International Virtual Conference on
Biomaterial-Based Therapeutics, Engineering and Medicine

BIOTEM-2021

December 17 - 20, 2021

Pre Conference Workshops
December 16, 2021

Organized by
Departments of
Biotechnology, Biomedical Engineering and Chemical Engineering
Manipal Institute of Technology, MAHE

Under the aegis of
Society for Biomaterials & Artificial Organs India (SBAOI)
and
Society for Tissue Engineering and Regenerative Medicine India (STERMI)

Co-organized by
The American Ceramic Society (ACerS)

BIOTEM 2021 Inauguration Schedule

5.00 PM - 5.20 PM	**Rejuvenation of SBAOI** **Bikramjit Basu** President, SBAOI
5.25 PM - 5.30 PM	**Welcome Address** **Anil Rana** Director, Manipal Institute of Technology, India
5.35 PM - 5.40 PM	**Theme of the Conference** **Bharath Raja Guru** Convener-BIOTEM2021, MAHE, Manipal, India
5.45 PM - 6.00 PM	**Guest of Honour's address** **Padma Vibhushan M. S. Valiathan** National Research Professor, India
6.05 PM - 6.15 PM	**Chief Guest's address** **Debashish Bhattacharjee** Vice President, Technology & New Materials, Tata Steel
6.20 PM - 6.25 PM	**Overview of IUSBSE's activities** **Jaochim Kohn** President, IUSBSE
6.30 PM - 6.35 PM	**Global outreach activities of ACerS** **Andrea Ross** American Ceramic Society, ACerS
6.40 PM - 6.45 PM	**Overview of ROYCE BIO activities** **Jonny Blaker** Henry Royce Institute, UK
6.50 PM - 6.55 PM	**Chair, Bioceramics 32 Congress** **Anna Tampieri** ISTEC - CNR, Italy
7.00 PM - 7.05 PM	**MAHE, MIT Documentary**
7.10 PM - 7.15 PM	**Overview of STERMI activities** **Biman Mandal** President, STERMI
7.20 PM - 7.25 PM	**Felicitation Address** **C.P Sharma** Founder President – SBAOI, STERMI, Former Senior Scientist G & Head Biomedical Technology Wing, SCTIMST, Trivandrum India
7.25 PM - 7.30 PM	**C.P. Sharma Award Announcement** **Bikramjit Basu** President, SBAOI

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In January 2021, to maintain ACerS members' engagement during the pandemic, we created a **no cost** monthly webinar series. Over the past year, the **Frontiers of Ceramics & Glass webinar series** has provided educational opportunities to over 1,000 members and non-members.

A sampling of the 2021 topics and presenters are listed below:

Bioceramics: Additive Manufacturing and Nanoclays for Biomaterials Applications
presented by Julian Jones, Imperial College London; and Kalpana Katti, North Dakota State University

Years of Glass – How the chemical durability of glass is predicted over millennia and beyond
presented by Joseph Ryan, Pacific Northwest National Laboratory

New Materials for Three Dimensional Ferroelectric Microelectronics
Susan Trolier-McKinstry, The Pennsylvania State University

Understanding Ideation and Opportunity analysis for designing high performance materials via different case studies
Surojit Gupta, University of North Dakota

Synthesis and performance of ceramic-based biological composites
David Kisailus, University of California, Irvine

High Entropy Environmental Barrier Coatings
Elizabeth Opila, University of Virginia

Join us for the 2022 **Frontiers of Ceramics & Glass webinar series** where we will host another year of exceptional topics and presenters!

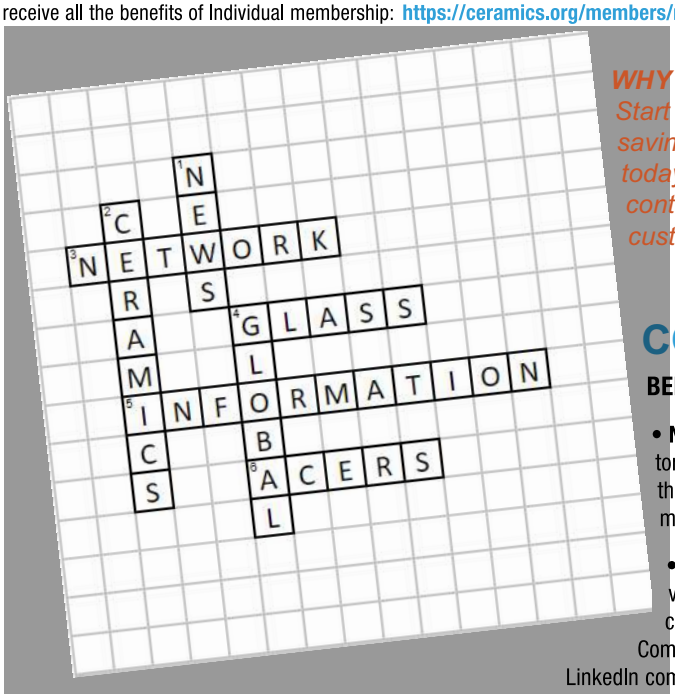
Check out current webinars offered, as well as the ACerS webinar archives at *www.ceramics.org/webinars*

The American Ceramic Society
www.ceramics.org

SPECIAL OFFER TO CONFERENCE ATTENDEES

ASSOCIATE MEMBERSHIP PROGRAM

The American Ceramic Society (ACerS) provides an opportunity to first-time members by offering a complimentary 12-month ACerS Associate Membership ($120 value). Additionally, ACerS offers a second year of Associate membership at a discounted rate of $40. Associate members receive all the benefits of Individual membership: https://ceramics.org/members/membership-types



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- **Network Globally:** ACerS online membership directory helps you connect with colleagues and friends throughout the Society's global network, as well as make new contacts within the materials community.
- **Be Social**: Participate in thought-provoking conversations and discussions through our social channels, which include our Online Member Communities, Facebook, Twitter, LinkedIn group, LinkedIn company, and Google+ pages.
- **Utilize the Ceramic and Glass Career Center:** Job seekers may post their resume and search the online career center for the latest job postings from leading organization in the ceramic and glass industry.
- ***ACerS Bulletin***: ACerS membership magazine focuses on news and new developments in the ceramic and glass community. Members receive both print and online access.
- ***ceramicSOURCE*** is ACerS annual buyer's guide for everything related to the ceramic and glass. It is published as an annual supplement to the December issue of the Bulletin, and brings ceramic and glass industry buyers and sellers together.
- ***Ceramic Tech Today*****, ACerS ceramic and glass material, application, and business blog:** The CTT digest email is sent three times per week, delivering the most relevant news directly to your inbox, saving you time and keeping you informed.
- **Professional development and technical webinars and sessions online and at in-person meetings:** Targeted career preparation and technical content is available exclusively for members both in free webinar format and at ACerS technical conferences.
- **Other resources:** There is a wealth of additional education, online tools and publications, including DVD short courses, ACerS-NIST Phase Equilibria Diagrams Database, and scientific books and articles, available to members at discounted rates.

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American Ceramic Society (ACerS) Corporate Partnerships allow your company to gain exposure to a global community of ceramic and glass professionals, access technical resources, recruit talent, and gain professional development resources for you and your employees—all while supporting your industry and ACerS, the leading professional society for ceramic and glass professionals.

SPECIAL PROGRAM FOR START-UP COMPANIES AND SMALL & MEDIUM SCALE ENTERPRISES (SMES) LOCATED IN DEVELOPING AND UNDERDEVELOPED COUNTRIES

In an effort to support startup companies and SMEs located in developing and underdeveloped countries (as identified by the World Bank), ACerS is pleased to announce the availability of a new Corporate Membership program for these companies at discounted rates.

A Startup Company is defined as a young company founded by one or more entrepreneurs to develop a unique product or service and bring it to market. By its nature, the typical startup tends to be a shoestring operation, with initial funding from the founders or their friends and families or investors.

A 'SME' in ceramic and glass manufacturing industry is typically defined as an enterprise having plant and machinery or equipment of worth in total of typically less than 2 million USD (this amount may vary in different countries).

> "We like the discounted rates on the expos, and the exposure is even better now because of the Corporate Partnership program. It's perfect for building awareness and letting customers know that we support the Society."
>
> – Mary Stevenson, President Deltech Furnaces

WHAT YOU SHOULD KNOW ABOUT THE AMERICAN CERAMIC SOCIETY

The American Ceramic Society is a non-profit, professional society whose mission is to advance the study, understanding and use of ceramic and glass materials for the benefit of our members and society.

More than 10,000 scientists, researchers, engineers, manufacturers, plant personnel, educators, students, and marketing and sales professionals from more than 70 countries make up the membership of ACerS.

Since 1898, ACerS has been the hub of the global ceramics community and one of the most trusted sources of ceramic and glass materials and applications knowledge.

WHO SHOULD BE AN ACERS CORPORATE PARTNER?

Any company involved in providing materials, products, or services designed for use with technical ceramics and glass, as a supplier, manufacturer, service provider, consultant, or end user.

If ceramic and glass materials and technologies are a significant part of what you do, then ACerS Corporate Partnership is for you.

WHY BECOME A CORPORATE PARTNER OF THE AMERICAN CERAMIC SOCIETY?

The ACerS Corporate Partnership program is designed for companies who wish to grow their business through networking and exposure to ceramics and glass professionals around the world, engage with the Society, and support their industry. In addition to excellent visibility in the marketplace, you gain access to a wide array of technical resources, professional development, and recruitment opportunities for you and your employees.

To achieve new heights with ACerS Corporate Partnership and to begin taking advantage of the valuable benefits, please contact:

Kevin Thompson Director of Membership **614-794-5894 | kthompson@ceramics.org**

ACerS supports startup companies and SMEs in developing and underdeveloped countries and desires to assist in their success and growth. To better serve the entire cross-section of the technical and economic sectors of the ceramics and glass community, startup companies and SMEs are eligible for discounted corporate membership annual dues.

Startup and SME corporate memberships enable ceramic and glass companies to connect with colleagues from around the world. Eligible countries are based on those defined as Low-Income or Lower-Middle-Income Economies by the World Bank.

Start-up Companies – who qualify as a startup company, and have been in existence less than five years, are eligible to join ACerS as a Corporate Partner for just $250 per year for up to three years. After three years the company will be expected to pay the regular dues rate of $750 per year.

Small & Medium Scale Enterprises (SMES) – who qualify as a SME, and have been in existence less than ten years, are eligible to join ACerS as a Corporate Partner for just $375 per year for up to three years. After three years, the company will be expected to pay the regular dues rate of $750 per year.

CORPORATE PARTNER BENEFITS

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- *ACerS Bulletin*: one free ¼ page, four-color ad
- Print and electronic media: 5% discount off all advertising
- Website: landing page with link to your site
- Expos: $200 booth discounts at ACerS expos
- Meetings:10% discount off sponsorships
- Career Center: unlimited complimentary online job postings
- Corporate Awards: only corporate partners are eligible
- Visibility: gain exposure to ACerS 10,000+ members and subscribers
- BCC Research Reports: 15% discount off all orders
- *Ceramic & Glass Manufacturing* magazine: be seen in Corporate Partner News section
- Product Directory Source: enhanced listing in ACerS new and improved *CeramicSource*
- Webinars: opportunity to present webinars to ACerS members at discounted rates

Individual/Employee Benefits

- Membership: Two (2) ACerS Individual memberships
- Meetings: One (1) complimentary registration to any ACerS-hosted meeting
- Workshops/Short Courses/Online Courses: Discounted member rates for all company employees
- *Ceramic Manufacturing Solutions Conference at Ceramics Expo* additional 10% discount off member rates for all employees
- Networking: invited to exclusive events at select ACerS meetings
- Webinars: free business, management and professional development webinars available for all employees

Companies interested in a "Startup and SME Corporate Partnership", or have questions regarding qualification, please contact Kevin Thompson, Membership Director, kthompson@ceramics.org or 1-614-794-5894.

ACERS INDIVIDUAL MEMBERS ENJOY THE FOLLOWING BENEFITS:

- Members-only access to online Communities and Member Directory
- Online access to ACerS technical journals
- ACerS *Bulletin* magazine and *Bulletin Archives Online*
- ACerS *Ceramic & Glass Manufacturing* magazine
- *Ceramic Tech Today*, the latest in industry news and trends
- Discounted registration rates at ACerS technical meetings, workshops and training courses
- Discounts on technical publications, Phase Equilibria Diagrams and ceramic materials courses
- Invaluable networking opportunities

PLEASE NOTE: Corporate partnerships are on a calendar-year membership (January 1 – December 31). Annual dues and benefits will be pro-rated based upon join date.

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Message from the Founder

It gives me great pleasure to learn that the Departments of Biotechnology, Biomedical Engineering and Chemical Engineering, Manipal Institute of Technology, MAHE is organizing BIOTEM-2021 an International Conference on "Biomaterial-based Therapeutics, Engineering and Medicine" during 17-20 December, 2021 at Manipal Institute of Higher Education (MAHE), Manipal in association with SBAOI and STERMI.

The development of affordable medical devices, artificial and regenerated organs is very much needed as a priority in India. The interdisciplinary areas like biomaterials, medical devices, diagnostics & therapeutics and tissue engineering have grown significantly that paved the way for the development of smart biomaterials, which can emulate natural healing mechanisms by regenerating damaged tissues by specific reactions of the cells. Biomaterials and medical devices represent a fast emerging market that is projected to reach USD 47.5 billion globally by 2025, with India's share of only less than 2%. Indian medical device market is driven by 80% imports from countries like US, China and Germany. Union Ministry of Health and Family Welfare started initiative for framing a new Drugs, Cosmetics and Medical Devices Bill. This may increase the acceptability of Indian medical devices in the global market and India's share is expected to reach USD 10 billion in 2025.

Efforts to upbringing innovations in research and development in biomaterials and medical device sector with Make in India concept of our honourable Prime Minister need more attention. This conference will certainly help in integrating, analyzing and strengthening these areas.

I take this opportunity to thank all the colleagues for their outstanding contribution and the organizers and participants for making this conference a great success. The initiative of Dr. Bharath Raja Guru and the support of the Manipal Institute of Higher Education made this conference a reality. We hope this conference will provide an important forum for scientists, medical professionals, engineers, students and industrialists for learning and exchange of ideas for pursuing innovative research and initiate future collaborative projects in creating futuristic hybrid therapeutic products, functionalities and encouraging knowledge base for artificial intelligence and robotics towards organ regeneration programmes.

I wish conference a great success and hope this will provide an excellent learning experience.

Chandra P. Sharma FBSE, FBAO

Founder, SBAOI & STERMI

Former Senior Scientist G & Head, Biomedical Technology Wing,
Sree Chitra Tirunal Institute for Medical Sciences & Technology, Trivandrum (SCTIMST)

Former Adjunct Professor, Department of Pharmaceutical Biotechnology,
Manipal College of Pharmaceutical Sciences, Manipal University, India

Hon. Emeritus Professor, CBEAS, Purbanchal University, Kathmandu, Nepal

Vice President Asia Pacific Society for Artificial Organs (HQ: Japan)

Message from the President SBAOI

I am deeply honored to welcome you to the International Virtual Conference "Biomaterial-Based Therapeutics, Engineering and Medicine (BIOTEM-2021)" organized by Departments of Biotechnology, Biomedical Engineering and Chemical Engineering, Manipal Institute of Technology, MAHE, under the aegis of Society for Biomaterials & Artificial Organs India (SBAOI) and Society for Tissue Engineering and Regenerative Medicine India (STERMI). This conference is preceded by two pre-conference workshops, Bioelectronic Medicine and 3D Graphy Workshop – 3D Bioprinting for Hard & Soft Tissue.

Our society has presently more than 900 members, including Life Members (Indian and Foreign), Fellows, Honorary and Regular members. Several global and national leaders in the field of Biomaterials, Tissue Engineering, Additive Manufacturing, Regenerative Engineering will present their pathbreaking research at the forthcoming conference and pre-conference workshops.

At SBAOI, we will remain committed to discuss many unanswered issues at the challenging interface of Engineering, Biology, and Medicine. In particular, my vision as President of SBAOI is as follows,

a) to enhance the global outreach of SBAOI and particularly to nurture biomaterials activities in South Asia

b) to promote diversity and inclusiveness in SBAOI activities

c) to make SBAOI a more useful platform to young researchers and biomaterials professionals

d) to establish stronger linkages with stakeholders, industry professionals, and clinicians.

I believe that the outcome of the professional activities of SBAOI will intensify the development of the next-generation biomaterials and biomedical implants, which will enhance healthcare quality in India and many developing nations around the world. As President, I will strive to encourage the members and students to be actively involved in SBAOI activities, by providing an enriching intellectual environment and opportunities.

Finally, I, on behalf of SBAOI, would like to thank our Gold Sponsor, TATA Steel as well as silver sponsors, Manchester BIOGEL, United Kingdom and Orthotech India Private Limited, Gujarat, and Altem Technologies. The contribution of 3D Graphy for organizing the pre-conference workshop on 3D Bioprinting is appreciated. I also express my gratitude to Scheme for Promotion of Academic and Research Collaboration (SPARC program) of Ministry of Human Resource Development, Government of India for funding both the pre-conference workshops. SBAOI also thank Henry Royce Institute, UK and American Ceramic Society for their financial support towards this conference. At the close, I would like to thank Prof. Bharath Raja Guru and his team at Manipal University as well as members of the Executive Committee, SBAOI for their painstaking efforts in organizing BIOTEM 2021.

I wish you all have an intellectually stimulating time during December 16-20, 2021 during the virtual conference and pre-conference workshops. We are currently living in very challenging times. The pandemic has disrupted everyone's lives and heightened concerns about safety and health. I wish you all a very safe year ahead.

Bikramjit Basu C.Eng. FNA FNAE FASc FNASc FAMS FIMMM FBSE FACerS FIAMBE
President, Society for Biomaterials and Artificial Organs India, SBAOI
Professor, Indian Institute of Science, Bangalore

Message from the Director, MIT

It gives me great pleasure to announce that MAHE/MIT is organizing a virtual conference on an International scale on Bio-material based Therapeutics Engineering and Medicine (BIOTEM-21) under the aegis of society for bio-materials and artificial organs, India (SBAOI) and society for tissue engineering and regenerative medicine, India (STERMI)

MAHE and MIT have always believed in nurturing and promoting research activities of global standards. It has a special focus in providing opportunities to the students and staff to engage themselves in translational research that can influence and improve the lives of the people in the community. I am also happy to share that in this conference researchers from multi-disciplinary areas and institutes such as MIT, MCOPS and MCODS, all under MAHE, are coming together on a common platform.

The conference will provide an excellent opportunity to our students and staff to learn, share and exchange ideas with eminent researchers in the field. At the same time, it will serve as a platform to the MAHE young researchers to explore newer areas of technical advancements and knowledge, find experts with common interests as well as an opportunity to publish their work.

I wish the International conference great success. Jai Hind !

Commander (Dr) Anil Rana
Director, Manipal Institute of Technology,
MAHE, Manipal

Message from the President, STERMI

India has been aspiring to provide affordable healthcare for all. Realizing the tremendous progress and potential of Biomaterials and Regenerative Medicine over the years, it is time we collectively put our efforts to realize this dream through translation. A common platform for experts from different multidisciplinary fields to communicate, exchange knowledge and collaborate is desirous and need of the hour.

To achieve this goal, it is heartening to see Departments of Biotechnology, Biomedical Engineering and Chemical Engineering, Manipal Institute of Technology, MAHE under the aegis of Society for Biomaterials & Artificial Organs India (SBAOI) and Society for Tissue Engineering and Regenerative Medicine India (STERMI) in collaboration with The American Ceramic Society

(ACerS) is organizing International Virtual Conference on “Biomaterial-Based Therapeutics, Engineering and Medicine (BIOTEM-2021) between December 17 - 20, 2021.

This will be the 31st SBAOI and 14th STERMI annual meeting(s). Through the great efforts of Dr. Chandra P Sharma and other eminent colleagues both the Society(s) were initiated in India.

First meeting of the STERMI society was organized at IIT Madras on December 13, 2007 with an inaugural address of Prof. DF Williams, Editor-in-Chief, Biomaterials. Since the many years of existence, both the societies have tremendously contributed in India’s dream to be an international leader in the field of Biomaterials and Regenerative Medicine.

As the current President of STERMI, I would like to take this opportunity to welcome all the delegates and participants to BIOTEM-2021 International conference. I sincerely hope that this endeavor will pave the way for new discoveries and be deemed fruitful in generating keen interests amongst the participants so that young minds pursue science with vigor in order for a better future for all.

My best wishes to all the participants and organizers for a successful BIOTEM-2021.

Biman B. Mandal
President, STERMI

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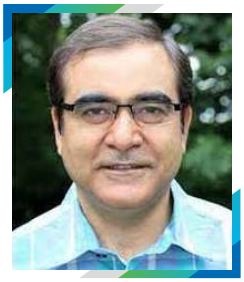

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Society for Biomaterials and Artificial Organs SBAOI

Newsletter

Vol.1, Issue 1, July 2021

BIOMATERIA

This society, one of the world's largest biomaterials societies was founded in 1986 by Dr. C.P. Sharma as a non-profit professional organization and was registered under the Travancore-Cochin Act XII of 1955 (act for registration of literary, scientific, and charitable societies) with the name **Society for Biomaterials and Artificial Organs - India**, (SBAOI). SBAOI is a member of the International Union of Societies for Biomaterials Science and Engineering (IUS-BSE) since 2003. The Society is administered by its office bearers consisting of the President, two Vice Presidents, the General Secretary, Treasurer and members of the executive committee, elected during the general body meeting of the society.

Society's website: http://https://biomaterials.org.in/

C.P. Sharma
Founder

President's message

As the current president of society, it is my proud privilege and honor to welcome you all to the SBAOI Newsletter. SBAOI works at the forefront of biomaterials science and technology, while providing an interdisciplinary platform to stimulate innovation and translation of biomaterials, implants, and biomedical devices. My vision is, **(a)** to enhance the global outreach of SBAOI particularly to nurture biomaterials activities in South Asian countries; **(b)** to promote diversity and inclusiveness in SBAOI activities; **(c)** to make SBAOI a more useful platform to young researchers and biomaterials professionals; **(d)** to establish stronger linkages with stakeholders, industry professionals, and clinicians.

Bikramjit Basu
President (2021-24)

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Forthcoming Activity:

SBAOI XXVIII National Conference & next Annual General Meeting at Manipal University (Online), December 2021.

Condolence Message Prof. Rinti Banerjee

With a heavy heart and profound sadness, SBAOI condoles the passing away of Professor Rinti Banerjee, Department of Biosciences and Bioengineering, IIT Bombay (https://www.bio.iitb.ac.in/people/faculty/banerjee-r/). She was the Chairperson of the Department of Biosciences and Bioengineering during 2016-2019 and has been lately steering the 'Digital Health' program at IIT Bombay.

A clinician-scientist by training, she is globally known for her pioneering research in the area of Biomaterials, Nanomedicine, and Drug Delivery. She is an elected fellow of the Indian Academy of Sciences and Society for Biomaterials and Artificial Organs India (SBAOI). She is also the recipient of the National Bioscience Award from the Government of India. She has contributed significantly to the advisory committees of various governmental funding agencies as well as professional societies, like SBAOI. She was in ICU for the last few weeks due to post-covid complications and succumbed to a massive heart attack on 08 July 2021.

On my personal behalf and on behalf of the SBAOI, I express my deepest condolences to the members of the bereaved family. May God gives them the strength to bear such a loss.

With deep sorrow,
Bikramjit Basu

Society of Biomaterials and Artificial Organs-India

C P Sharma Awardees (Partial list)

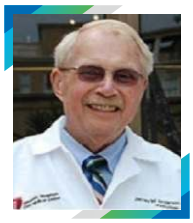
- **Cato T. Laurencin** (2020), The University of Connecticut, USA
- **James Kirkpatrick** (2019), Johannes Gutenberg Univ. of Mainz, Germany.
- **Ashutosh Chilkoti** (2018), Duke University, USA.
- **Gilson Khang** (2017), Chonbuk National University, South Korea.
- **John L. Brash** (2016), McMaster University, Canada.
- **John A. Ramshaw** (2015), Chief Scientist, CSIRO Australia
- **Seeram Ramakrishna** (2014), NUS, Singapore
- **Myron Spector** (2013), Brigham and Women's Hospital, Boston, USA
- **Sung Wan Kim** (2012), University of Utah, USA
- **Yasuhiko Tabata** (2011), Kyoto University, Japan
- **Young Ha Kim** (2010), Gwangju Institute of Science and Technology, Korea
- **Buddy D. Ratner** (2009), University of Washington, Seattle, USA.
- **David F. Williams** (2008), Wake Forest Institute for Regenerative Medicine, USA
- **Larry L. Hench** (2007), Florida Institute of Technology, USA
- **Dr. Avi Domb** (2006), The Hebrew University of Jerusalem, Israel
- **Robert E. Baier** (2005), SUNY at Buffalo, USA

Speakers

Inaugural Address

Dr. M. S. Valiathan
Padma Vibhushan Awardee
India

C.P. Sharma Award Lecture



Prof. James M. Anderson
Case Western Reserve University
United States

Plenary lecture

Prof. B. Ravi
IIT Bombay
Mumbai, India

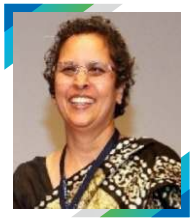
Plenary Lecture

Prof. Rohit Srivastava
IIT Bombay
Mumbai, India

Plenary Lecture

Prof. Michael Gelinsky
Technische Universität Dresden
Dresden, Germany

Plenary Lecture



Prof. Vrisha Madhuri
Christian Medical College Hospital
Vellore, India

Plenary Lecture

Prof. Rui L. Reis
University of Minho
Portugal

Plenary Lecture

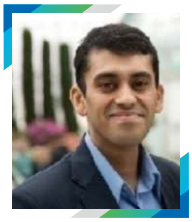
Prof. K.V. Venkatesh
IIT Bombay
Mumbai, India

Plenary Lecture

Prof. Biman B. Mandal
IIT Guwahati
Guwahati, India

Prof Guangzhao Mao
The University of New South Wales
Sydney, Australia

Dr. Vinoy Thomas
University of Alabama at Birmingham
United States



Dr. Ameya Kirtane
Harvard Medical School
Cambridge, Massachusetts
United States

Prof. Jayanth Panyam
Temple University
Philadephia, United States

Prof. Srinivas Mutalik
Manipal College of Pharmaceutical Sciences
Manipal, India

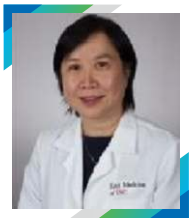
Dr. Swati Biswas
BITS Pilani
Hyderabad Campus, India

Dr. Venkata Vamsi Krishna Venuganti
BITS Pilani
Hyderabad Campus, India

Dr. Usha Y Nayak
Manipal College of
Pharmaceutical Sciences
Manipal, India

Dr. Finosh G. Thankam
Western University of
Health Sciences
Califonia, United States

Prof. Huinan Liu
University of California Riverside
Califonia, United States



Dr. Bo Han
University of Southern California
Califonia, United States

Speakers

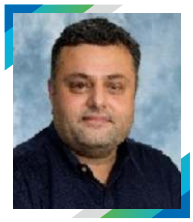
Dr. Kishore Ginjupalli
Manipal College of Dental Sciences
Manipal, India

Dr. Haruka Yoshie
CELLINK group (BICO Company)
Kyoto, Japan

Dr. Dhivya S.
Altem Technologies (P) Ltd.
Bangalore, India

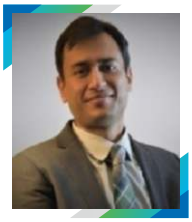
Dr. Abhijit Majumder
IIT Bombay
Mumbai, India

Prof. Balendra Pratap Singh
King George's Medical University
Lucknow, India



Prof. Ketul Popat
Colorado State University
United States

Prof. Uwe Gbureck
University of Wuerzburg
Germany



Dr. Ashutosh Goel
Rutgers, The State University
of New Jersey
United States

Prof. M.N.V. Ravi Kumar
The University of Alabama
United States

Dr. Harishkumar Madhyastha
University of Miyazaki
Japan

Dr. Manish Baldia
Jaslok Hospital and Research Centre
Mumbai, India

Dr. Ashutosh Kumar Dubey
IIT (BHU)
Varanasi, India

Dr. Balaram Ghosh
BITS Pilani
Hyderabad Campus, India

Prof. Quazi Syed Zahiruddin
Datta Meghe Institute of Medical Sciences
Wardha, India

Dr. Neetu Singh
IIT Delhi
India

Prof. Deepthy Menon
Amrita Vishwa Vidyapeetham
Kochi, India

Dr. Vibha Shetty
Ramaiah Dental College
Bangalore, India

Dr. Kinshuk Dasgupta
Bhabha Atomic Research Centre (BARC)
Mumbai, India

Dr. Subrata Mukherjee
Tata Steel Limited
Jamshedpur, India

Dr Krishnaraj Somayaji
Manipal College of Dental Sciences
Manipal

Program Schedule

DAY 1 Thursday, 16-12-2021

10.00 AM- 8.00 PM	**Pre-conference workshop - I** International Workshop "BIOELECTRONIC MEDICINE", Organised by IIT(BHU) & IISc, Bangalore and co-hosted by Henry Royce Institute, UK

DAY 2 Friday, 17-12-2021

2.00 PM - 4.30 PM	**Pre-conference Worshop - II** "3D Graphy Workshop – 3D Bioprinting for Hard & Soft Tissue" Organised by 3D Graphy and IISc
5.00 PM - 7.30 PM	**BIOTEM- 2021 Inauguration**
5.00 PM - 5.20 PM	**Rejuvenation of SBAOI** **Bikramjit Basu,** President, SBAOI
5.25 PM - 5.30 PM	**Welcome Address** **Anil Rana,** Director, Manipal Institute of Technology, India
5.35 PM - 5.40 PM	**Theme of the Conference** **Bharath Raja Guru,** Convener-BIOTEM2021, MAHE, Manipal, India
5.45 PM - 6.00 PM	**Guest of Honour's address** **Padma Vibhushan M. S. Valiathan,** National Research Professor, India
6.05 PM - 6.15 PM	**Chief Guest's address** **Debashish Bhattacharjee,** Vice President, Technology & New Materials, Tata Steel
6.20 PM - 6.25 PM	**Overview of IUSBSE's activities** **Jaochim Kohn,** President, IUSBSE
6.30 PM - 6.35 PM	**Global outreach activities of ACerS** **Andrea Ross,** American Ceramic Society, ACerS
6.40 PM - 6.45 PM	**Overview of ROYCE BIO activities** **Jonny Blaker,** Henry Royce Institute, UK
6.50 PM - 6.55 PM	**Chair, Bioceramics 32 Congress** **Anna Tampieri,** ISTEC - CNR, Italy
7.00 PM - 7.05 PM	**MAHE, MIT Documentary**
7.10 PM - 7.15 PM	**Overview of STERMI activities** **Biman Mandal,** President, STERMI
7.20 PM - 7.25 PM	**Felicitation Address** **C.P Sharma,** Founder President – SBAOI, STERMI, Former Senior Scientist G & Head Biomedical Technology Wing, SCTIMST, Trivandrum India
7.25 PM - 7.30 PM	**C.P. Sharma Award Announcement** **Bikramjit Basu,** President, SBAOI

Session - 1: Chandra P. Sharma Award Lecture

Chair: C. P. Sharma and **Co-Chair:** Bikramjit Basu

7.30 PM - 8.30 PM **Clinical and basic science perspectives of the foreign body reaction**
James M. Anderson, Case Western Reserve University, USA

DAY 3 Saturday, 18-12-2021

Session - 2 Saturday, 18-12-2021

Chair: Biman Mandal and **Co-Chair:** A. Siddharthan

9.00 AM - 9.20 AM **Invited Lecture**
Engineering Material Surfaces for Blood Contacting Medical Devices
Ketul C. Popat, Colorado State University, USA

9.30 AM - 10.15 AM **Plenary Lecture**
Personalized Medical Devices Using Additive Manufacturing Technology
B. Ravi, IIT Bombay, India

10.25 AM - 10.55 AM **Keynote Lecture**
Biosensing based on carbon nanotube aerogel: A wonder material
Kinshuk Dasgupta, BARC, Mumbai, India

11.05 AM - 11.50 AM **Plenary Lecture**
Systems Engineering Perspective of Human physiology - Multiscale Models for Disease Characterization: Towards drug-discovery, Clinical Study, Disease management and Personalization
K. V. Venkatesh, IIT Bombay, India

12.00 PM - 12.30 PM **Industry Lecture**
Recent advancement of 3D bioprinting technologies in Therapeutics and Tissue Engineering
Haruka Yoshie, CELLINK, BICO, ALTEM Technologies

12.30 PM - 12.45 PM **Inauguration of Poster Session**

LUNCH BREAK

Session - 3 Saturday, 18-12-2021

Chair: Debrupa Lahiri and **Co-Chair:** Rachit Agarwal

2.00 PM - 2.30 PM **Keynote Lecture**
Targeted Drug Delivery to Respiratory Neurons Using Nanoparticles Functionalized by Neural Tracing Proteins
Guangzhao Mao, University of New South Wales, Australia

2.40 PM - 3.25 PM **Plenary Lecture**
Affordable Healthcare Technologies in Sensing, Drug Delivery and Therapy
Rohit Srivstava, IIT Bombay, India

3.35 PM - 3.55 PM **Invited Lecture**
Indigenouslydeveloped highly pure and crystalline Hydroxyapatite powder for Biomedical applications
Subrata Mukkherji, TATA Steel R &D, Jamshedpur, India

Session - 4 Saturday, 18-12-2021

Chair: Kaushik Chatterjee and **Co-Chair:** Pramod K

4.05 PM - 4.35 PM	**Industry Lecture** **Integrated approach of materials in pharmaceutical drug discovery and development** **Dhivya Shanmugarajan,** ALTEM TECHNOLOGIES, Bengaluru, Karnataka
4.45 PM - 5.15 PM	**Industry Lecture** **Tuneable peptide hydrogels to provide physiologically relevant 3D cultures for *in vitro* studies** **Adedamola (Dammy) Olayanju,** Manchester BIOGEL
5.25 PM - 5.45 PM	**Invited Lecture** **How to conduct clinical trial: An evidence based approach** **Balendra Pratap Singh,** KGMU, Lucknow, India
5.55 PM - 6.15PM	**Invited Lecture** **"Viscotaxis"-directed migration of mesenchymal stem cells in response to loss modulus gradient** **Abhijit Majumder,** IIT Bombay, India

Session - 5 Saturday, 18-12-2021

Chair: A Balamurugan and **Co-Chair:** Bharath Raja Guru

6.25 PM - 6.55 PM	**Keynote Lecture** **Gastric resident drug delivery systems for sustained oral delivery** **Ameya R. Kirtane** Harvard University, USA
7.05 PM- 7.35 PM	**Keynote Lecture** **Revving up the Immune System: TLR7/8-based Anticancer Nanovaccines** **Jayanth Panyam** University of Minnesota, USA
7.45 PM - 8.05PM	**Invited Lecture** **Making a polyesters' difference to nano pill** **M.N.V. Ravi Kumar** The University of Alabama, USA
8.15 PM – 9.30 PM	**SBAOI- Annual General Body Meeting**

DAY 4 Sunday, 19-12-2021

Session - 6 Sunday, 19-12-2021

Chair: H. K. Varma and **Co-Chair:** V. P. Shrivastava

9.00 AM - 9.30 AM	**Keynote Lecture** **Demineralized Bone Matrix: Activities and Applications** **Bo Han,** University of Southern California
9.40 AM - 10.00 AM	**Invited Lecture** **Cardioprotective Phenotypes and Regenerative Vesicles of Epicardial Adipose Tissue Derived Stem Cells in Translational Cardiac Regeneration** **Finosh Thankam,** Western University of Health Sciences, USA
10.10 AM- 10.55 AM	**Plenary Lecture** **Articular Cartilage restoration - A road map to clinical translation** **Vrisha Madhuri,** CMC, Vellore, India
11.05 AM- 11.35 PM	**Keynote Lecture** **Regeneration of intervertebral disc in a mouse disc degeneration model using bone marrow derived mesenchymal stem cell** **Manish Baldia,** Jaslok Hospital, Mumbai, India
11.45 AM- 12.05 PM	**Invited Lecture** **Engineering New Materials for Healthcare: A Chemist's Perspective** **Neetu Singh,** IIT Delhi, India
12.15 PM- 12.35 PM	**Invited Lecture** **Development of Lipidic Nanoplatform for Oral Delivery of Chlorhexidine: Characterization, Biocompatibility and Assessment of Depth of Penetration in Extracted Human Teeth** **Krishnaraj Somayaji,** MCODS, Manipal

LUNCH BREAK

Session - 7 Sunday, 19-12-2021

Chair: P. T. Reddy and **Co-Chair:** Mathew Peter

1.30 PM- 1.50 PM	**Industry Lecture** **Building 3D bio-printers in India for R&D and industrial applications** **Sumant Bhutoria,** ALFATEK, Kolkata, India
2.00 PM - 2.30 PM	**Keynote Lecture** **Viscoelastic tissue in Dermal Tissue regeneration** **Harish Madhyastha,** University of Miyaziki, Japan
2.40 PM - 3.25 PM	**Plenary Lecture** **Silk based bioengineered human tissues & organs: The way forward** **Biman B. Mandal,** IIT Guwahati, India
3.35 PM - 4.05 PM	**Keynote Lecture** **Dental Implants –Biomaterials in action** **Vibha Shetty,** Ramaiah University of Applied Sciences, Bangalore, India
4.15 PM - 4.35 PM	**Invited Lecture** **Strategies for cementation of all-ceramic restorations** **Kishore Ginjupalli,** Manipal College of Dental Sciences, Manipal, India
4.45 PM - 5.05 PM	**Invited Lecture** **Nanofibrous polymers for instructive design of biomaterial devices** **Deepthy Menon,** Amrita Vishwa Vidyapeetham, India

Session - 8 Sunday, 19-12-2021

5.15 PM - 7.15 PM **SBAOI-MAHE Young Scientist Award Contest**

Session - 9 Sunday, 19-12-2021

Chair: R.S. Jayasree and **Co-Chair:** Raviraja NS

7.30 PM - 8.00 PM **Keynote Lecture**

Design of third-generation bioactive glasses for soft tissue engineering – Challenges and open questions

Ashutosh Goel, Rutgers, The State University of New Jersey, USA

8.10 PM - 8.40 PM **Keynote Lecture**

Plasma Engineering of Biomaterials for Improved Bio-interfaces

Vinoy Thomas, The University of Alabama, USA

DAY 5 Monday, 20-12-2021

Session - 10 Monday, 20-12-2021

Chair: S. Kanagaraj and **Co-Chair:** Kishore Ginjupalli

9.00 AM - 9.30 AM **Keynote Lecture**

Engineering Bioresorbable Implants and Structures for Biomedical Applications

Huinan Liu, University of California, Riverside

9.40 AM - 10.00 AM **Invited Lecture**

Functionalized LbL patches for targeted delivery of chemotherapeutics in colon cancer

Venkata Vamsi Krishna Venuganti, BITS Pilani, Hyderabad, India

10.10 AM- 10.30 AM **Invited Lecture**

Mesoporous Silica Nanoparticles (MSNs): Versatile Multifunctional Carriers

Usha Y Nayak, Manipal Academy of Higher Education, Manipal, India

10.40 AM- 11.00 AM **Invited Lecture**

Development of HPMA-based Polymeric Micellar Systems for the Delivery of Anticancer Chemotherapeutic

Balaram Ghosh, BITS Pilani, Hyderabad, India

11.10 AM- 11.30 PM **Invited Lecture**

Lipidic Nanoparticles for drug delivery and targeting: Overview and case studies

Srinivas Mutalik, Manipal College of Pharmaceutical Sciences, India

11.40 AM- 12.00 PM **Invited Lecture**

'SMART' self-assembling micelles as chemo-photodynamic therapy in cancer

Swati Biswas, BITS Pilani, Hyderabad, India

12.10 PM- 12.40 PM **Keynote Lecture**

3D Printing from bench to Bed side Challenges and opportunities

Quazi Syed Zahiruddin, Datta Megha Institute of Medical Sciences- Wardha

LUNCH BREAK

Session - 11 Monday, 20-12-2021

Chair: Bikramjit Basu and **Co-Chair:** Willi Paul

2.00 PM - 2.45 PM	**Plenary Lecture** **Combining technologies, materials and cells in 3D bioprinting** **Michael Gelinsky,** TU Dresden, Germany
2.55 PM - 3.40 PM	**Plenary Lecture** **New approaches for the engineering and regeneration of different tissues** **Rui L. Reis,** University of Minho, Portugal
3.50 PM - 4.20 PM	**Keynote Lecture** **Bone regeneration capacity of magnesium phosphate minerals** **Uwe Gbureck,** University of Wurzburg, Germany
4.30 PM - 5.00 PM	**Industry Lecture** **Evolving Medicine with 3D Bioprinting** **Mauro Petretta,** RegenHU, Switzerland

TEA BREAK

Session - 12 Monday, 20-12-2021

5.10 PM - 6.30 PM	**SBAOI-BAJPAI-SAHA Student Award and Manipal Academy of Higher Education (MAHE) Awards**
7.00 PM	**Valediction & Announcement of Awards**

PARC
Scheme for Promotion of Academic and Research Collaboration

Project under MHRD
GOVERNMENT OF INDIA
सत्यमेव जयते

भारतीय विज्ञान संस्थान

HENRY ROYCE INSTITUTE

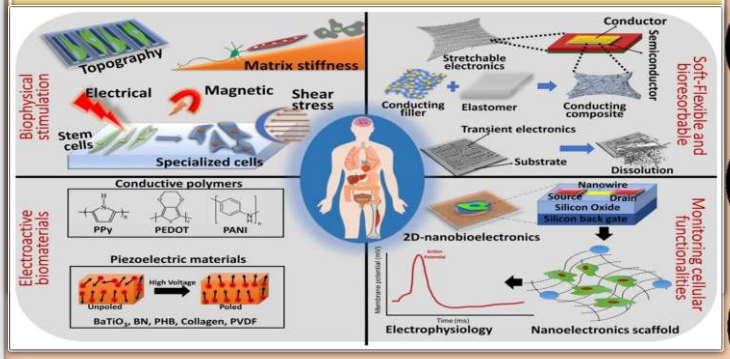
INTERNATIONAL WORKSHOP
BIOELECTRONIC MEDICINE

Theme and Relevance

The field of bioelectronic medicine represents the convergence of concepts from multiple disciplines, including Biomaterials Science, Biomedical Engineering, Neuroscience and Medicine, in a fast-developing way to treat chronic diseases. The significant progress in the field of bioelectronic medicine has resulted in the development of implantable devices, *e.g.*, neuromodulation devices for chronic pain management.

Our ability to precisely control the cell functionalities has been identified as the key underpinning factors in such impressive development. However, many research outcomes from academia have still not been translated to bioelectronic devices. In particular, the intermittent delivery of properly tuned pulsed dynamic electrical stimulation demonstrated the potentiality in modulating neurogenic/ osteogenic/ myogenic/ chondrogenic differentiation of stem cells. However, many such research outcomes are still not translated to clinical studies.

In this perspective, the bioengineering approach of integrating electronic systems with biomaterial-based scaffolds will be discussed in this workshop, by the global experts as well as young researchers. The present status of understanding the applications of electroactive biomaterials to deliver bioelectrical cues for regulating cell fate processes will be reviewed. Along with the fundamental physical phenomenon at the tissue-electrode interface, advancements in nanoelectronic devices will be presented in some of the lectures, together with the emergence of the soft and flexible electronics as next-generation bioelectronic devices with a more stable and compatible biointerface. Clinically-led bioelectronics medicine to regulate the electrical signaling at the neural interface will be highlighted. It is hoped that the discussion in this workshop will accelerate innovation to translate biomaterials-based biophysical stimulation towards the development of bioartificial organs.



Panda and Basu; Mat. Sci. and Engg.: R 146 (2021) 100630

Workshop schedule:
December 16, 2021 (Thu): 9 am – 8 pm IST
Registration deadline: December 10, 2021

Who should attend?
Graduate/Masters Students, Scientists and faculty members, working in the field of Bioelectronic Medicine.

Registration link: https://forms.gle/oNedCSB3KrfXXzUJ6

OUR SPEAKERS


Prof. John A. Rogers
Northwestern University, USA


Prof. George Malliaras
University of Cambridge, UK


Prof. K. Yamashita
Tokyo Medical and Dental University, Japan


Prof. Surya K. Mallapragada
Iowa state university, USA


Prof. Miho Nakamura
University of Turku, Finland


Prof. Sarah Cartmell
The University of Manchester, UK


Dr. Manus Biggs
National University of Ireland


Prof. S. Lanceros-Mendez
University of Minho, Portugal


Dr. Alok Kumar
Harvard Medical School, USA


Dr. Roberto Portillo Lara
Imperial College London, UK


Dr. Greeshma T.
IIT Madras, India


Dr. Sunil Kumar Boda
University of Minnesota, USA


Dr. Ravikumar K.
University of Pittsburgh, USA


Asish K. Panda
IISc Bangalore, India

Conveners


Dr. Ashutosh Kumar Dubey
IIT (BHU), Varanasi


Prof. Bikramjit Basu
IISc, Bangalore

Co-host


Dr. Jonny Blaker
Research Area Lead Biomedical Materials,
Henry Royce Institute, The University of Manchester

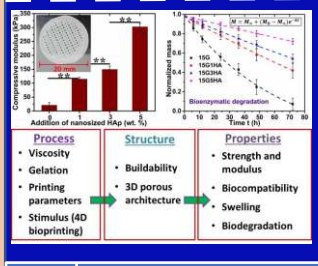
3D GRAPHY WORKSHOP – 3D BIOPRINTING FOR HARD & SOFT TISSUES

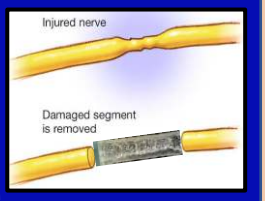
What is 3D Bioprinting?

3D Bioprinting works on the principle of layer-by-layer manufacturing of the artificial scaffolds with pre-defined design architecture, using bioinks. Bioink is mostly composed of cells and viscoelastic polymers, that envelop the cells. This technique effectively combines cells, growth factors, and biomaterials to fabricate functional tissues, largely driven with the aim of imitating natural tissue characteristics and architecture. 3D bioprinting can be used for a broad range of medical applications, from drug discovery to potential clinical treatments.

What are the various applications?

It can be used to print tissues and organs for conducting research on drug discovery. Drug testing is an important part for pharmaceutical companies to get an approved drug, prior to commercialization. In addition, 3D bioprinting is also used for printing tissue-engineered scaffolds. These scaffolds can be used to regenerate joints and ligaments, bone, skin, muscles, cartilage, blood vessels, bladder, cardiac tissues, heart valves etc. This is expected to revolutionize human healthcare.





Peripheral nerve repair and regeneration

Sr. No.	Speakers	Time (IST)
	Chair : Prof. Kaushik Chatterjee and Dr. Shibu John	
1	Welcome address by Prof. Bikramjit Basu	2:00 pm To 2:05 pm
2	Documentary on MAHE	2:05 pm To 2:10 pm
3	Welcome Address by Dr. Shibu John, Trinity Media/ 3D GRAPHY & Manipal Academy	2:10 pm To 2:25 pm
4	Piyush Padmanabhan, Co-Founder, Next Big Innovation Lab, India.	2:25 pm To 2:55 pm
5	Dr. Carlos Carvalho, Team Leader, Bioprinting Department, Envisiontech, Germany.	2:55 pm To 3:25 pm
6	Saroop Chand, Managing Director, Adroitech Informations Systems, India.	3:25 pm To 3:55 pm
7	Sumant Bhutoria, CEO, Alfatek Systems, India	3:55 pm To 4:25 pm
8	Closing Remarks by Dr. Shibu John	4:25 pm To 4:30 pm

Convener

Prof. Bikramjit Basu
IISc, Bangalore

Organiser

Dr. Shibu John
Founder, Trinity Media,
Managing Director, 3D GRAPHY LLP

Workshop schedule: December 17, 2021 (Friday): 02:00 pm - 04:30 pm, IST

Registration Deadline : December 12, 2021

Who should attend?

Graduate/Masters Students, Doctors, Surgeons, Scientists and faculty members, working in the field of Medicine, Surgery, Pharma, 3D Bioprinting and Tissue Engineering .

Registration link:

https://docs.google.com/forms/d/e/1FAIpQLSca9wRDyehpCN9pQav8u-77NF8bkpWxeB_hbXi1Lu5NHy-6OA/viewform

REGISTRATION IS FREE

ORGANISERS

PLATFORM

OUR SPEAKERS

Dr. Shibu John
Founder, Trinity Media,
Managing Director, 3D GRAPHY LLP,
Mumbai, India

Mr. Piyush Padmanabhan
Co-Founder, Next Big Innovation Lab, Bengaluru, India

Dr. Carlos Carvalho
Team Leader, Bioprinting Department, Envision Tech, Germany

Mr. Saroop Chand
Director, Adroitec Information Systems, Delhi, India

Mr. Sumant Bhutoria
CEO, Alfatek Systems, Kolkata, India

BIOTEM-2021

CP Sharma awardee Lecture

Dr. James Anderson

Dr. James Anderson received his Ph.D. at Oregon State University in 1967. In 1976, he graduated from the Case Western Reserve University School of Medicine with an M.D. degree and finished his Anatomic Pathology residency at the Institute of Pathology of University Hospitals of Cleveland in 1979. Following the completion of his residency, Dr. Anderson joined the faculty of the Institute of Pathology at Case Western Reserve University.

Dr. Anderson has worked in the area of biomaterials, medical devices, and prostheses for the past 40 years and his current activities range from the clinical pathology evaluation of retrieved implants from humans to fundamental studies of cellular interactions with biomaterials.

Dr. Anderson is the recipient of a NIH MERIT (Method to Extend Research In Time) Award (1993 to 2003). He is a founding member of the Society for Biomaterials and the Controlled Release Society and serves as a consultant to the National Institutes of Health Artificial Heart Program, the Food and Drug Administration, and the International Standards Organization where he is the Co-Chair of Working Group 1 for the development of the ISO Standard on Biological Evaluation of Medical Devices, ISO 10993. He is the Editor-in-Chief of the Journal of Biomedical Materials Research. In 2003, he was elected to the Institute of Medicine of the National Academies of Science. In 2005, Dr. Anderson received the Elsevier Biomaterials Gold Medal Award given to the individual who has made the most significant contributions to biomaterials science over the 25 year period from 1980 to 2005. He received this award at the Tissue Engineering Science International Conference held in Shanghai, China, in October of 2005. Dr. Anderson is the recipient of the 2006 Chugai Mentoring Award given by the American Society for Investigative Pathology to senior investigators who have distinguished their careers with a dedication to mentoring and education. In 2006, Dr. Anderson was awarded the Honoris Causa Degree (honorary Doctorate of Philosophy Degree) by the University of Geneva, Switzerland.

In 2008, Dr. Anderson was elected to the American Association of Physicians. Dr. Anderson was elected Fellow of the American Association for the Advancement of Science (AAAS) in 2011. In 2012, Dr. Anderson was awarded the title of Distinguished University Professor by Case Western Reserve University. He is the recipient of the 2013 ActaBiomaterlia Gold Medal for his contributions to biomaterial science and engineering and was elected to the National Academy of Engineering (NAE) in 2013.

Clinical and Basic Science Perspectives of the Foreign Body Reaction

James M. Anderson, MD Phd

Departments of Pathology and Biomedical Engineering
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Dr. Anderson will present information from his Implant Retrieval and Evaluation Program and the extensive research by him and his students on "The Foreign Body Reaction". Starting with his observations as a Surgical Pathologist, he initiated his research program to investigate the immunological and inflammation bases for the foreign body reaction. Following implantation of a medical device or biomaterial, a sequence of events described as the tissue response continuum occurs. These events are injury, protein adsorption, provisional matrix (thrombosis) formation, acute inflammation, foreign body giant cell formation, chronic inflammation, granulation tissue formation, and fibrous capsule formation. Utilizing a wide variety of in vivo animal models and in vitro cell culture methods, immunology and immunohistochemical techniques, and surface analysis techniques including FTIR and SEM, we have identified key mechanisms in the sequence of events in the tissue response continuum. The identification of these key mechanisms and pathways serve as potential sites for modulating or inhibiting the foreign body reaction. Results from our studies over four decades will be presented. It should be noted that there are implanted medical devices and biomaterials that require a foreign body reaction, i.e the development of adherent macrophages and foreign body giant cells at the implant interface and the development of a fibrous capsule. Our research results can be found in: Foreign body reaction to biomaterials, James M. Anderson, et al. Seminars in Immunology, 2008;20(2):86-100. These results provide a foundation for understanding anticipated tissue responses to new medical devices, new biomaterials, and in particular tissue engineered constructs with and without cellular components.

BIOTEM-2021

Plenary Lectures

Prof. B. Ravi

Prof. B. Ravi is an Institute Chair Professor of Mechanical Engineering at IIT Bombay. He is well known for his work in metal casting through AutoCAST, E-Foundry and SMART Foundry projects. In 2014 he set up BETIC – Biomedical Engineering & Technology Innovation Centre, whose team members developed and patented 50+ medical devices, incubated 16startup companies, licensed several products to industry, and won many prestigious awards. In 2019, he took over as the head of DS School of Entrepreneurship, which has trained over 2000 students in entrepreneurship and led to over 30 start-ups during the last five years. As a member of governing or advisory councils of several institutes and expert committees of various government agencies, Prof. Ravi also contributes to project reviews, policies and practices related to translational research, product innovation and entrepreneurship.

Personalized Medical Devices Using Additive Manufacturing Technology

Prof. Bhallamudi Ravi

Institute Chair Professor, Mechanical Engineering
PI, Biomedical Engineering & Technology Innovation Centre
Professor-in-Charge, Desai Sethi Centre for Entrepreneurship
Indian Institute of Technology Bombay, Mumbai-400076

ABSTRACT

Medical devices are critical for healthcare. This sector is growing rapidly, driven by market pull and technology push. Medical device industry also contributes to economic growth (via startups and SMEs) and social impact (via job creation and affordable healthcare). At present, there is considerable interest in personalized medicine driven by medical imaging, CAD, bio-materials and additive manufacturing (AM). In this session, we will explore the application of AM to fabricate patient-specific anatomical models, surgical jigs and implants (cranial, dental, maxillofacial, orbital, orthopaedic, spinal, etc.) with high quality and long life at continuously reducing costs. AM also plays a critical role in medical device innovation via rapid prototyping for early clinical feedback, thereby accelerating the journey to the market. These applications are illustrated by real-life examples of patient-specific devices as well as innovative medical products developed at BETIC centres in IIT Bombay and other partner institutes.

Dr KV Venkatesh

Dr KV Venkatesh is a professor of Chemical Engineering in IIT Bombay. He is also an associate faculty of School of Bioscience and Bioengineering at IIT Bombay. He got his B. Tech from chemical engineering from IIT Madras and later he pursued his PhD at Purdue University, USA. He joined the faculty of IIT Bombay in 1993 after his PhD. He has an extensive research experience in the areas of Systems and Synthetic Biology and Biosystems Engineering. He has contributed significantly to research in the areas of quantification of biological networks including genetic, signaling and metabolic pathways. He has 145 journal articles and book chapter to his credit. In recognition, he has won many national awards like the prestigious Swaranjayanthi fellowship from DST, INSA young scientist and INAE Young Engineers awards. He is an associate editor of BMC systems biology. He is an elected Fellow of Indian Academy of Sciences.

Systems Engineering Perspective of Human physiology - Multiscale Models for Disease Characterization: Towards drug-discovery, Clinical Study, Disease management and Personalization

K. V. Venkatesh

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Human physiology is an ensemble of various biological processes spanning from intracellular molecular interactions to the whole-body phenotypic response. Systems biology endures to decipher these multi-scale biological networks and bridge the link between genotype to phenotype. The structure and dynamic properties of these networks are responsible for controlling and deciding the phenotypic state of a cell. Several cells and various tissues coordinate together to generate an organ level response which further regulates the ultimate physiological state. The overall network embeds a hierarchical regulatory structure, which when unusually perturbed can lead to undesirable physiological state termed as disease. Here, we treat a disease diagnosis problem analogous to a fault diagnosis problem in engineering systems. Accordingly, we review the application of engineering methodologies to address human diseases from systems biological perspective. The research work highlights potential networks and modeling approaches used for analyzing human diseases. The application of such analysis is illustrated in the case of arthritis, Non-Alcoholic fatty acid Liver disease and child wellness platforms. We put forth a concept of cell-to-human framework comprising of five modules (data mining, networking, modeling, experimental and validation) for addressing human physiology and diseases based on a paradigm of system level analysis. The work emphasizes on the importance of multi-scale biological networks and subsequent modeling and analysis for drug target identification and designing efficient therapies.

Rohit Srivastava

Dr. Rohit Srivastava is Head and Professor of Department of Biosciences and Bioengineering at the Indian Institute of Technology, Bombay. Dr. Srivastava completed his Bachelor of Engineering in Electronics Engineering from VNIT Nagpur in 1999 with distinction and subsequently went on to finish a Master of Science and a PhD in Biomedical Engineering from Louisiana Tech University, Ruston, LA, USA after which he joined IIT Bombay in 2005. His specialization lies in POC Diagnostic devices, Biomedical Microsystems devices (MEMS), nanoengineered biosensors, photothermal therapy in cancers and nanoengineered orthopedic applications. Dr Srivastava's lab in collaboration with Biosense Technologies Pvt Ltd have already developed and commercialized "UChek" a portable urine analysis system based on the mobile platform and have also made a low-cost reader for quantitatively analyzing urine dip sticks for which he has received the DBT Biotech Process and Product Commercialization Award 2015 and the OPPI Young Investigator Award 2014.

Dr Srivastava has also been awarded the DBT National Bioscience Award 2017 for his efforts in translating technologies from lab. He has been awarded the prestigious NASI Reliance Industries Platinum Jubilee Awards 2018 for Application Oriented Innovations in Physical Sciences. He has recently been awarded the prestigious Om Prakash Bhasin Award 2018 for excellence in Health and Medical Sciences, considered the highest honour in the country in this field. Prof. Rohit Srivastava has been conferred the prestigious Dr. Shanti Swarup Bhatnagar Prize 2021 in Medical Sciences and has been elected a Fellow of INAE in 2021. He has been elected a Fellow of the National Academy of Sciences, INDIA, 2019 and Fellow of Royal Society of Chemistry, London in 2019 and a Fellow of Royal Society of Biology, London 2019. Dr. Srivastava's lab is focusing on developing technologies that can be commercialised and brought to use for the common man in India.

Affordable Healthcare Technologies in Sensing, Drug Delivery and Therapy

Rohit Srivastava

IIT Bombay

Our lab at IIT Bombay is well recognized for translation research in the field of Biosensors and affordable Point-of-care diagnostic technologies for rural and maternal healthcare. Our team has already commercialized several point-of-care diagnostic devices including SYNC- Bluetooth integrated glucometer for diabetes management; UChek- routine urine analysis system; Care Mother- a smartphone-based platform to integrate doctors and pregnant women to screened and identify risk-prone pregnancies for maternal and neonatal healthcare in the rural areas through student start-ups. We have also clinically validated and transferred numerous healthcare technologies such as Smartsense™- affordable and portable blood electrolyte analyzer with integrated blood plasma centrifuge; Uridsa™- a low-cost, portable colorimetric deice to diagnose kidney-related disorders etc. We have also clinically validated several technologies like PorFloR™- Fluorescence strips and device for detection of orthopedic implant-associated infection such as C-reactive protein (CRP) and interleukin-6 (IL-6); CholcheckTM- Affordable LFA-based complete cholesterol panel and detection device. Our group has also indigenously developed economical, novel, resorbable bone screw and drug loaded chitosan sponges for orthopedic applications. We strongly believe in bringing a positive change in India's underdeveloped healthcare sector via developing affordable healthcare technologies with the collaboration of industries and generating funds via transferring technologies for commercialization.

Dr. Vrisha Madhuri

Dr. Vrisha Madhuri is a professor of Paediatric Orthopaedics at CMC. She received her MS in Orthopaedics from CMC, and she went on to receive her M.Ch in Orthopaedics from Liverpool University in the U.K. She has received many accolades, including an award from the National Research and Development Council Government of India for societal innovation. Dr. Madhuri is widely published, has several patents, and numerous research projects which have transformed paediatric orthopaedics and helped to deliver quality care for children.

Articular cartilage restoration- A road map to clinical translation

Dr.Vrisha Madhuri MS Orth, MCh Orth

Professor Orthopaedics, Adjunct Scientist Center for Stem Cell Research
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ABSTRACT

The chondral injuries of the joints are seen in 10-15% of all arthroscopies and lead to osteoarthritis. Autologous and other forms of biological cartilage repairs are currently taking place in collaboration with industry involved in regenerative cell therapies. In India, many leading institutes are involved in studying cartilage tissue regeneration and tissue engineering with most publications pertinent to establishing and testing the different scaffold materials and drug delivery to repair the defects. Internationally numerous strategies are being tested to prepare the tissue-engineered graft using autologous chondrocyte, minced cartilage, chondrocytes prepared from the mesenchymal stem cells or induced pluripotent stem cells. The most extensively studied approach is the use of chondrocytes laden 3D scaffolds, and many different materials have been explored as a scaffold and shown useful for cartilage tissue engineering in *in vitro* and *in vivo*.

Our lab used various strategies to promote the regeneration of articular cartilage defects, which includes testing cell-laden 3D scaffolds developed with in the country and targeting the malfunction pathways using small molecules and biomolecules. Initially two foam based scaffolds developed at SCTIMST- 1. Polyvinyl alcohol-poly (caprolactone) (PVA-PCL) monophasic 2. A biphasic, PVA–PCL incorporated with bioglass as the lower layer scaffold and the regeneration potential of these two were tested using a rabbit model. The two months outcomes showed a cartilage-like tissue formation by both scaffolds. But, at 1-year follow-up, there was a deterioration of regenerative tissue

due to the slow degrading profile of both PVA-PCL scaffolds. From this study, we learned the optimal condition required for cartilage repair. Subsequently, in collaboration with IIT, Kanpur, we have tested several scaffolds based on our earlier rabbit study experience The two scaffolds 1. Chitosan-gelatin blended with laponite 2. Carrageenan-gelatinwere designed to mimic the ECM components of the articular cartilage 3. Multi-layered chitosan-gelatin (ML) scaffold was to imitate the ultrastructural arrangement of the tissue, and 4. Randomly aligned chitosan-gelatin scaffold, which is used as a control for ML. In vitro and in vivo testing of these four scaffolds formed a hyaline cartilage tissue in the defect. Among these, the multi-layer chitosan-gelatin and carrageenan-gelatin scaffold alone (without cells) repaired the defect using endogenous stem cells. Further studies are ongoing to test its regenerative potential using a larger animal model in preparation for human translation.

The low or uncontrolled differentiation of stem cells causes fibrosis or hypertrophic cartilage formation, respectively. These are the major setback in articular cartilage tissue engineering. To address this issue, we have improved the MSCs differentiation protocol. The transforming growth factor is typically used to differentiate the MSCs, and it was shown to promote hypertrophic differentiation. We have demonstrated that the supplementation of the parathyroid hormone-related peptide on the fourth day of culture induces chondrogenesis of MSCs, and also it prevents hypertrophic cartilage formation (11). We anticipate this protocol will enable us to create hyaline cartilage for the treatment.

Studies illustrated that the diseased/damaged tissue in the vicinity stimulates the hypertrophic differentiation of transplanted graft, necessitating an inhibition of hypertrophy promoting genes. We have identified a miRNA combination that enables the spontaneous and controlled differentiation of MSCs into hyaline cartilage and sustained delivery of these miRNAs using hydrogel (miRNA activated matrix) formed a hyaline-like cartilage tissue with minimal hypertrophy without the addition of any growth factors. We anticipate that miRNAs' sustained delivery facilitates the maintenance of tissue phenotype even in the diseased state. An in vivo testing of this strategy for the treatment of goat articular cartilage defect is underway and the way forward towards translation.

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Dr. Biman B.

Dr. Biman B. Mandal is Professor at Department of Biosciences and Bioengineering and Associate Dean, Academics (UG) at the Indian Institute of Technology Guwahati (IITG). His group is working on Tissue Engineering, Biomaterials and Stem cells towards developing a number of affordable healthcare products which includes bioartificial skin, smart wound dressings, bioartificial liver devices, vascular grafts, cardiac patches, intervertebral disc, corneal grafts, bone, cartilage, minimally invasive drug eluting injectable gels, targeted anti-cancer drug delivery devices, skin care products, affordable bioreactors and bio-instrumentation etc.

Dr. Mandal received his bachelor's from Presidency College, Calcutta University (2003)and his master's in Biotechnology, H.P. University (2005). He earned his Ph.D in Biotechnology from Indian Institute of Technology Kharagpur, and was a CSIR-Fellow (2005-2009). Dr. Mandal completed his Post Doctoral Research at Department of Biomedical Engineering, Tufts University, USA (2009-2011).Dr. Mandal is a recipient of numerous National and International awards which includes the APA-Young Scientist award 2019; NASI-SCOPUS Young Scientist Award 2016; INSA- Medal for Young Scientists 2015; NASI- Young Scientist Platinum Jubilee Award 2013; DST-INSPIRE Faculty award 2013; Gandhian Young Technological Innovation Award 2014; DAE-Young Scientist Award 2011; SYIS- TERMIS Asia-Pacific Young Investigator Award2011; MAHE Young Scientist Award 2012; DBT-RGYI Award 2012; DST- Young Investigator Grant Award 2012; He was awarded "Indo-Swiss Student Exchange Award" during his Ph.D in 2006. Dr. Mandal has been invited to deliver talks both Nationally and Internationally including at MIT, Boston and is a visiting faculty toKTH, Sweden, UCL London, Justus-Liebig University, Germany and Nanyang Technological University (NTU), Singapore.

Silk Based Bioengineered Human Tissues & Organs: The Way Forward

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ABSTRACT

Every year, millions of patients suffer loss or failure of an organ or tissue as a result of accidents or disease. Tissue or organ transplantation is a commonly accepted norm under these circumstances. However, constant shortage of donor tissue and organ transplants coupled with high morbidity and mortality has spurred great interest for lab grown bioengineered tissues/organs as promising substitute. Our laboratory at IIT Guwahati specifically focuses on recreating these functional tissues, organs and implants at an affordable cost using naturally derived biodegradable biomaterials i.e. Indian endemic silk in combination with stem cells. We have developed methods using conventional and latest 3D bioprinting techniques to intricately mimic the architecture of organs/tissues in great details in an attempt to understand the underlying cell-material crosstalk and its role in tissue regeneration. As an outcome of our research endeavor at IITG, we have developed a number of affordable prototypes which are in various phases of animal/clinical validation. These include smart wound dressings for diabetic foot ulcers, skin grafts for burn injuries, vascular grafts for by-pass surgery, vascularised bone grafts as orthopaedic implants, beating cardiac patch for myocardial infarction, bioartificial pancreas releasing insulin for type-1 diabetes, 3D printed intervertebral disc and knee meniscus as orthopaedic grafts and minimally invasive anti-cancer drug eluting injectable gels for cancer treatment. Similarly, we have developed multiple in vitro human disease models which can contribute to Industry in high throughput drug screening and drug development.

Prof Michael Gelinsky

Michael Gelinsky received his PhD in Chemistry from Freiburg University (Germany). In 1999, he moved to Dresden University of Technology (Germany) and worked for around 10 years in the Institute for Materials Science, heading his own group at the newly founded Max Bergmann Center of Biomaterials from 2002. In 2010, he was appointed as Professor at the Faculty of Medicine and is currently head of the Centre for Translational Bone, Joint and Soft Tissue Research. Gelinsky's work is focused on biomaterials and scaffold development, tissue engineering and regenerative therapies, mostly for musculoskeletal tissues. His group is also very active since more than 10 years now in the field of additive manufacturing of degradable implants and biofabrication technologies. His lab is mostly using microextrusion methods but also has started with melt electrowriting and inkjet. The team published the first papers on bioprinting of live microalgae and plant-derived cells ("green bioprinting").

Michael Gelinsky was conference chair of the annual meeting of the European Society for Biomaterials in 2019 and is currently Vice President of the German Society for Biomaterials. In addition, he is serving as a board member of the International Society for Biofabrication. In 2020, he was elected as a member of the International College of Fellows of Biomaterials Science and Engineering (ICF-BSE).

Combining technologies, materials and cells in 3D bioprinting

Michael Gelinsky

Centre for Translational Bone, Joint and Soft Tissue Research, TU Dresden

Human tissues are complex objects, consisting of highly organised extracellular matrix components and in most cases several cell types, arranged in a spatially strictly controlled manner. With bioprinting we are able to deposit living cells in combination with biomaterials, creating three-dimensional, tissue-like constructs. However, we are not yet able to realise the necessary complexity and simultaneously resolution when we want to print volumetric constructs as they would be needed for medical applications.

More complexity could be achieved when different materials and cell types are combined during the bioprinting process and also the combination of different additive manufacturing technologies within one print might help to mimic the real tissues better. Our lab is interested in such combinations, e.g. of bioinks with calcium phosphate bone cements, of melt electrowriting and extrusion printing or bringing together two cell types in a core/shell fashion. Furthermore, additional functionalities can be achieved when cell types are combined that cannot be found together in nature like photosynthetically active micro-algae and human cells.

Rui L. Reis

Rui Luís Reis is a professor of tissue engineering, regenerative medicine and stem cells at the Department of Polymer Engineering, School of Engineering of the University of Minho, in Braga and Guimarães. He is the Director of the 3B's Research Group, part of the Research Institute on Biomaterials, Biodegradables and Biomimetics (I3Bs) of UMinho (www.i3bs.uminho.pt), which specializes in the areas of regenerative Medicine, tissue engineering, stem cells and biomaterials. He is also the Director of the ICVS/3B's Associate Laboratory of UMinho. He is also the CEO of the European Institute of Excellence on Tissue Engineering and Regenerative Medicine. Rui L. Reis is also, since 2013, the Vice-Rector (Vice-President) for research and innovation of UMinho. Since 2007 he is also editor-in-chief of the Journal of Tissue Engineering and Regenerative Medicine. He is since 2016 and until 2018 the Global (World) President of the Tissue Engineering and Regenerative Medicine International Society (TERMIS). He is the responsible and PI of the EU funded project for the creation of the new center of Excellence, with headquarters in AvePark in Caldas das Taipas - Guimarães, the Discoveries Center for Regenerative and Precision Medicine in a Teaming process between University of Minho, University College London, University of Porto, University of Aveiro, University of Lisbon, University NOVA Lisbon

New approaches for the engineering and regeneration of different tissues

Rui L. Reis [1,2,3]

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The selection of a proper material to be used as a scaffold or as a bioink in 3D bioprinting approaches in order to supportor encapsulate cells is both a critical and a difficult choice that will determine the success of failure of any tissue engineering and regenerative medicine (TERM) strategy.

In our research group we have been using natural origin polymers, including a wide range of marine origin materials, for many different approaches that allow for the regeneration of different tissues. Several innovative bioinks with quite specific properties were proposed. We have also been optimizing the respective formulations for using these novel materials in distinct biomanufacturing strategies. This will be presented and discussed during the keynote talk.

Furthermore, an adequate cell source should be selected. In many cases efficient cell isolation, expansion and differentiation methodologies should be developed and optimized. We have been using different human cell sources namely: mesenchymal stem cells from bone marrow, mesenchymal stem cells from human adipose tissue, human cells from amniotic fluids and membranes and cells obtained from human umbilical cords.

The potential of each combination materials/cells, as related to different manufacturing technologies, with details focusing on bioprinting, to be used to develop novel useful regeneration therapies will be discussed. The use of different cells and new ways to assess their interactions with different natural origin degradable scaffolds and bioinks will be described. Several examples of TERM strategies to regenerate different types of tissues will be presented.

BIOTEM-2021

Keynote Address

Biosensing based on carbon nanotube aerogel: A wonder material

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Carbon nanotube aerogel (CNT aerogel) is a 3D network of long carbon nanotubes synthesized by floating catalyst chemical vapour deposition (FC-CVD). We were able to synthesize CNT aerogel based electrodes with isotropic properties and with very high electrical conductivities by a simple scalable process. A label-free biosensor has been prepared which was able to detect the hybridization of DNA very rapidly with very high sensitivity. Also sensing of volatile organic compounds (VOC) was possible with this sensor making it useful for cancer detection. The talk will focus on the engineering and the sensing aspects of this wonder sensor material.

Recent advancement of 3D bioprinting technologies in Therapeutics and Tissue Engineering

Haruka Yoshie
CELLINK, BICO Company

Over the recent years, 3D bioprinting technologies have made substantial advances in the field of tissue engineering. Using 3D bioprinting technologies, researchers canprint living cells to create complex tissue models. To recapitulate biology and physiology, and to create the appropriate microenvironment for the cells, the choice of the biomaterials, bioinks, plays an important role.

3D bioprinting technologies have been applied to study various tissue models mimicking different organs in the body. Other applications include studying diseases. It has been used for cancer research; some researchers apply this technology to study infectious disease. Additionally, it provides a platform for high-throughput method for drug discovery and toxicology studies with its efficient and reproducible procedures.

In this talk, I will introduce the basic 3D bioprinting principles, bioinks, and CELLINK 3D bioprinting technologies. The talk will also cover various application areas from tissue engineering to pharmaceutics.

Targeted Drug Delivery to Respiratory Neurons Using Nanoparticles Functionalized by Neural Tracing Proteins

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Respiratory failure is the leading cause of death in spinal cord injury (SCI) patients. Persistent respiratory recovery in rats can be achieved by multiple administrations of adenosine receptor antagonists such as theophylline, which suggests that chronic drug administration induces functional plasticity in the respiratory circuitry. However, while theophylline works in humans in a similar manner as in rats, most SCI patients cannot tolerate theophylline due to its side effects. To directly address the problem of the drug's side effects, we have developed a novel approach that combines nanotechnology with proven neurobiological principles to selectively target the respiratory neurons responsible for diaphragm muscle function. Our nanotherapeutic design consists of a targeting neural tracing protein, wheat germ agglutinin conjugated to horseradish peroxidase (WGA-HRP), chemically linked to a gold nanoparticle, which in turn is chemically conjugated to a pro-drug, pro-theophylline or pro-DPCPX. Our targeted drug administration can induce recovery of the hemidiaphragm in SCI rats by using a fraction of the systemic dose. For comparison, the systemic dose of theophylline in rats is 15 mg/kg, while the theophylline content in the nanoconjugate is only 0.12 mg/kg. The systemic dose of DPCPX in rats is 0.1 mg/kg, while the DPCPX content in the nanoconjugate is 0.15 µg/kg, ~0.1% of the systemic dose. This talk will focus on our recent work to demonstrate quality control in the synthesis of the nanoconjugate, its storage and biological stability, sustained release of the drug in biological pH, and retrograde movements of individual particles from axon to cell body in neurons compartmentalized in microfluidic channels. We apply the microfluidic method to screen for protein-nanoconjugates capable of delivering and releasing drug cargos at precise locations in the motor neuron circuitry to reduce and possibly eliminate the drug's side effects.

Integrated approach of materials in pharmaceutical drug discovery and development

Dhivya Shanmugarajan and Sharath Chandra

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Biomaterial-based therapeutics is a rapidly burgeoning niche domain in the pharmaceutical industry. The primary focus is gained more towards drug discovery and delivery. Treating many diseases is turning into a daunting task due to poor bioavailability and pharmacokinetic properties of the drugs. This is due to inappropriate site of administration of drugs or uncontrolled release systems. To overcome this major concern a suitable drug carrier or vehicle are needed to be identified to transport the active pharmacophore ingredients.

There are various materials such as polymers, polymer-composites, co-polymers, carbon nanotubes, metal-based nanoparticles, nanoemulsions, micelles, chitosan, natural and synthetic collagen, etc., that can be utilized as drug delivery vehicles but the feasibility of the carriers is a prerequisite to be analyzed before introducing into *in vivo* system.

The integrated utilization of Dassault Systemes BIOVIA life science solutions such as materials studio to analyze the properties of various materials efficacy will lead to choosing a better drug vehicle and Discovery studio to analyze drugs or natural products ADMET properties and drug-likeness properties will enhance pipelines of drug discovery and development. Both systems have high efficient modeling and simulation tools that will condense hurdles of painstaking pharmaceutical research. Moreover, the significant importance of selecting a specific drug carrier, can be revealed through the implementation of these tools will leverage the resources. Also, it improves its efficacy, safety and controlled sustainable site release of drugs in the body

Key words: Biomaterial-based, drug discovery and delivery, polymers, drug vehicle, materials, ADMET.

Gastric resident drug delivery systems for sustained oral delivery

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The oral route remains the preferred route of drug administration for patients, care givers and drug makers. Despite its long history, oral drug delivery systems can be used for only limited applications. For example, while injectable/implantable systems have the capacity to deliver drugs for months-years, typical oral drug delivery systems last for just 1-2 days. Hence, *truly* long-term drug delivery is not possible with most orally administered products. Long-term oral delivery cannot be achieved due to the limited gastrointestinal residence time of orally administered products. To overcome this problem, we have developed a gastric resident drug delivery system. This system has a stellate shape and can be folded into a gelatin capsule for ingestion. On reaching the stomach, the capsule dissolves allowing the dosage form to unfold and assume a size larger than the pylorus. The drug delivery system resides in the stomach of a large animal for 1-4 weeks, and can be used for delivering drugs for this duration. These systems stand to have to have a significant impact on the treatment of diseases needing chronic therapy.

Revving up the Immune System: TLR7/8-based Anticancer Nanovaccines

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Agonists of toll like receptors (TLRs) are promising anticancer vaccine adjuvants because of their ability to induce proinflammatory cytokines necessary to generate a robust immune response. However, currently available TLR agonists suffer from several limitations including self-regulatory immunosuppression and unfavorable local pharmacokinetics resulting in poor availability within dendritic cells. Further, current TLR agonist-based anticancer vaccines generate a robust cytotoxic CD8 T cell response but not CD4 Th1 helper T cell response, which is critical for induction of effective, long-term antitumor immunity. We are addressing these important challenges through a synergistic combination of drug discovery and drug delivery efforts. Our team has developed a suite of highly substituted imidazoquinolines, which activate TLR 7 and/or 8 and induce significantly higher levels of cytokines compared to imiquimod, an FDA approved TLR7 agonist. Our studies show the balance between pro-inflammatory and immunosuppressive cytokines can be tuned through structural modifications. Encapsulation of these agonists in acidic pH responsive nanoparticles (NPs) resulted in robust activation of CD4 and CD8 T cells as well as natural killer (NK) cells, leading to a stronger anticancer immune response than free agonist or that encapsulated in non-pH responsive NPs. Importantly, intradermal delivery of NP vaccine using a hollow microneedle platform led to an enhanced Th1 immune response, which is essential for effective induction of long-term anti-tumor immunity. We are further optimizing the new agonists for efficient encapsulation in pH responsive NPs, tune the NP properties for improved targeting of dendritic cells following delivery via hollow microneedles, and investigate potentiation of NK cell-mediated antibody-mediated cellular cytotoxicity.

Demineralized Bone Matrix: Activities and Applications

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Allogenic demineralized bone matrix (DBM) is widely used as a bone graft substitute in orthopedics and dentistry. It has been used successfully to regenerate bone as a powder, in the form of segments or perforated slabs alone or mixed with different carriers. Despite its success in many applications, questions continual to be raised regarding its use, largely due to the variability in results. Our studies indicate that the osteoinductivity of DBM can vary with donor age, gender, site of implantation, method of preparation and other factors such as particle size, geometry, conditions of storage, and selections of the carriers.

DBM osteoinductivity is derived from the endogenous bone morphogenetic proteins (BMPs) that are impregnated in collagen scaffolds. The activity and cellular accessibility to BMPs are two important factors associated with the osteoinductive potential of DBM. In addition, inflammatory phase and interaction between the inflammatory cells and the implanted bone matrix is of critical importance for osteogenesis. Understanding the intricate mechanisms of cell-material response and repair processes will allow for better designed DBM based bone graft materials.

Regeneration of intervertebral disc in a mouse disc degeneration model using bone marrow derived mesenchymal stem cell

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Background:

Back pain and radicular pain due to disc degeneration is probably the most common problem encountered in neurosurgical practice. The experience and results of stem cell therapy in animal disc degeneration model will help us while doing clinical trials.

Objective:

To study the effect of bone marrow derived mesenchymal stem cells in an established mouse disc degeneration model.

Methods:

An easily reproducible mouse coccygeal (Co) 4-5 disc degenerated model by CT-guided per-cutaneous needle injury was established. The MSCs were cultured from mouse bone marrow and validated. By an established technique, 24 mice disc degenerative models were generated and divided equally into 3 groups (Test, Placebo and Control). The test group received MSCs with fibrin glue scaffold and placebo group received only scaffold after six weeks of degeneration. The control group did not receive any injection. The effects of MSCs were analyzed eight weeks post injection.

Results:

The test group showed a significant change in disc height index (%) in micro CT, whereas in the placebo and control group there was no change. The Safranin O staining showed an increase in glycosaminoglycan content and the polarized imaging of picrosirius red staining showed restoration of the collagen fibers in AF which was statistically significant.

Conclusion:

Intra discal MSC injection restored disc height and promoted regeneration in the discs at the end of 8 weeks. MSC's niche depends on the microenvironment of the host tissue. These findings will be helpful for the clinical trials.

Visco-elastic scaffold in dermal tissue regeneration

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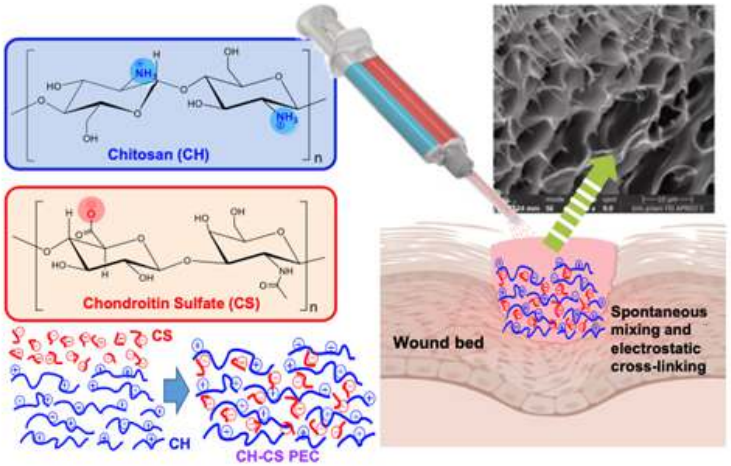
Pathological state of non-healing cutaneous chronic wounds in diabetic and venous ulcers represents a major burden and disturbs the mental and economic status of patients. The resource-intensive and slow-acting treatment modalities further deepens severity of pathogenesis of wound. Recently alternate approach of scaffold aided drug deliver is being attempted at clinical trials. Present study reveals the efficacy of injectable *in-situ* gel forming, biodegradable thermostable viscoelastic material namely chitosan-chondroitin sulphate, poly-electrolyte complexation (CH-CS-PEC) towards the dermal wound healing[1]. Schematic is explained in figure 1. CH-CS-PEC conjugate displayed the highest rheological nature of matrix viscoelasticity with micro-porous architecture. Solid state CP-MAS ^{13}C NMR, X-Ray diffraction, XPS characterization showed the perfect chemo-molecular interaction to form the stable matrix. Fibroblast and keratinocyte cells displayed the higher degree of migration upon co-culture with CH-CS-Pec complexes. Higher mRNA expression status of *involucrin, HGF, Col-1/Col-III* and -SMA was noticed in both fibroblast and keratinocyte cells. Western blot analysis of PCNA confirmed that CH-CS-PEC conjugate have positive impact on the cell migration. Immuno-histochemical for early and mature migratory markers, α-SMA and β -integrin showed enhanced expression further confirmed the suitability of the conjugates as wound healing material. In addition, no clear toxic effects and cell stress phenomenon of synthesized materials was noticed towards fibroblast and keratinocytes [2]. Nonetheless, CH-CS-PEC could be used or taken as suitable scaffold material for dermal wound



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Dental Implants –Biomaterials in action

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A stable prosthesis for a missing tooth or missing part of the face is critical for the patient for function, comfort and appearance. A dental implant enables stability for the prosthesis through osseointegration. With an aging population increasing worldwide, the dental implant market is expected to touch over 11 million dollars with Asia Pacific region anticipated to have the highest growth rate for the implant industry. Therefore, with the need for indigenous implants being the order of the day, a titanium implant with predictable outcomes in terms of sustained mechanical and biological properties over several years is warranted. The implant must also have a variety of prosthetic options to permit the clinician to use them in varied clinical situations. To meet these requirements, an improved design of dental implant was developed. The implant stability in synthetic and natural bone samples were tested using insertion and removal torque analysis. The implants were also subjected to animal studies with positive results.

Design of third-generation bioactive glasses for soft tissue engineering – Challenges and open questions

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The concept of third-generation biomaterials is based on the principle of activating a synchronized sequence of genes at the cellular level to stimulate the regeneration of living tissues. The resorbable bioactive glasses are a subset of third-generation biomaterials where the glass resorbs, when in contact with body fluids, while the ionic dissolution products released from the glass into the body stimulate specific biological responses, for example, gene expression of human osteoblasts, promote angiogenesis and induce insulin-like growth factor II mRNA expression. Considering slow and incongruent dissolution kinetics of silicate-based bioactive glasses when in contact with physiological fluids, they do not meet the criteria to be used as third-generation biomaterials. Therefore, the next generation of bioactive glasses are expected to (1) be fully biodegradable; (2) release functional ions in a controlled manner while matching their dissolution rate with the recovery rate of the injured tissue; and (3) not promote calcification of tissues. While considerable effort is being made to design such glasses, there are several challenges that need to be addressed to achieve this goal. The presentation will discuss a few of these challenges and open questions from the perspective of glass science and propose the topics on which future research needs to be directed to accomplish the abovementioned goal.

Plasma Engineering of Biomaterials for Improved Bio-interfaces

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Low temperature Plasma (LTP) can initiate chemical reactions, producing different oxygen radicals, charged particles, ions and UV light. Active species can be used for biomedical, agricultural and food safety applications. Active species can also be very toxic to biological tissue, selectively killing bacteria, fungus, and viruses as different gases produce different charged species and reactive neutrals. There is significant interest in the field of tissue engineering in plasma surface modification of biomaterials and tissue scaffolds to promote adhesion/conjugation of biomolecules and proteins that accelerate the proliferation of cells onto them, and drug molecules for controlled release or cellular growth factors to promote biointegration. In plasma treatment, three surface phenomena are anticipated, i.e., etching (degradation) of the surface through reactions of high-energy atomic or ionic gases with the organic carbon of the surface and formation of various functional groups at the surface depending on the gas (O, N, F containing gases) through reaction of active species from the plasma and surface carbons of the biomaterials or plasma-assisted polymerization on the irradiated substrate using organic monomeric gases [1-4]. We have recently studied LTP effect on the 3D printed polymeric tissue scaffolds for both cellular and anti-bacterial properties. This talk presents the plasma engineered surface modification research on 3D printed PLA and PCL polymeric materials and tissue scaffolds.

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Engineering Bioresorbable Implants and Structures for Biomedical Applications

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Engineered bioresorbable materials provide promising solutions for tissue engineering and regenerative medicine. Bioresorbable implants and devices are designed to degrade harmlessly in the body over time as new tissues grow, which eliminates the need for secondary surgeries and associated complications. Recent researches on biodegradable polymers and metals have demonstrated their potentials for clinical translations, but there are still major challenges yet to be addressed, e.g. (1) how to match their degradation rates with tissue healing rates, and (2) how to control their bioactivity to promote healing functions of desirable cells while inhibiting bacterial infections. In this presentation, our recent progress on developing bioresorbable alloys and composites as the next-generation biomaterials, and creating new surface modification strategies and biodegradable composites to regulate their degradation rates, will be discussed.

Degradation of bioalloys and composites and their *in vitro* cytocompatibility with relevant host cells, and functional evaluation in animal models *in vivo* will be presented.

Bone regeneration capacity of magnesium phosphate minerals

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Bone defects exceeding a critical size require a filling with either autologous bone transplants or synthetic materials to fill the space and to prevent fibrous tissue ingrowth. Currently available synthetic materials for bone replacement are usually based on calcium phosphate phases such as hydroxyapatite or ß-tricalcium phosphate. But despite clinical use and decades of research, there are still decisive drawbacks of these materials when used as bone substitutes, e.g. insufficient mechanical properties and limited resorption speed, especially of hydroxyapatite. Magnesium phosphate (MgP) minerals such as struvite ($MgNH_4PO_4{\cdot}6H_2O$), K-struvite ($MgKPO_4{\cdot}6H_2O$), newberyite ($MgHPO_4{\cdot}3H_2O$) or cattiite ($Mg_3(PO_4)_2{\cdot}22H_2O$) are discussed as suitable alternatives [1] due to their higher solubility and their bone regeneration capacity previously demonstrated even in large animal models.

This lecture aims to give an overview on the use of MgP for bone replacement, starting with general aspects on magnesium phosphate chemistry, the transfer of the materials into clinically suitable application forms such as self-setting cements, granules or macroporous scaffolds, as well as the influence of MgP minerals on bone healing in various animal models. Here, usually no signs of inflammation are observed after implantation, while the implanted materials show a continuous degradation with simultaneous new bone formation. Previous studies showed that even larger partial load-bearing defects can be successfully treated with magnesium phosphate cements with practically full resorption and bone regeneration after 10 months [2]. More recent studies also revealed that the degradation speed can be adjusted by altering the phase composition, e.g. a substitution of ammonium ions in struvite by potassium shows an accelerated degradation behavior. Although this is accompanied by a temporarily soft tissue formation at the implant – bone interface, K-struvite granules are finally resorbed after two months and replaced by newly formed bone already after four months of implantation.

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3D Printing from bench to bedside: Challenge and opportunity

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3D Printing technology has expressed its advantage by offering design freedom, mass customization, waste minimization, the ability to manufacture complex structures and fast prototyping. The last two decades have witnessed the emerging arena of additive manufacturing in terms of its applicability in a vast field of science and technology. In healthcare, additive manufacturing has been utilized for customization in implant, development of surgical guideway,a mock surgical model for disease organs, organ development, device development etc. Organ availability and its transplantation is always an issue and technological intervention like 3D printing, bioprintingproves to be an alternative toward this. However, the bedside translation of 3D printing has been astonishingly decelerated due to challenges on the way to technology development. These challenges are not just limited to the technical issues but also to the regulatory and commercial hurdles that are impeding the translational cycle. Despite such hurdles, this technology has entered into the dynamic phase of clinical adoption. Recent progress in clinical studies and trials shows exceedingly encouraging results proving the performance and stability of 3D printed structures in biological conditions.

This talk aims to emphasize challenges; the scientific community is facing to bring 3D printing technology to bedside and clinics along with the opportunities we have to engage interdisciplinary services around the key translational hurdles to drive quality improvements in healthcare delivery.

BIOTEM-2021

Invited Talks

Engineering Material Surfaces for Blood Contacting Medical Devices

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Hemocompatibility of biomaterials remains a challenge for successful development of blood-contacting medical devices. When biomaterial implants come in contact with blood, the initial event is the adsorption of plasma proteins, followed by platelet adhesion and activation and further thrombus formation, which can cause the device failure[1]. Thus, there is a vital interest in developing novel surfaces that prevent blood from clotting. It is well known that titanium has good biocompatibility and has been widely used as a biomaterial since the late 1970s. However, even titanium-based implants can cause the same adverse effects when interacting with blood. Therefore, one approach that has been recently studied is enhancing hemocompatibility by using superhydrophobic surfaces (i.e., surfaces that repel blood) [2]. In our work, we have investigated the hemocompatibility of superhydrophobic and superhydrophilic surfaces by studying the adsorption of key blood plasma proteins and the platelet adhesion and activation. Our results indicate that the surfaces can be fabricated and stable over a period of 28 days under physiological conditions. They also control protein adsorption on the surface which may prevent blood clotting on the surfaces. Further, the surfaces reduced platelet adhesion and activation, which may result into less thrombus formation.

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Nanofibrous polymers for instructive design of biomaterial devices

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Nanofibrous materials show diverse and promising applications in filtration, wound-dressing materials, protective textiles, tissue scaffolds, and biomedical devices. Majority of the nanofibrous matrices are fabricated by the process of electrospinning. By utilizing innovative approaches that combine the techniques of electrospinning and textile technology, highly complex and intricate scaffold designs have been engineered. Our group has innovated a unique technique of bundling electrospun nanofibers into yarns, which can be manoeuvred into diverse architectures using the textile techniques of plying, weaving, knitting, etc. Various biomedical constructs including drug eluting patches, vascular patch, vascular grafts, drug eluting sutures, drug eluting stents, etc have thus been developed. This talk will address how nanofibrous polymers can be utilized for instructive design of such biomaterial devices, so that the properties desirable for the device are attained, without compromising its biocompatibility or functionality.

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"How to conduct clinical trial: An evidence based approach"

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As new biomaterials are developed by in-vitro test in the laboratory; utilization of these materials in human being can not be done straight away. This should be done by a clinical trial of high-level evidence in human being; otherwise it will be unlawful. The purpose of interaction is that dentistry and Orthopedics doctors involve in rehabilitation and restoration of lost tooth/ bony structure with biocompatible substitutes. These substitute range from lost enamel, dentin, bone to dental implant. In this era of interdisciplinary research, there is a need of collaboration between biomaterial scientists, medical specialists and dentists for the better patient care.

This presentation will focus on what are the prerequisites of clinical trial like approval from CDSCO, ethical approval, and clinical trial registry. It also cover how to conduct clinical trial in collaboration.

"Viscotaxis"-directed migration of mesenchymal stem cells in response to loss modulus gradient

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Cell migration is a crucial biological process in both physiological and pathological conditions. It has been shown that the adherent and migratory cells crawl from low elastic modulus (*E)* region to high *E* region on a substrate with gradient rigidity. However, tissues in our body are not purely elastic but rather viscoelastic. Effect of viscoelasticity on cellular functions and behaviour is a poorly addressed question. Here, we ask what will happen if we put a cell on a substrate with loss modulus (G") gradient. To address this question, we monitored the migration pattern of human mesenchymal stem cells (hMSCs) on polyacrylamide gels with a gradient of *G″* but constant *G′*. We found that cells show a strong preference in migrating towards low loss modulus from high loss modulus region. As expected, this migration bias is dependent on the strength of the gradient. Further analysis indicates that this bias results from asymmetry in focal adhesion stability and cellular traction. On the substrates with low loss modulus, cells can apply high traction and can create stable and matured adhesion points. However, on thesubstrates with high loss modulus, the material compliance increases at longer timescale. As a result, cells are unable to apply high traction and form stable adhesions. Due this asymmetry in adhesion and tractions, cells preferentially migrate from high loss region to low loss region of the gel. When cellular traction is perturbed with pharmacological inhibitors, this process gets disturbed, and the directionality of the migration is lost. While earlier literature has shown that microorganisms can sense the fluid viscosity and swim towards higher viscosity region, a phenomenon known as viscotaxis, this is the first report to demonstrate that the mammalian cells can sense the solid viscoelasticity and in response migrate from high to low loss modulus region.

Making a polyesters' difference to nanopill

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Polymer nanoparticles present an exciting opportunity to deliver pharmaceutical drugs orally. While promising, this approach is currently limited by two major problems, ***1)*** out-competition of nanosystem ligands by higher concentration, endogenous ligands and ***2)***lack of polymer structural versatility, which does not allow optimization of ligand-receptor stoichiometry for maximizing transport efficiency. In pursuit of the clinical translation of polymer nanoparticles, my lab has focused on the synthesis of polyesters with controlled topologies for probing transcytosis at the blood-GUT barrier using relevant *in silico, in vitro, ex vivo,* and *in vivo* models. In this talk, I will discuss the progress we have made over the eight years.

Cardioprotective Phenotypes and Regenerative Vesicles of Epicardial Adipose Tissue Derived Stem Cells in Translational Cardiac Regeneration

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The conventional management strategies of myocardial infarction (MI) including coronary artery bypass graft (CABG) surgery are effective to sustain life; however, myocardial regeneration has not been achieved owing to the sustenance of ischemic insults and inherently poor regenerative capacity of the native myocardium. Stem cell-based therapies are promising; however, lineage specificity and undesired differentiation profile are challenging. Our investigations using a translationally worthwhile CABG model unveiled sustained ischemia with fatty deposits and aggravated inflammation in the myocardium suggesting the possibilities of epicardial fat (EF) in cardiac regeneration. Herein, we focused on the EF as an ideal source for mesenchymal stem cells (MSCs) owing to the proximity and anatomical similarities with cardiac muscle. Epicardial adipose tissue derived stem cells (EATDS) were isolated from three hyperlipidemic Yucatan microswine. The regenerative secretome unveiled versatile healing/protective mediators in the secreted vesicles offering a promise in cardiac regeneration. The treatment of these vesicles with isolated swine cardiac fibroblasts resulted in the upregulation of cardiomyocyte specific transcription factors and regenerative mediators with downregulation of fibroblast biomarkers. The EATDS remain understudied regarding their phenotype heterogeneity and cardiac regeneration potential. As EF closely reflects the cardiac pathology during ischemia, we investigated the EATDS subpopulations under simulated ischemic and reperfused conditions employing single cell RNA sequencing (scRNAseq) which revealed 18 unique cell clusters suggesting the existence of heterogeneous phenotypes. Finally, we developed a hydrogel-based cardiac tissue engineering template for incorporating the EATDS phenotypes destined for cardiac regeneration offering the sustained bioavailability of regenerative secretome and a translationally relevant minimally invasive swine-MI model for ongoing investigations. Thus, the multidisciplinary approach of unique regenerative EATDS, regenerative vesicles, and cardiac tissue engineering open significant translational avenues for myocardial regeneration and cardiac management benefitting millions of MI sufferers across the globe.

Development of LipidicNanoplatform for Oral Delivery of Chlorhexidine: Characterization, Biocompatibility and Assessment of Depth of Penetration in Extracted Human Teeth.

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Microorganisms are the major cause for the failure of root canal treatment, due to the penetration ability within the root anatomy. However, irrigation regimens have at times failed due to biofilm mode of bacterial growth. Liposomes are vesicular shaped structure coated with phospholipids, might help in better penetration efficiency into dentinal tubules and increase the antibacterial efficacy. In the present work, twenty percent chlorhexidine was lyophilized and chlorhexidine liposomes were formulated. Liposomal chlorhexidine was characterized by size, zeta potential, Transmission and cryo-electron microscope. Twenty-one extracted single-rooted premolars were taken, irrigated with Liposomal and 2%chlorhexidine to evaluate the depth of penetration. Invitro cytotoxicity and cell uptake study was performed for Liposomal chlorhexidine on L929 mouse fibroblast cell line. The average particle size of liposomes was 48±4.52 to 223±3.63 nm with a polydispersity index of 0.27. Transmission and cryo-electron microscope images showed nearly spherical and vesicular structures. Depth of penetration of Liposomal chlorhexidine was higher in the coronal, middle and apical third of roots compared to plain chlorhexidine in human extracted teeth when observed under Confocal Laser Scanning Microscope. Pure drug exhibited a CTC50 value of 65.67± 3.1 µg/ml and Liposomal chlorhexidine exhibited a CTC50 value of above 1000 µg/ml on L929 cells. Liposomal chlorhexidine showed better cell uptake compared to control. Antimicrobial analysis showed less number of bacterial cells when treated with Liposomal Chlorhexidine compared with 2% chlorhexidine. Liposomal chlorhexidine morphology resembled the bilayered morphology. Nano-liposomal novel chlorhexidine was less cytotoxic when treated on mouse fibroblasts L929 cells and more effective as an antimicrobial agent along with higher penetration ability.

Strategies for Cementation of all-Ceramic Restorations

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Dental restorations are cemented using a fluid luting material that flows between the irregularities on the surface of the restoration and the tooth to provide retention. Traditionally, cements based on zinc oxide were popularly used. However, with ever increasing demand for the aesthetics, there has been a shift in the formulation of luting cements from opaque zinc oxide based matrix to translucent glass or polymeric matrix based materials. Resin based luting cements are currently the most widely used for the cementation due to their excellent aesthetics combined with high strength and low solubility. They are formulated much like dental composite restorative materials and consist of a polymerizable matrix with fillers and reaction controlling additives.

Conventional ceramics based on feldspathic porcelains are used mostly for the anterior restorations due to their inferior mechanical properties. Over the years, advancements in the materials made it possible to develop newer and improved materials with higher strength and toughness such as machinable, glass-infiltrated, high-purity alumina, and zirconia ceramics. Such ceramics, popularly known as all-ceramics, are used both as anterior and posterior aesthetic restorative materials.

Long-term clinical success of restorations also depends on the bond strength between the tooth and the restoration which is influenced by the luting cement used. Conventional cements achieve this through mechanical interlocking whereas resin luting cements achieve this through micromechanical bonding. Conventional resin cements use etching of tooth surface with phosphoric acid which is rinsed prior to the application of the cement. Alternatively, self-etch or self-adhesive resin cements have been formulated to reduce the number of steps involved in the process of bonding. Similarly, ceramic surfaces too are surface pre-treated to facilitate bonding. Ceramics based on glass are amenable for hydrofluoric acid etching whereas those based on stable oxides such as alumina, zirconia, etc. are difficult to etch. For such ceramics, alternative methods such as sand blasting, tribochemical/pyrochemical silica coating, application of silane coupling agents, etc. are used to improve the bonding.

Selection of an appropriate surface preparation of a ceramic restoration as well as luting cement play an important role in the retention and thus its service life. This presentation provides an overview of various types of surface preparation techniques used with all-ceramic restorations and resin luting cements.

Engineering New Materials for Healthcare: A Chemist's Perspective

Neetu Singh

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Among myriad of health issues of global populace today, the problems associated with better means of diagnosis, and repair and regeneration of organs, bones, cartilages, etc. remain a big challenge. The prospect of using nanoscience and nanotechnology as a tool to answer questions arising out of these healthcare issues are exciting and form the basis of this talk. Nanostructures, due to their similar size scale as bio-macromolecules and cellular components, provide an unprecedented opportunity to target and potentially modulate important biological processes. Some of the key nanotechnology based scientific and technological contributions from our laboratory that are impacting disease diagnostics and tissue engineering will be discussed. Briefly, examples illustrating how knowledge of chemical science& nanotechnology has enabled us to develop platform technologies for easy quantification of cell growth, migration and disease progression. The technologies developed allow detecting diseases faster and achieving complex cell organization as seen in real organs for developing *in vitro* 3D organoid platforms for various applications.

Functionalized LbL patches for targeted delivery of chemotherapeutics in colon cancer

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The delivery of chemotherapeutics to a target cancer site in a non-invasive fashion is a challenge. Here, we demonstrate the selective binding of functionalized layer-by-layer (LbL) assembled polymeric patches to colon cancer to deliver chemotherapeutics. The LbL patch was fabricated by sequential adsorption of biomaterials chitosan and alginate. One side of the patch was coated with polycaprolactone as a backing layer. On the other side, folic acid-conjugated chitosan was coated for selective binding to cancer lesions. Oxaliplatin and STAT3 siRNA-chitosan nanoparticles were entrapped within the LbL patch. Coating Eudragit S100 delayed the release of patch from the gelatin capsule. The patches and nanoparticles were characterized for particle size, zeta-potential, mechanical strength. Cell studies in Caco-2 cells showed significantly greater growth inhibition and STAT3 protein suppression. *In vivo* studies in chemically-induced orthotopic colon cancer, Balb/c mice showed that the functionalized patch selectively binds to the colon tumors. In contrast, the non-functionalized patch would only bind to normal tissue. The oral administration of functionalized LbL patch showed superior tumor inhibition compared with intravenous administration of oxaliplatin and STAT3 siRNA. Together, functionalized patches can be developed for selective localized chemotherapeutics delivery in colon cancer.

Mesoporous Silica Nanoparticles (MSNs): Versatile Multifunctional Carriers

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Recent breakthroughs in drug delivery technologies utilising a range of carriers have resulted in a paradigm shift in the current approach to diagnosis and therapy. The Mesoporous silica nanoparticles (MSNs) because of their unique characteristics of uniform and tunable pore size, easy independent functionalization of the surface, internal and external pores, and the gating mechanism of the pore opening; these ordered porous materials have attracted a lot of attention as drug carriers. They are cost effective since they can be synthesised with a relatively simple method. A tremendous growth in research on MSNs as drug carriers over the last few years, highlighting their potential benefits in drug delivery. Their broad use for loading small molecules as well as macromolecules like proteins, siRNA, and other molecules has made them a versatile carrier. In recent years, researchers have made many changes to the architecture of MSNs in order to investigate their potential in drug-resistant chemotherapy and antimicrobial therapy. The advancements are made in MSNs to widen the scope of their application, particularly in the field of biomedicine. The talk highlights the properties of MSNs as drug delivery carrier and its applications.

Development of HPMA-based Polymeric Micellar Systems for the Delivery of Anticancer Chemotherapeutics

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Biodegradable and tumor-micro-environmental responsive polymers are desired for targeted anticancer drug delivery. Development of pH sensitive drug delivery system tocarry anticancer drugs to tumor is considered to be a promising strategy where the delivery system targets the acidic extracellular micro- environment as well as the intracellular organelles of solid tumors. *N*-(2-hydroxypropyl) methacrylamide-based block co-polymers (pHPMA) have received special attention due to their hydrophilicity, non-immunogenicity, biocompatibility and possibility of functionalization by various ligands. The hydrophilic HPMA monomers can be modified with hydrophobic moieties and the resultant amphiphilic polymers could self-assemble to form nanoparticles. In addition to entrapping drugs physically in the nanoparticles, multiple drug molecules can be conjugated on the monomers. In our recent report, a polymeric micelles constituted of HPMA and methoxypoly (ethylene glycol) (mPEG)-based co-polymer, mPEG-b-HPMA was studied for the delivery of an anticancer drug, doxorubicin (DOX) by physically loading the drug into its core. The DOX-loaded micelles were prepared at different drug to polymer ratios by thin film hydration method. The optimized DOX loaded system displayed promising anticancer effect in different in vitro system. In the next attempts, a novel HPMA-based polymer, p(HPMA)-p(HPMA-NH-N-DOX)-bmPEG(P6) has been developed for the delivery of anticancer drug, Doxorubicin (DOX) where themonomer, HPMA was conjugated to DOX via pH- responsive hydrazone linker, which was further reacted along with free HPMA in the radical polymerization reaction using (mPEG)2–4,4-azobis-(4-cyanopentanoic acid) (mPEG2-ABCPA) as a macroinitiator. The synthesized polymers were characterized and different biological study have been carried out that showed pH-responsive triggered delivery of DOX in in vitro system. In our next project, a novel nanocarrier for the delivery of DOX, all-trans-retinoid acid (ATRA) conjugated polymeric micelles were developed for the enhanced anti-tumor effect. The block co-polymer of mPEG-b-HPMA was synthesized using radical polymerization technique. The carboxylic acid group of ATRA was conjugated to hydroxyl group of HPMA of mPEG-b-HPMA to form mPEG-b-HPMA-ATRA. This amphiphilic polymeric conjugate could self-assemble to form micelles for loading of hydrophobic drugs that nano construct was studied till the in vi vivo system using 4T1 xenografted BALB/C mice. The extensive exploration of the newly developed ATRA conjugated mPEG-b-HPMA based DOX loaded micelles showed to have the potential to be utilized successfully in breast cancer treatment.

Lipidic Nanoparticles for drug delivery and targeting: Overview and case studies

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Drug delivery systems were considered only as a means of getting the drug into the patient's body. But it has a significant effect on safety, Efficacy and Patient compliance/ convenience. Novel drug delivery systems including nanopharmaceuticals provide various advantages over conventional drug delivery systems. Nanotechnology is the vital aspect for targeted drug delivery. Nanocarriers possess attractive properties such as biodegradability, bio-compatibility, conjugation, complexation/ encapsulation, etc. Lipidic nanocarriers such as liposomes, solid lipid nanoparticles, nanostructured lipid carriers, etc provide the advantage of sustained release as well as drug targeting. They can be conjugated with a ligand for specific delivery to the cells.

'SMART' self-assembling micelles as chemo-photodynamic therapy in cancer

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Photodynamic therapy (PDT) has been a promising non-invasive treatment modality in several cancers, including head and neck cancers. However, the sub-optimal delivery of photosensitizing agents limits the clinical applications of PDT. Photosensitizers are porphyrin-based molecules, which suffer from low aqueous solubility, poor tissue penetration, and the tendency to form aggregates. A delivery system to carry the PSs to the tumor site is highly desirable, which solubilizes the PSs in the nanoparticles' hydrophobic core compartment, thus preventing aggregation and enhancing the pharmacokinetic properties. Another significant challenge associated with photodynamic therapy is the hypoxic tumor microenvironment. PDT requires oxygen in the vicinity to generate reactive oxygen species. Here, we have developed a 'SMART' oxygen-generating nanoparticles polymeric system with chlorin e6 (Ce6) as the PS and m(polyethylene glycol) and poly(lactide) as the polymers, which are conjugated together via a platinum(IV)-azide complex. The nanoparticles delivered Ce6 effectively in the tumor and reduced cell hydrogen peroxide levels by converting it to molecular oxygen. A laser (660 nm)-sensitive polymeric nanomicelles were also prepared to deliver Ce6, where a 2-nitrobenzyl (2NB) linker was introduced between hydrophilic PEG and hydrophobic Ce6. The laser irradiation causes micellar disassembly (Figure 1) and on-demand release of Ce6. The multifunctional 'SMART' nanocarriers systems were therapeutically effective in the *in vitro* cancer cells and *in vivo* tumor models.

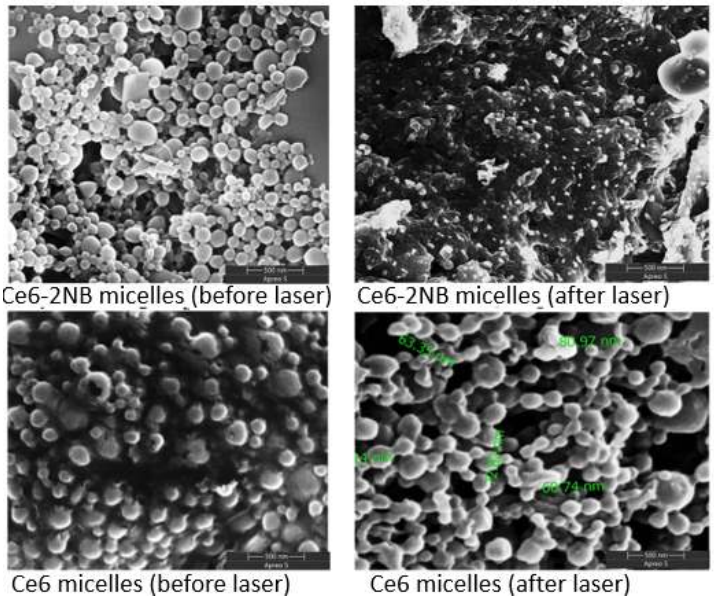

Figure 1: Assessment of degradability. SEM image of Ce6-2NB micelles in comparison with Ce6 micelles (without light-sensitive linker). Laser irradiation (660 nm, 15 min) caused complete disassembly.

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BIOTEM-2021

Industrial Talk

Indigenously developed highly pure and crystalline Hydroxyapatite powder for Biomedical applications

Subrata Mukkherji

TATA Steel R&D, Jamshedpur, India

The growth of demand for synthetic bone substitutes, over last few decades, has been driven by factors such as rise in number of injuries/trauma and inborn bone defects. Natural bone is made up of hydroxyapatite (HAp) nanocrystals embedded in a biopolymeric collagen matrix, where HAp contributes ~70% dry weight of the healthy human bone. Therefore, HAp, being a major bone mineral, has been recognized for numerous applications in bone tissue engineering primarily in the fields of cranial, dental, maxillofacial, orthopedic (total heap joint-Stem/acetabular cup), and spinal treatments. Presently, synthetic HAp finds a wide range of applications in the form of powders, dense or porous blocks/scaffolds, composites with glasses, metals and polymers for bone repair and regeneration. However, ironically in India, a large volume of HAp and its derivative products are still imported, perhaps, because scalability with uncompromised quality remains a major technological challenge. The challenge was accepted by Tata Steel.

Tata Steel, through its New Material Business, aspires to become one of the major players in Medical Materials and Devices. Development of indigenous Phase pure, crystalline HAp was the first baby step towards this exciting journey. In this talk, we will discuss how Tata Steel's collaboration with world renowned academic institute (IISc-Bangalore) and dynamic entrepreneurs (Ants Ceramic) inspired to successfully develop HAp at commercial scale. We have successfully produced phase pure HAp, validated by plasma spray coating on metallic implants, quality and chemical fingerprint were probed using TEM, SEM, RAMAN, FTIR, XRD, ICP etc, and biocompatibility is being studied in detail. The similar manufacturing protocol will be extended to develop other CaP variants. I will narrate the story of our journey so far which is decorated with numerous technological challenges encountered at different stages of value chain, how we have overcome those to finally arrive at a product which is at par, if not better, with world benchmarked products. We believe this effort will assist India to be self-reliant in the field of Bioceramics.

Building 3D bio-printers in India for R&D and industrial applications

Sumant Bhutoria

ALFATEK, Kolkata, India

3D Bio-printing has given a fresh lease of life to the area of tissue engineering, allowing researchers to fabricate 3D cultures that better mimic the in-vivo conditions of living cells and tissues. We talk about the various 3D bio-printing technologies that are currently popular - extrusion, inkjet, laser, ultrasonic and how we have built some of these technologies into our own home-grown 3D bio-printer offerings. Early this year, we launched our second generation 3D bio-printer, ANGA with liquid spill protection, modular and customizable printheads, advanced UV-C sterilization, HEPA filtration and climate control, and this has been very well received by the 3D bio-printing community in India. We have also developed a number of add-ons and accessories of 3D bio-printers - hand-held UV curing lamps, co-axial bio-printing set-ups, etc.

In the last 5 years, we have also had the opportunity to work closely with some of the R&D groups in India, and we showcase some of the innovations that we have developed: 3D Bio-printing on a rotating spindle to fabricate blood vessels, stents, etc., development and characterization of bio-inks, etc. Finally, we also talk about our work with our industrial partners - fabricating skin models, and 3D printed tablets.

Tuneable peptide hydrogels to provide physiologically relevant 3D cultures for in vitro studies

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3D cell culture is an increasingly reliable method to mimic the *in vivo* environment *in vitro*; however, some widely used biomaterial scaffolds have limitations as they are animal derived and lack tuneability and reproducibility. Recent advancements in synthetic tuneable peptide hydrogels have shown potential to overcome these limitations by better simulating tissue microenvironments, allowing the generation of more physiologically and clinically relevant data. Here we will demonstrate the use of such systems - PeptiGels® and PeptiInks® for the growth of 3D organoids, tumour models, and their applications more broadly within regenerative medicine and drug discovery.

Evolving Medicine with 3D Bioprinting

Mauro Petretta, Senior Scientific Advisor

Regen HU, Switzerland

3D bioprinting represents a disruptive technology with an ever-growing impact in many aspects of healthcare. Through the accurate spatial localization of biomaterials, bioactive stimuli and living cells, this technique offers unique possibilities for applications ranging from biofabrication of patient-specific tissues and organs to the implementation of personalized diagnostic tools and therapeutic treatments, as for example by exploiting in vitro tissues and disease models and the realization of custom-made pharmaceutical formulations. This presentation will provide a brief overview of 3D bioprinting basic principles and main features, as well as of our approach to biofabrication. In conclusion, you will learn more about different applications performed with this technique in the biotech field.

BIOTEM-2021

Abstracts for SBAOI-MAHE Young scientist Award

Design and modification of decellularized plant cellulose as functional scaffolds for tissue engineering applications

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The utility of plant tissues as scaffolding materials is gaining significant interest in recent years owing to its unique material characteristics that are ideal for tissue engineering applications. In this study, the degradation and biocompatibility of natural cellulosic scaffolds derived from Borassus flabellifer (Linn.) (BF) immature endosperm was improved by chemical oxidation and surface functionalization process. Briefly, thus obtained cellulosic scaffolds were sequentially processed by detergent exchange decellularization process followed by sodium periodate mediated oxidation and organosilanes based surface modification using amino (NH_2)-terminated 3- aminopropyltriethoxysilane (APTES) and methyl (CH_3)-terminated octadecyltrichlorosilane (OTS). Post oxidation and surface functionalization the scaffolds showed improved physiochemical, morphological and mechanical properties. Especially, the scaffold swelling capacity, total porosity, surface area, degradation kinetics and mechanical behavior were significantly higher in modified scaffold groups. The in vitro studies demonstrated favorable adhesion, proliferation and differentiation of osteoblasts with an evident up regulation of mineralization. The scaffolds when implanted subcutaneously in a rat model showed active angiogenesis, enhanced degradation and excellent biocompatibility with concomitant deposition of collagen matrix. Taken together, the native cellulosic scaffolds post chemical oxidation and surface functionalization can exclusively integrate the potential properties of native soft tissue with ameliorated in vitro and in vivo support in bone tissue engineering for non-loading bearing applications.

Key words: Cellulosic scaffolds, Decellularization, Chemical oxidation, Organosilanes, Bone tissue engineeringThe results of this demonstrated a proof-of-concept in improving the biodegradation and biocompatibility of cellulosic scaffolds through chemical oxidation and surface functionalization. Both OCS-APTES and OCS-OTS scaffolds in comparison with OCS scaffold showed adequate morphological, physical and mechanical features. The in vitro studies proved that all the studied scaffold groups supported osteoblast adhesion, proliferation and differentiation. The overall cell-material interaction study results were in accordance with physiochemical and morphological features of the scaffolds. Furthermore, the in vivo results expounded that under sub cutaneous implantation all the scaffold groups exhibited minimal inflammatory response with active angiogenesis, enhanced

degradation and excellent biocompatibility with concomitant deposition of collagen matrix.

In summary, this study elucidates that the openness of BF endosperm scaffold modification is highly instrumental in improving the overall biodegradation and biocompatibility of plant derived cellulosic scaffolds that is fully accepted as a subcutaneous implant. In conclusion, we suggest that plant derived cellulosic scaffolds with suitable modification can be used as implantable scaffolds which can be complementary to the existing bacterial cellulose scaffolds which has received good acceptance in tissue engineering applications.

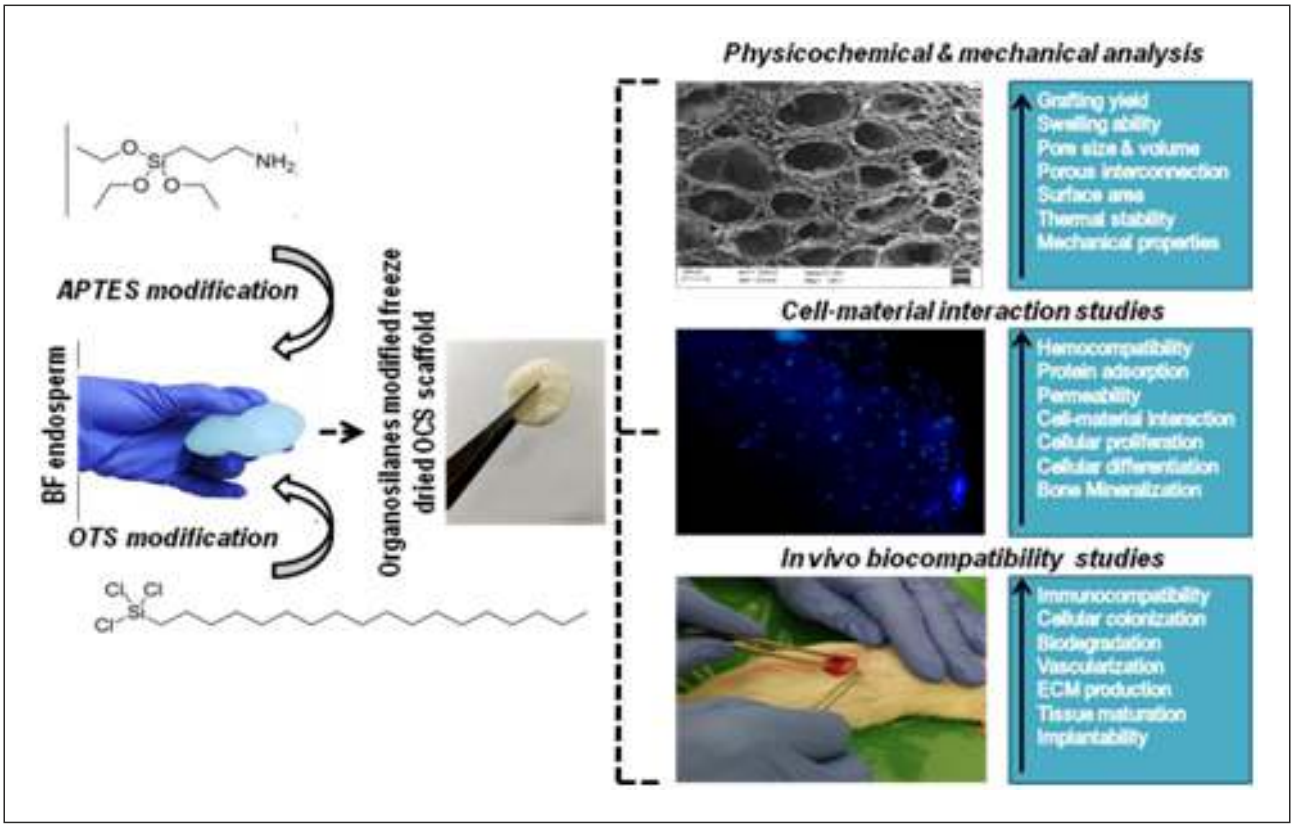


Figure 1: Graphical representation of BF endosperm isolation, decellularization and chemical oxidation to produce OCS scaffolds and surface functionalization of OCS scaffolds with APTES and OTS by chemical grafting.

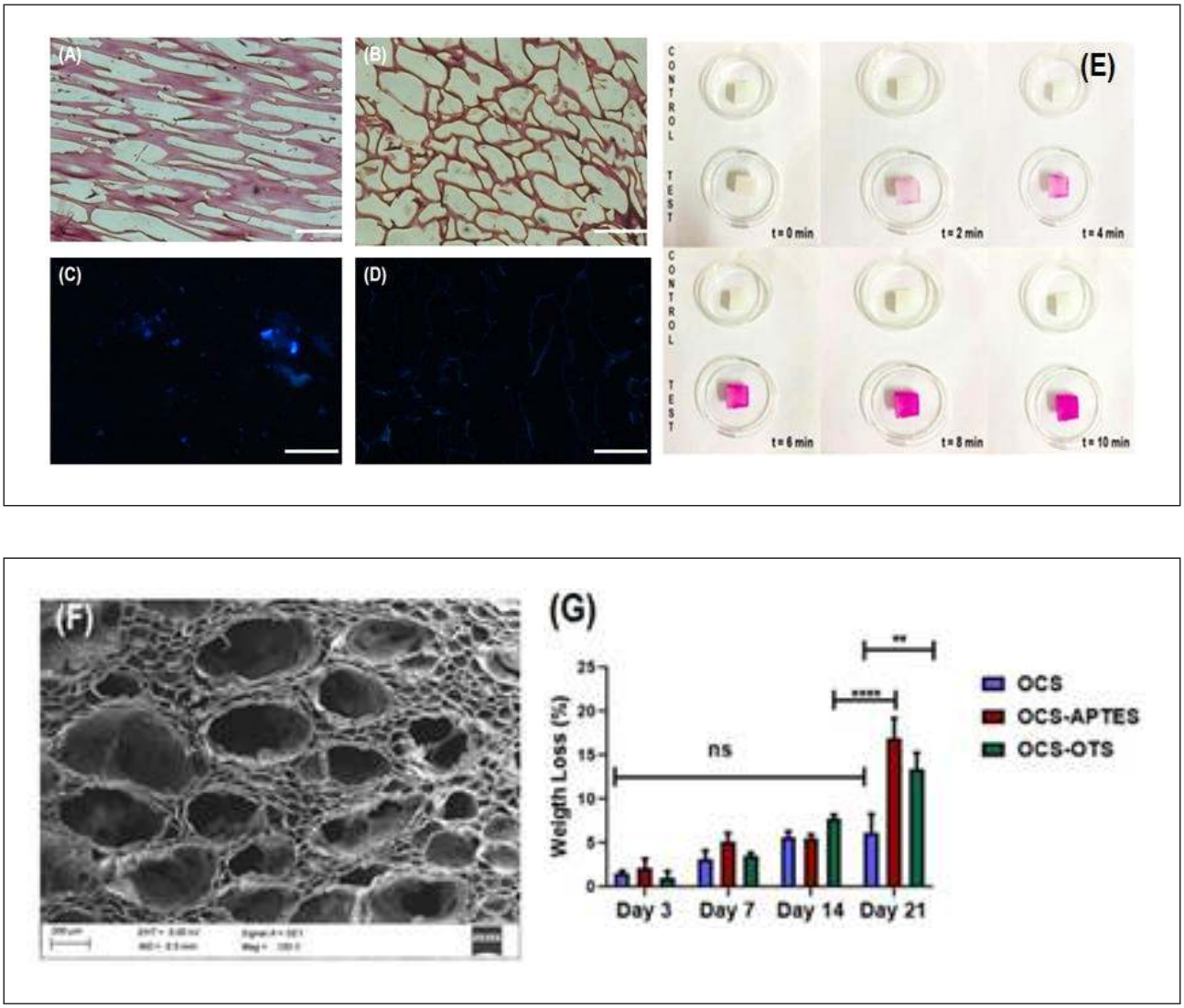
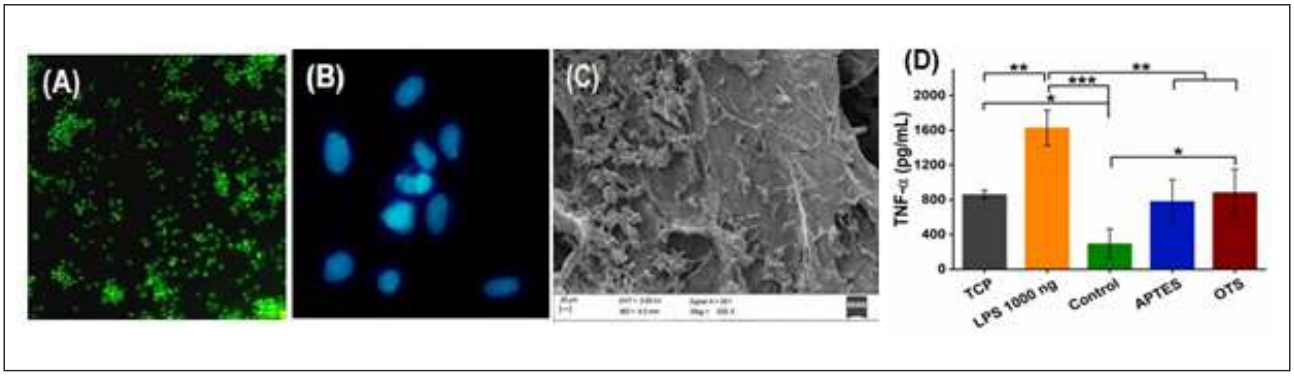


Figure 2: The effect of decellularization process on BF sample before and after SDS treatment. (A): H&E staining of native BF sample. (B): H&E staining of decellularized BF sample after SDS treatment. (C): Hoechst staining of native BF sample. (D): Hoechst staining of decellularized BF sample after SDS treatment. (E): Photographic illustration of chemically oxidized samples treated with Schiff's reagent as function of time. (F): Morphology of the scaffold. (G): Scaffold biodegradation in physiological solution.



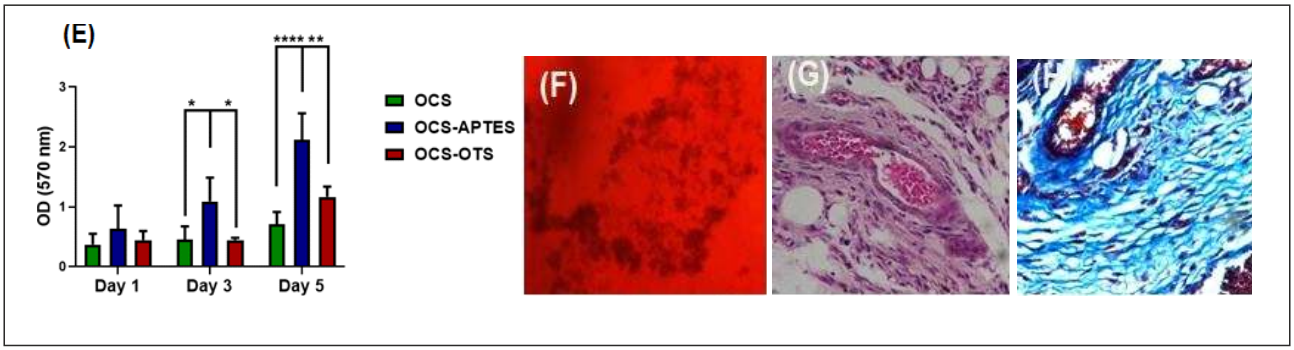


Figure 3: (A): Live/dead assay images. (B): Cell colonization analyzed by Hoechst staining. (C): Cell attachment and distribution by SEM. (D): TNF-α secretion by macrophages. (E): Evaluation of cell proliferation by MTT assay. (F): Microscopic images of ARS staining. (G): H&E staining. (H): Masson trichrome staining post 4 weeks of sub cutaneous implantation in a rat model.

3D printed bio-props for tissue regeneration

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Recent advancements in tissue engineering have proven its potential in the regeneration of tissue using additive manufacturing techniques. 3D printing is a promising technique for the development of scaffolds with biomimetic properties that provides a proper microenvironment for cell proliferation as well as tissue regeneration. In the present study, we have developed biomaterial-based ink for the development of 3D printed scaffolds for skin and nerve tissue regeneration (Figure 1).

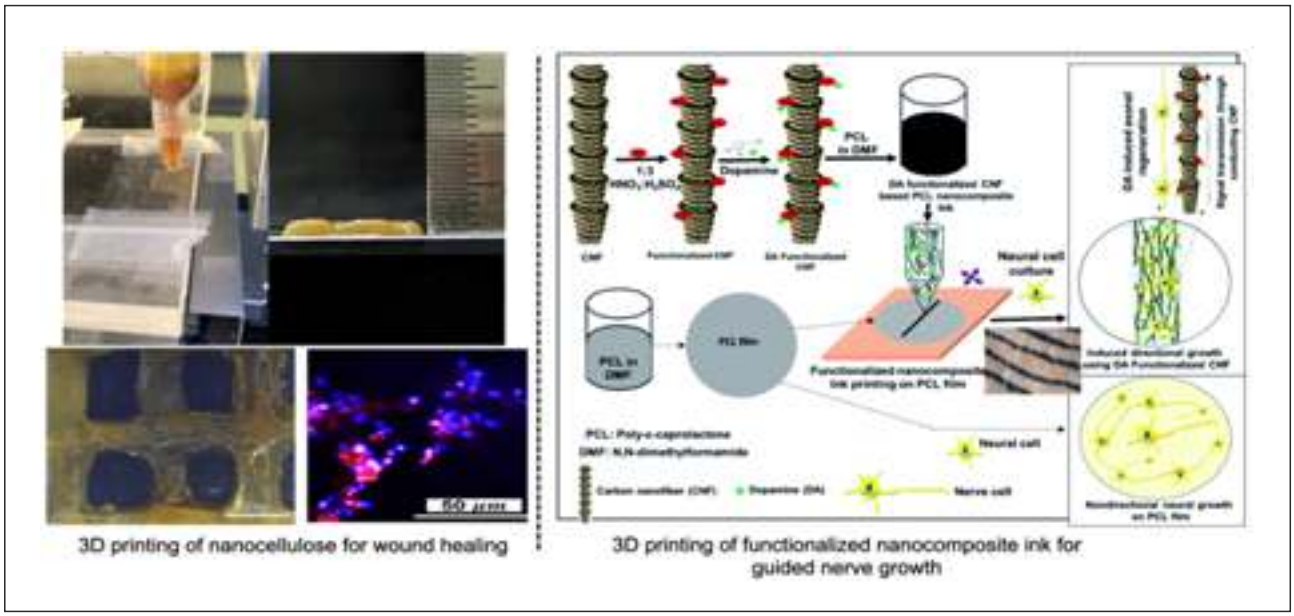

Figure 1. 3D printed bioprops for skin and nerve tissue regeneration

Nanocellulose is a natural biomaterial with ideal properties to be used as a biomaterial for tissue engineering. Herein, we have grown nanocellulose from the symbiotic colony of bacteria and yeast (SCOBY) known as kombucha sheets. This cellulose-based sustainable kombucha (KBC) sheets possess high mechanical stability and biological properties, however, its main limitation is poor processability for 3D printing. To address this, we have partially hydrolyzed the KBC to enhance extrusion and shape formation ability. This study is the first report on the processability of

nanocellulose for 3D printing. These 3D printed scaffolds showed promising potential for skin tissue regeneration [1]. Nerve tissue regeneration strategies are advancing day by day as it affects the quality of patients' life. 3D printing is a promising approach for the development of scaffolds with patterned structures to enhance guided nerve regeneration. Herein, we have formulated a novel conducting nanocomposite biomaterial-based ink composed of dopamine, carbon- nanofibers (CNF) and polycaprolactone (PCL) for the development of bio-props for nerve regeneration. We have 3D printed the ink on a PCL film and studied its potential application in guided nerve regeneration. The in vitro cell study of human glioma cells showed that the printed lines with dopamine functionalized nanocomposite ink provided support for neural cell attachment, migration and differentiation toward the targeted end. Thus, this scaffold is a promising candidate for nerve guide application based on its signal transmission and navigating neurons in a correct pathway towards the targeted end [2].

Results and Discussion: Herein, for SCOBY culture, 200 g of sugar was dissolved in 2 L of boiling water. 4 bags of dry green tea (2 g each, commercially available from local market) were dipped for 15 min and cooled to room temperature in a plastic tray (cleaned using ethanol). Apple cider vinegar (200 ml) and live kombucha SCOBY (200 g, 90 mm diameter) were added and the tray was closed with a piece of cloth to avoid the contaminations. It was kept in a place away from sunlight. After two weeks (day 14), the top layerwas separated from the fermentation medium. The separated layer was washed with distilled water and then allowed to dry at room temperature. Thus, prepared sheets are marked as pure KBC in the present study. The acid-induced partial hydrolysis was carried out using 30% (v/v) sulphuric acid for 4 h at 70 °C. Acetic acid and different concentrations of hydrochloric acid (with and without combination with sulphuric acid) were also tried for the partial hydrolysis of KBC as initial trials. However, the best results for the extrusion 3D printing application were found after the treatment with 30% sulphuric acid. Further the acid hydrolysed kombucha was used for characterizations such as surface morphology, functional group analysis, mechanical property, suitability for 3D printing and cytocompatibility analysis. The mechanical property of the hydrolysed nanocellulose showed similar to soft tissue like skin. Further, the 3D printed hydrolysed KBC was seeded with human adult dermal fibroblast cells and found to have promising results.

For the regeneration of nerve, biomaterial based conducting nanocomposite ink was developed. Dopamine (DA) concentration was optimised first in neuro 2a cells and it was used as a functionalizing agent for the enhanced nerve cell proliferation. CNF and CNF–DA was mixed in PCL and were printed via an extrusion- based process using a bioprinter. A 5 mL syringe was fitted with a 20-gauge blunt-ended needle as the nozzle. The CNF-based inks were printed in parallel lines with a distance of 5 mm between each line in a single layer on the prepared PCL film at room temperature. The lines were deposited over a fixed time interval. U87MG cells, which are human glioma cells and a representative of central neurons, were used to evaluate the biocompatibility and the possibility of supporting nerve

growth on a selected path on each material. The presence of functionalized CNF in the conductive ink to imprint scaffolds led to the controlled release of DA, which provided support for neural growth and neuron proliferation during the recovery time. The printed PCL films showed thermomechanical properties comparable with human nerves. This new printed scaffold with nanocomposite ink shows potential for guiding and supporting neural cell migration, growth and extension of axons and dendrites (Figure 2).

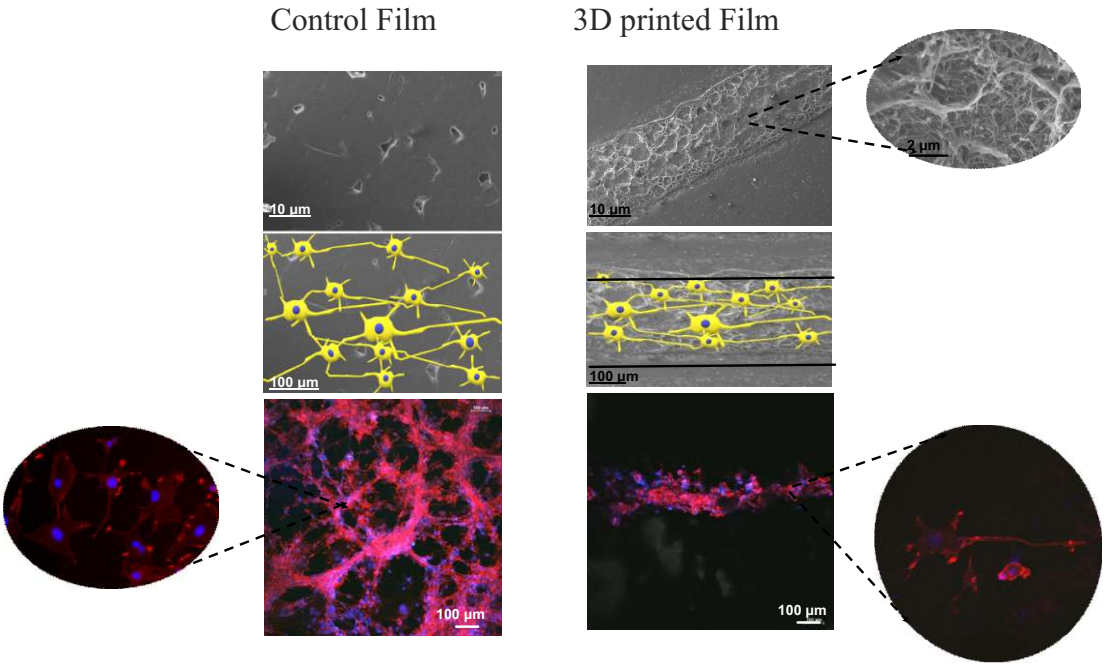

Figure 2. Growth and proliferation of neural cell networks on pure PCL film with no directional preference and directional growth of nerves cells, migration and movement to the printed lines then extending axons and dendrites,

Keywords: Bioink, 3D bioprinting, nanocellulose, nerve conduit, conducting nanocomposite, peripheral nerve

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Effect of surface grafting coefficient and chain length of fatty acids on the near infrared luminescence intensity of Neodymium doped Lanthanum fluoride nanoparticles

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Near-infrared (NIR) luminescent lanthanide doped insulating nanomaterials (wideband gap) have found application as bioanalytical reporters, sensors and in the field of imaging.[1] Low native autofluorescence from biological systems and less scattering in the NIR range of electromagnetic spectrum results in higher detection sensitivity and resolution due to an improved signal-to-noise ratio.Both f-f and d-f transitions in lanthanides involve electrons that are localized in atomic orbital of the ions. Therefore, size dependent quantization effect is not observed in lanthanide doped insulating nanoparticles. However, luminescence from nanostructure is affected by the environment surrounding it. Different strategies like surface coating with organic molecules and core-shell architecture were used to reduce such quenching by keeping OH- ions away from the nanoparticle surface. [2]Hence, understanding the relation between luminescence intensity and surface grafting coefficient is vital to develop highly luminescent lanthanide doped nanoparticles.This study explores the influence of surface density and length of fatty acid on nanoparticle surface on the luminescence of Nd^{3+} doped LaF_3nanoparticles.[3] Oleic acid was selected as coating molecule on nanoparticle for this study. It was observed that the increase in surface grafting coefficient of oleic acid from 0 to 5.7 resulted in a 14 fold increase in the luminescence intensity and for the nanoparticles having oleic acid surface grafting coefficient 5.7 to 7.5, luminescence intensity remained almost same. A fourfold increase in the luminescence of nanoparticles above surface grafting coefficient of 3.9 was observed and attributed to the formation of a complete monolayer. The second aspect considered in this study was the length of the fatty acid coating. Almost 3 fold increase in luminescence intensity was observed for an increase of 1 nm length (difference in the chain length of hexanoic acid and oleic acid).

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Evolution of the Dental Implant System from Design and Surface to the Clinical Setting- A multidisciplinary team approach

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The total global dental implant market is expected to reach $13 billion in 2023. In India 19% of the population is completely edentulous and approximately 1.5 to 2 lacs dental implants are placed every year. India needs to import the implants and technology is still costly hence not affordable to masses. There is no Indian FDA certified Indian manufacturer and exponential market growths needed the development of indigenous system.

Main objective of this research work was to evolve an indigenous dental implant system. The entire process needed the knowledge and experience of multidisciplinary team and a step by step team approach. In this research work a new design was proposed and validated by finite element analysis. Machining of this new patented design was done on 10 axis CNC machine as per ISO standards. The sandblasting and acid etching process and parameters were optimized. The surface modification, characterization, mechanical testing, cleaning & packaging, quality control, biological testing and clinical trials were done as per FDA guidelines using various ASTM and ISO standards.

A non-inferiority randomized controlled clinical trial of the developed implant system was done at Maulana Azad Institute of Dental Sciences. This clinical trial established the equivalency of the indigenous dental implants to the marketed surface.

Engineering Vascularized and Intrafibrillar Mineralized Stem-Cell Laden 3D Microenvironments On-Demand

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Bone is a hierarchically structured tissue formed by multicellular networks of osteocytes that are densely cemented within a 3D mineralized collagenous matrix with interconnected vasculature [1]. However, existing synthetic bone replacement grafts are developed by culturing osteogenic cells onto rigid and highly porous composite scaffolds, or within soft, non-calcified cell-laden hydrogels systems. Such systems grossly fail to replicate the native bone microenvironment, where bone precursors get entrapped within a 3D matrix that transitions from a soft, poorly calcified collagenous network to a stiff, densely mineralized scaffold. Recapitulating such a dynamic transition of the cell-rich bone microenvironment, while simultaneously replicating its ultrastructural features from nano- to micro-scale in-vitro, has never been possible. Hence, this study establishes the facile fabrication of biomimetic 3D microenvironments recapitulating the multicellular and architectural complexities of native mineralized tissues at all levels of hierarchy from nano-to-macro scale. A highly controllable one-step materials chemistry approach involving a protein-guided mineralization mechanism was adopted for the confined deposition of nano-apatite crystals within the molecular interstices of individual collagen fibrils (intrafibrillar mineral) and between fibrils (extrafibrillar mineral) in a 3D collagenous matrix encapsulated with human mesenchymal stem cells (MSCs) [2]. The resultant mineralized construct exhibited nanoscale mineralization, physical, structural and osteoinductive properties in-vitro, with unprecedented biomimetic features, approximating that of native bone microenvironement (positive control). Further, mature pericyte-supported vasculature was created within these mineralized constructs and their spontaneous engraftment was established in-vivo by transplanting into the subcutaneous pockets of SCID mice. In summary, it is envisaged that these striking results will greatly transform the field of tissue engineering by providing one step closer solutions for regenerative processes, research on bone targeting diseases, and drug screening.

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Immuno-Modulation to Promote Diabetic Wound Healing

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A common secondary complication in diabetic individuals is the development of foot ulcers. A significant number of diabetic foot ulcers (DFU) do not heal and eventually result in amputation. Current treatment strategies, such as debridement, bandaging, use of antibiotics, and growth factor ointments, while effective, do not heal all ulcers. Hence, there is a need for newer strategies. In this talk, I will present our approach for promoting wound healing, which uses an immuno-modulatory drug-loaded bandage to alter the chronic inflammatory micro-environment at the wound site. Our data in a pre-clinical diabetic wound model suggests that such an approach could significantly improve healing outcomes.

Biomaterial Carriers for Treatment of Osteoarthritis

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Osteoarthritis (OA), a chronic progressive joint disorder, has affected nearly 500 million people worldwide and these numbers are projected to increase in the coming years which poses a huge societal burden and health care expense. Current treatments for OA offer symptomatic relief but do not prevent or halt the disease progression. Several factors such as obesity, chronic inflammation, low autophagy, cellular senescence etc. are considered significant drivers of OA. In this talk, I will describe our efforts to deliver biomaterial encapsulated small molecules such as Specialized pro-resolution mediators (SPMs), rapamycin etc. to target this disease. We have been able to show that biomaterial assisted sustained release can promote cartilage ECM production and can be used to prevent and treat post-traumatic OA in mice models. Such controlled-release formulations could represent a patient-compliant treatment for OA.

Molecular structure of fibrin direct platelet response under mechanical stimuli

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Density, orientation, and molecular conformation of extracellular matrix proteins play key role in regulating cell function. Proteins with specific conformation exposing appropriate domains can direct not only initial cellular morphology, but also long-term function. As a result we are working to quantitatively relate Fibrin(ogen) protein morphology, molecular structure, and its response to cell function under mechanical stimuli. Fibrin hydrogel under mechanical tension not only showed change in fiber orientation and density but also resulted in a significant increase in thioflavin T binding and decrease in tissue-plasminogen activator (t-PA) binding, which is the first step catalysing fibrinolysis. At molecular level, fibrin under tension showed secondary structural change from α helix to β sheet transition. Moreover with these molecular changes of fibrin under tension, platelet integrin ($\alpha_{IIb}\beta_3$) coated beads showed 3 fold less binding on stretched fibrin hydrogel. Coincident with integrin experiment, stretched fibrin showed less human platelet attachment with limited ability to activate platelets in comparison to unstretched fibrin. Overall these findings suggest that molecular structural changes of Fibrin (ogen) under mechanical stimuli can not only influence fibrinolysis but can also influence platelet activity.

Engineered nanomaterials for diagnostics and therapy

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Appropriate surface chemistries of nanomaterials are crucial for creating biocompatible materials with targeted functions. In this seminar, I will discuss my research on the utility of functionalized nanoparticles and polymers in modulating the materials- biology interface to enable healthcare applications, including disease detection, biologics delivery and tissue engineering. We have fabricated an array of nanoparticle-protein assemblies that provide useful biosensor to detect proteins, cancer cells, and tissues in minutes. Furthermore, early detection of diseases demands high sensitivity, wherein we focused on creating smart platforms utilizing cascade enzymatic reactions to achieve ultrasensitive detection by the naked eye. Besides, these nanoparticle-biomolecule dyads provide efficient vehicles for biologics delivery, wherein hierarchical assemblies make the systems stimuli-responsive. Altogether, we have developed multifunctional bionanomaterials with great potential in disease detection at the point-of-care and therapy.

BIOTEM-2021

Abstracts for SBAOI-BAJPAI-SAHA Student Award and Manipal Academy of Higher Education (MAHE) Awards

Biomaterials-based biophysical stimulation for regenerative engineering

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World health organization (WHO) has recognized multiple degenerative diseases as the leading cause of mortality globally. The drug-based clinical treatment of chronic degenerative diseases such as multiple sclerosis, Parkinson's disease, arthritis, muscular dystrophy, etc., has been accomplished with limited success. In this perspective, "stem cell-based regenerative engineering" provides a new treatment option to repair and regenerate the damaged tissue or organ. Stem cells are the unspecialized cells, which can be differentiated to specialized cells, such as nerve/brain cells (neurons, glial cells), bone cells (osteoblasts), cartilage cells (chondrocytes), fat cells (adipocytes), etc. Stem cells have the unique capability to replicate themselves (self-renewal) unless they are provided with specific external factors (i.e. biochemical and biophysical cues). Among various biophysical cues, the efficacy of electrical stimulation, substrate stiffness, and conductivity have been demonstrated to direct stem cell differentiation (Figure 1). In the present work, cellular differentiation has been regulated using biophysical signals on multifunctional substrates to demonstrate the efficacy of such strategies in developing implantable biomaterials.

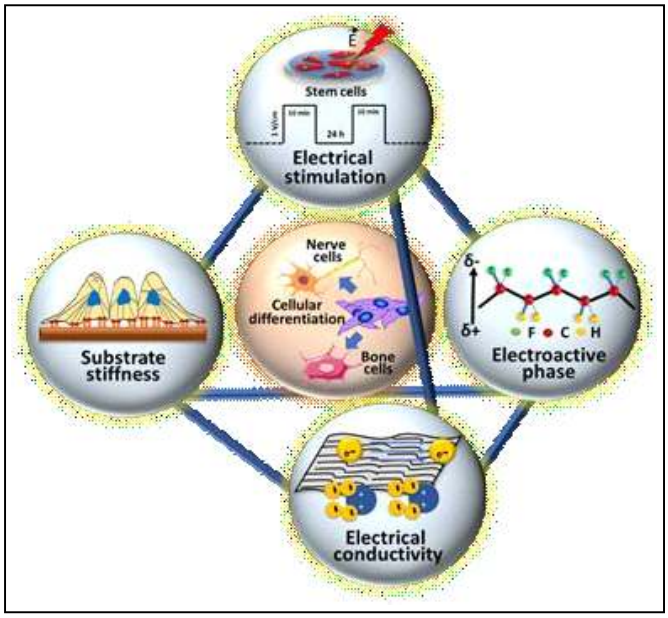

Figure 1: Schematic showing theme of presentation and strategies to induce cellular differentiation using electrical stimulation and substrate functionalities

The biomaterial functionalities such as conductivity, mechanical properties and electroactive β-phase have been tailored using Polyvinylidene difluoride (PVDF)-based composites to regulate cellular differentiation. The properties of multifunctional PVDF have been modulated using conducting nanofiller (multiwall-carbon nanotube, MWNT) and piezoceramic ($BaTiO_3$, BT) by an optimized processing approach (melt mixing-compression molding-rolling). The electrical stimulation on the conducting rolled-PVDF/MWNT composites guided the differentiation of human mesenchymal stem cells (hMSCs) towards neuron-like cells. The enhanced electroactive β-phase with the incorporation of BT supported the lineage commitment of hMSCs towards glial-like cells on moderately conducting rolled-PVDF/BT/MWNT. In addition to the phenotypical changes and genotypical analysis, the differential response of stem cells was further confirmed using Ca^{2+} oscillation and whole-cell patch clamp-based electrophysiological recordings (Figure 2a). The strategy to differentiate stem cells towards functional neurons has future implications in stem cell therapy treating neurodegenerative diseases.

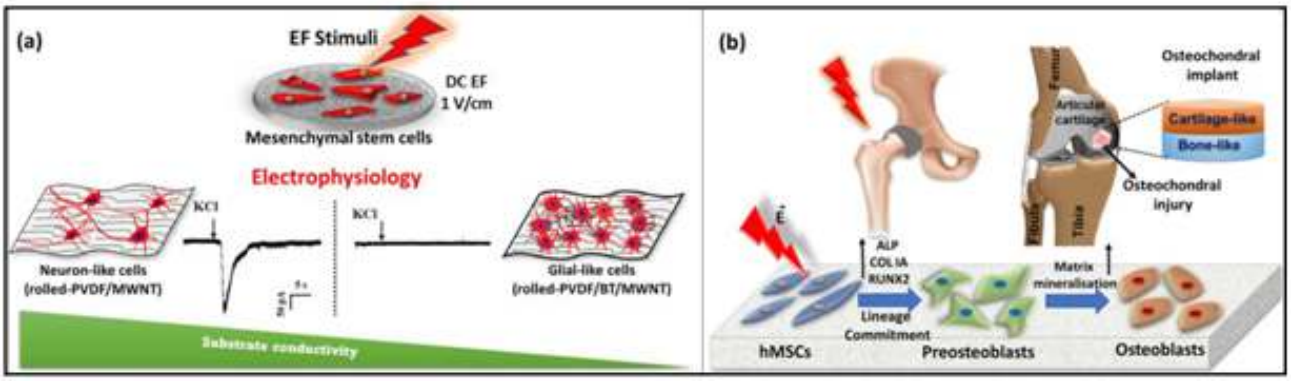

Figure 2. Graphical representation of the inventive insights demonstrated in the present work (a) schematic showing the neural differentiation of electrically stimulated mesenchymal stem cells on conductive MWNT reinforced PVDF composites (b) Electrical waveform and substrate stiffness dependent cellular differentiation on PVDF composites for osteochondral regeneration.

Next, the effect of the electrical waveform on the osteogenesis of hMSCs has been investigated on PVDF/BT composite using monophasic direct current (DC), square and biphasic wave stimulation in a patented cell stimulator, StimuCell®. To provide a functional platform for stem cells to differentiate, BaTiO3 reinforced PVDF has been developed with mechanical properties similar to bone. The phenotypical characteristics of DC stimulated hMSCs provided signatures of differentiation towards osteogenic lineage, which was subsequently confirmed using ALP assay, collagen deposition, and genetic expression (Figure 2b). Monophasic DC stimulation induced early osteogenesis in hMSCs with a higher level of intracellular ROS, whereas square wave directed late osteogenesis with a lower level of ROS.

Furthermore, the critical role of biomechanical cues has been investigated for osteochondral regeneration. In this regard, a fluoropolymer compatibilized thermoplastic polyurethane bilayer composite with an elastically stiff and compliant layer has been prepared following an optimized processing approach using melt-mixing and compression molding. The macromolecular non-covalent interaction such as hydrogen bonding of chemically functionalized fluoropolymer allowed the compatibilization of fluoropolymer blend with polyurethane, when processed in melt compounding route. Elastically stiff matrix exhibited bone-like elastic modulus (~2 GPa) to support the enhanced proliferation and maturation of pre-osteoblasts. The early differentiation of pre-osteoblasts on the stiffer substrate was confirmed using higher ALP activity together with an elevated level of collagen and matrix mineralization. The superior mechanical properties of the electroactive fluoropolymer with higher osteogenic activity compared to UHMWPE, indicate its potential for orthopedic implant applications. The polyurethane-based elastomeric soft matrix with lower elastic stiffness (~0.09 GPa) supported the chondrogenic functionalities of the goat chondrocytes. The synthesis of the chondrogenic matrix, such as collagen, glycosaminoglycans, and proteoglycan content, was clearly upregulated on the elastically compliant matrix. The pre-induction and maturation of osteochondral behavior have been rationalized as an interplay between substrate stiffness, surface free energy and electroactive properties. The hybrid bilayer polymer composite with an elastically stiff and compliant matrix layer has promising translational implications in developing implants for osteochondral repair.

Summarizing, an improved understanding of cellular behavior with the instructive biophysical cues will be provided in the presentation, which will allow the development of clinically relevant biomaterials for regenerative medicine.

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Sulfated polysaccharide with flexible structure for Osteogenic Differentiation of Mesenchymal Stem Cells for Bone Tissue Engineering

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Globally over million bone graft procedures are performed annually. Several materials from polymers, ceramics to growth factors have been used for the development of bone grafts. Natural polymers are another material that is gaining increasing attention in bone tissue engineering. The fucose containing sulfated polysaccharide (fucoidan), present in the cell wall of the brown algae which are one of the most interesting and more investigated phyla because of their spectra of biological activities. The bioactivities strongly depend on the structural features, which vary on various other factors, such as environment, time of harvest, and extraction and purification process.

Addressing the major issue concerning the medical application of fucoidan is achieving it's reproducible and pure quality. In the current study the fucoidan is isolated from a species of brown algae that is widely distributed in the Indian coastal region by a novel advanced extraction method. A comparison with the conventional method revealed, a two-fold increase in the obtained yield. The crude fucoidan with the higher yield showed 2.59, 27.8, and 4.2 percentage content of sulfates, sugar, and protein. Further, the purification of the crude fucoidan was performed by using DEAE-Cellulose anion-exchange chromatography. The results of the degree of sulfation, sugar, and protein content (4.29, 35.6, and 6.7 %) of the purified fucoidan were greater when compared to the crude fucoidan. The structural characterization of purified fucoidan was done by UV–visible spectroscopy, X-ray diffraction, Thermogravimetry, FTIR, and ^{1}H-NMR analysis. The findings of the structural study confirm the semicrystalline property of the purified fucoidan with the presence of sulfates that is considered as a structural marker for fucoidans, along with hydroxyl, and carboxyl groups. The ^{1}H-NMR results confirm the occurrence of α-L-Rhamnop and FucoP residues.

This study with an aim to investigate the relation between structure and biological activity of fucoidan, it was subjected to in vitro characterization. The antioxidant activity of fucoidan was measured by DPPH scavenging assay. The crude fucoidan with a lower IC50 value showed better antioxidant activity when compared to the purified. This might be because of the polyphenolic compounds present in the crude extract, which are further removed during purification.

Next, the ability of purified fucoidan to differentiate mesenchymal stem cells to bone cells was investigated. Initially, the cell viability of fucoidan at different concentration (1-100 µg/mL) was measured. The significantly ($p < 0.05$) increased proliferation in the purified fucoidan treated at 1 µg/mL and greater than ≥ 50% cell inhibition at higher concentration was observed. Besides, its effect on osteoblast differentiation was evaluated based on alkaline phosphatase (ALP) activity. The findings showed higher activity at 1 µg/mL when compared to the untreated control, followed by the reduced activity at higher concentration. Further, the calcium accumulation with 1 µg/mL of sample, at two-time points (day 14 and 21) was examined. The results confirmed the significant increase in the calcium deposition from day 14 to day 21 of differentiation.

Basically, the mesenchymal stem cells differentiate into osteogenic lineage cells in three phases that include cell proliferation, matrix maturation, and matrix mineralization. The first phase includes the expression of osteopontin, type 1 collagen, fibronectin, and transforming growth factor-beta (TGF)-b. In the second phase, cells start to differentiate and form matrix maturation. The early gene marker ALP is usually high in the second phase. In the last phase, mineralization can be observed which can be measured through osteocalcin expression (OCN) and expression of osteoblast markers. In our study, the effect of fucoidan on early and late osteogenic markers such as collagen-I and OCN respectively as indicated by immunofluorescence. After 21 days of treatment, the mesenchymal stem cells showed higher expression of OCN and moderate expression of collagen-I. Thus, the in vitro findings confirm the osteoinductive ability of the fucoidan, that can be an ideal biomaterial for bone regeneration.

Resolvin D1-loaded nanoliposomes promote M2 polarization of macrophages and are effective in the treatment of Osteoarthritis

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Osteoarthritis (OA) is the most common disorder of the joints and currently affects >300 million patients worldwide.[1] In this disease, the articulating cartilage undergoes progressive damage which leads to severe pain and loss of function. Current treatment for OA does not target the etiology of the disease but instead focuses only on alleviating pain by administration of steroidal analgesics. Steroidal analgesics are not ideal for the long-term treatment of the disease because they generate chronicchondrotoxicity and cartilage thinning.[2] Eventually, as the disease progresses towards severe stages, the patients have to undergo a highly invasive and costly joint replacement surgery. Currently, there is no disease-modifying OA drug (DMOAD) approved for human use.

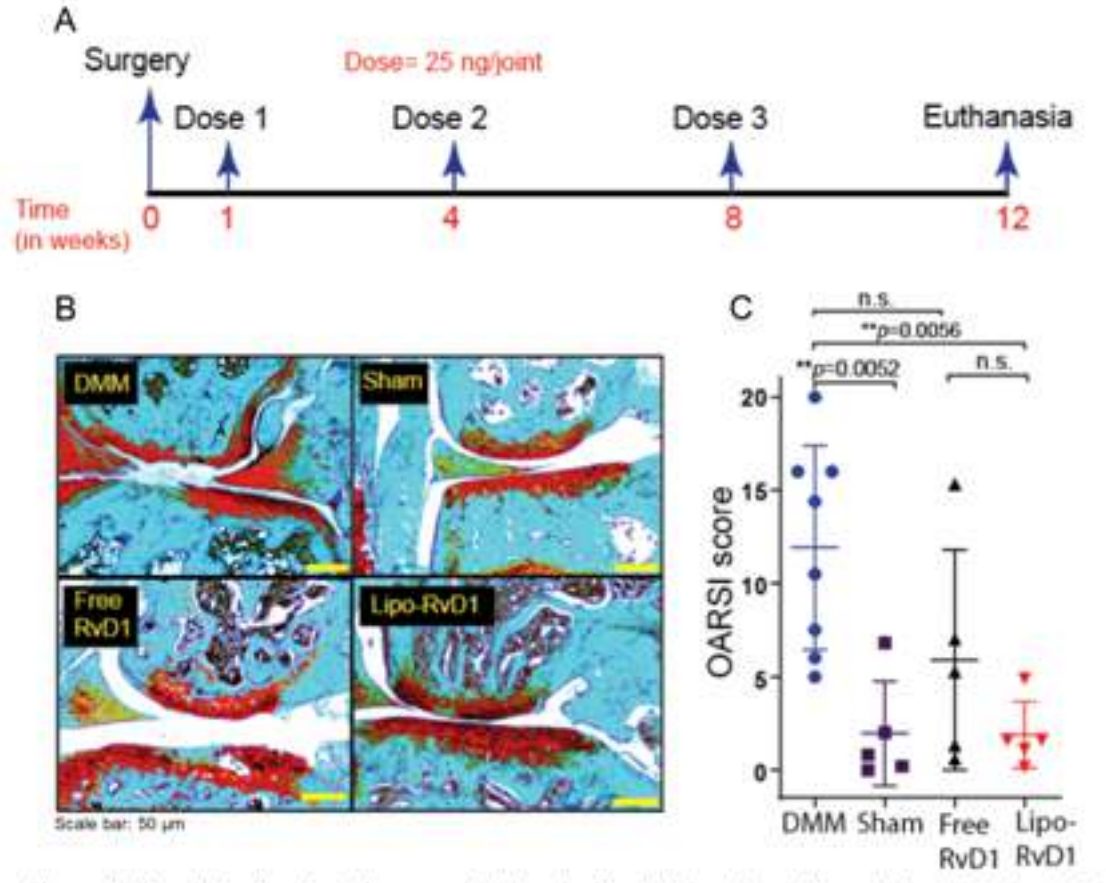

Figure 1: Prophylactic study in normal diet animals. (a)Timeline of the study. (b)Safranin O stained sections of the affected joints. (c)Histology (OARSI) scores of the affected joints.

OA-associated damage is driven by chronic low-grade inflammation, and several cells are involved in the cross-talk that contributes to the inflammation. Targeting the OA-related chronic inflammation using antagonists and antibodies against inflammatory cytokines is a viable strategy to treat OA and has shown promise in pre-clinical trials. However, previous attempts to deliver anti-inflammatory molecules to the site of damage did not translate into therapy for humans. The failure of these trials can be attributed to the fast clearance of the small molecules by synovial vasculature and of the macromolecules by the lymphatics, which results in short half-lives in the joint (1- 4h) for commonly used steroids. The limiting in vivohalf-lives of small-molecule drugs can be extended by encapsulating the molecules in particle-based systems. Liposomes are ideal for efficient delivery because of their biodegradability, low toxicity, stability, flexible synthesis methods, and ability to incorporate versatile cargo.

Specialized proresolution mediators (SPMs) are potent molecules that actively reduce inflammatory factors from the site of damage in a process called resolution of inflammation.[6] Chronic inflammatory diseases, including OA, are known to have impaired inflammation resolution pathways. Exogenously supplied SPMs like Resolvin D1 (RvD1) reducethe severity of OA, but strategies involving the direct IAinjection of such molecules require administration of doses before OA-causing injury has taken place.[7] In this study, we generate a liposomal-RvD1(lipo-RvD1) formulation to increase the bioavailability of the molecule in the pathology-affected joint. The liposomes were synthesized from Dipalmitoylphosphatidylcholine (DPPC), 1,2-Distearoyl-sn-glycero-3- phosphoethanolamine-Poly (ethylene glycol) (DSPE: PEG), and cholesterol in predetermined ratios by thin-film hydration technique followed by extrusion. Liposomes were actively loaded with RvD1 using a pH gradient strategy , which successfully encapsulated 71±28% of the added compound. This high encapsulation efficiency of an SPM into a nanocarrier has not been demonstrated earlier. The molar ratios of the liposomal components DPPC, DSPE:PEG, and cholesterol were optimized for maximum retention of RvD1, which finally was found to be 85:5:10. This formulation was stable and acted as a source of RvD1 for ~11 days *in vitro* in near-physiological conditions.

The size of the carriers is known to affect their IA retention.[9,10] After testing the IA retention of three different sizes- 150, 350, and 900 nm, we observed that smaller liposomes (≤350 nm) had longer retention than larger liposomes (~900 nm). For the rest of our studies, we used 350 nm liposomes due to their higher retention in the joint.

Upto 71% of the joint injury patientsdevelop OAlater in life.[11] Thus, effective, prophylactic anti-OA medication is required to arrest damage in the earlier stages of the disease. We evaluated the prophylactic efficacy of our formulation in the widely used, Destabilization of Medial Meniscus (DMM) mouse model of OA (figure 1A). Our histology results show that only lipo-RvD1 treated joints

reduced the severity of OA, whereas free RvD1 did not have any protective effect on the joint (figure 1B,1C).We conducted the same experiment in an obesity-related OA model in mice to reproduce the contribution of obesity on the pathology of the disorder. The pathology of obesity-related OA is much more severe due to the contribution of adipose tissue to OA-associated inflammation . In this model also, only the lipo-RvD1 treated joints had

shown efficacy whereas free-RvD1 had no protective effect on the joint (data not shown). The results from the latter model establishedthe ability of lipo-RvD1 to treat diseases in diverse stages of progression.

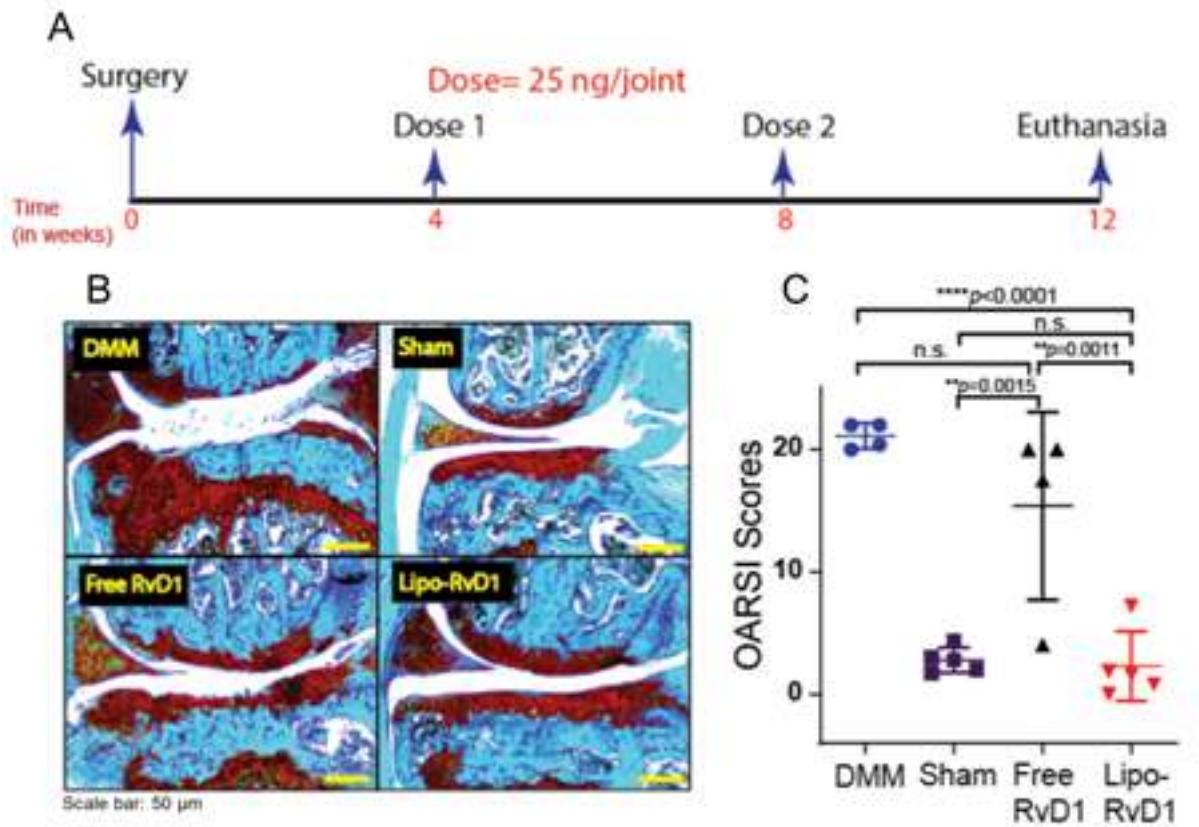

Figure 2: Therapeutic study in normal diet animals. (a)Timeline of the study. (b)Safranin O stained sections of the affected joints. (c)Histology (OARSI) scores of the affected joints.

Most OA patients report to the clinics in the later stages of the disease. Thus, there is a requirement for a good therapeutic agent for the treatment of OA. In the therapeutic study, we administered the formulation to the animals after significant damage is known to have ensued[12] (figure 2A). Lipo-RvD1 treated joints showed much healthier articular cartilage compared to free-RvD1 and surgery-only joints in both the mouse models (figure 2B,2C).

Pathological pain (allodynia) is one of the main clinical symptoms of OA. To test if resolvin formulations decreased pain, we tested the pain threshold of mice using Von Frey filaments. We observed that administration of lipo-RvD1 was effective in alleviating the allodynia than DMM mice and free RvD1 injected mice in the therapeutic regimen of administration. IA injection of free RvD1 did not generate sufficient analgesia, and the pain threshold of these mice was similar to that in DMM-operated mice. Our results show that the sustained presence of RvD1 in the affected knee joint helps alleviate OA-associated pain. The pain relief could be important translationally as not only would it provide immediate benefit but would also ensure patient compliance.

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Development of Orthopaedic Biomaterials for Resveratrol in Postmenopausal Osteoporosis

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Resveratrol (RSV) is a naturally occurring polyphenolic stilbene that plays a beneficial role in bone mineralization and improves microarchitecture structure in osteoporosis. Due to the wider physicochemical and biological barrier, the site-specific drug delivery system for RSV was initiated as a systematic approach towards bone tissue. In this work, the bone-targeted orthopaedic biomaterials containing RSV-loaded polylactic co-glycolic acid (PLGA) nanoparticles was developed using Alendronate (ALN) as a bone targeting ligand. The in vivo imaging system demonstrates the bone targeting ability and an effective carrier system towards skeletal tissue. The antiosteoporotic efficacy of the nanoformulation was further investigated in ovariectomized (Ovx) rats. PLGA-RSV-ALN nanoparticles (the equivalent of pure RSV doses as 5 and 10 mg/kg) were injected in Ovx rats for three months. The parameters like micro-computed tomography (μCT) scanning, biochemical, biomechanical, and histopathological investigation were analysed to evaluate the effect of formulation on skeletal micro-architecture. The present study demonstrated that alendronate anchored RSV-loaded PLGA biomaterial is an effective strategy to target osteoporotic bones at low doses with reduced frequency. It is an effective approach to treat the osteolytic degradation induced by osteoporosis.

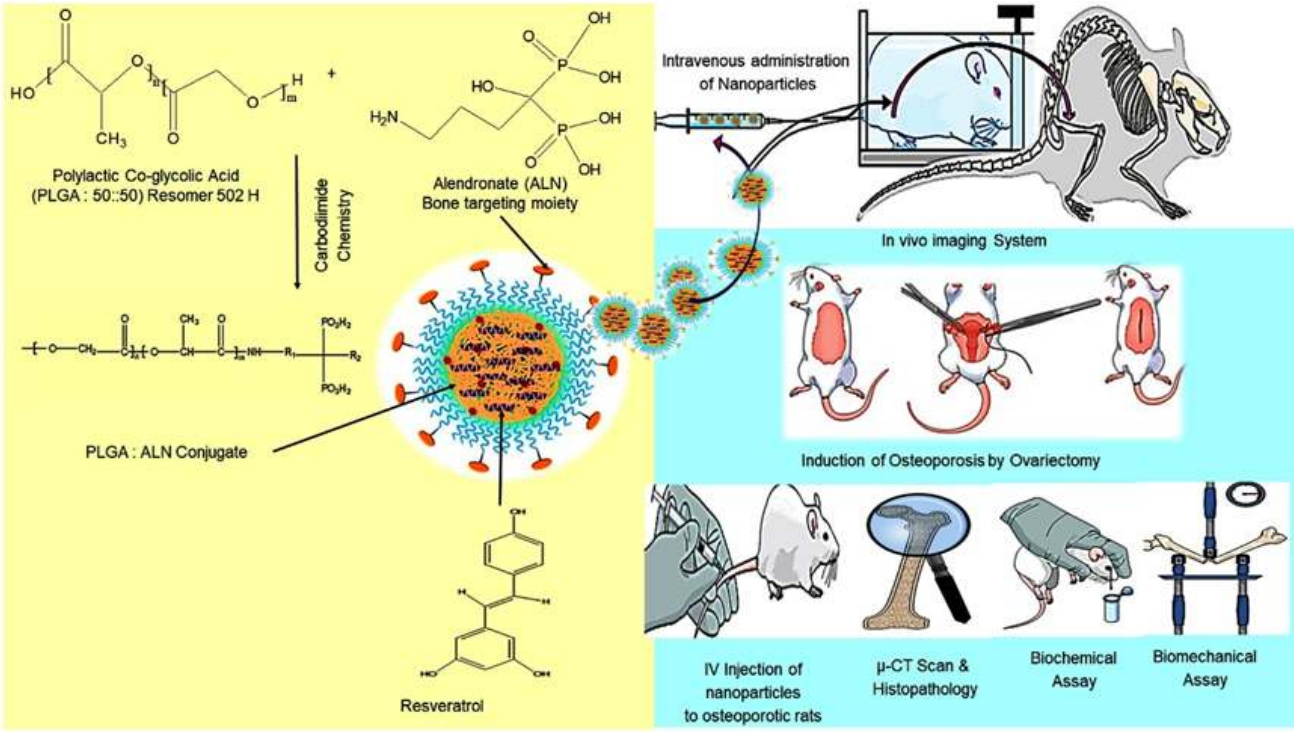


Figure 1: Summary schematic showing the experimental setup of carbodiimide-based approach for the synthesis of PLGA-ALN conjugate and it's in vivo evaluation in OVX rats.

1. Introduction

Resveratrol is chemically 3,5,4′-trihydroxystilbene, practically insoluble in water (aqueous solubility ~3 mg/100 mL), BCS class II highly hydrophobic with high membrane permeability compound.[1,2] As per several in vitro studies, RSV improves osteoblastic differentiation and prevents osteoclastic resorption.[3] Preclinical evidences suggesting the osteogenic potential of RSV in rodent models, [4-8] like age, estrogen deficiency, bone acquisition, and disuse bone loss conditions.[9,10] The short biological half-life, physicochemical labile properties, extensive metabolism, and rapid elimination of RSV developed the concept of a targeted drug delivery system towards bones to achieve specific biodistribution, the therapeutic concentration at a lower dose range with lesser side effects. [11] Therefore, the present is aimed to formulate an antiosteoporotic agent RSV into polylacticco-glycolic acid (PLGA) nanoparticles to target bone using Alendronate (ALN) as a targeting ligand. PLGA–RSVAlendronate (PLGA-RSV-ALN) nanoformulation can work as a novel tool as a site-specific drug delivery system for RSV with improved efficacy. As an adult bone is composed of mainly mineralized constituents (50–70%) in Hydroxyapatite {(Hap) ($Ca_{10}(PO_4)6(OH)_2$} form which is specific to the bones (except for teeth), provides a unique opportunity to design the drug delivery system targeting towards Hap.[12] Bisphosphonates (BPs) represent the class of antiresorptive agents, have a unique backbone structure sharing two phosphonates on a single carbon atom (P-C-P) which binds to the bone via chelation of calcium ions of Hap with high affinity. In addition to the strong

affinity towards skeletal tissue as BPs distribute faster and retains 100 times higher in skeletal tissue than in plasma.[13] In addition to the targeting specificity, BPs are also known to inhibit the differentiation as well as apoptosis of the osteoclast by blocking the mevalonate pathway and supports in reducing the osteolytic lesions associated with osteoporosis.[14] Thus, it was hypothesized that the proposed nanoparticles-based RSV entrapped functionalized system would target bone with a synergistic effect on bone degradation, and bisphosphonate will reduce bone complications by controlling osteoclast activity. The nanoparticles will retain for a longer time at the bone resorption site, and efficacy will be achieved at low doses. To the best of our knowledge, a bone-targeted drug delivery system of RSV for the treatment of osteoporosis has not been investigated. Therefore, this work is an attempt toward a newer concept of functionalizing anabolic agents to reduce skeletal complications.

2. Methodology:

Synthesis of PLGA-ALN conjugate

The fabrication of PLGA-ALN is the two-stage process; first, the activation of the carboxylic acid end group of PLGA, and second is the cross-linking reaction. Resomer RG 502 H was activated using EDC-NHS chemistry as per the reported method with slight modifications. [15]

Characterization of PLGA-ALN conjugate

The ^{1}H NMR spectra of PLGA, ALN, and PLGA-ALN conjugates were analysed by employing Bruker 500 MHz NMR while 13C NMR spectra were subjected to NMR analysis by an agilent-700 MHz spectrophotometer. The FTIR spectra of PLGA, ALN, and PLGA-ALN conjugate were screened by the KBR method in the JASCO spectrometer (model FT/IR-6300 type A). X-Ray Powder Diffraction (XRD) spectra were obtained by a Philips X´PERT-PRO X-ray diffractometer (PANalytical, Almero, Netherlands).

Development and Optimization of Nanoparticles

The formulation of nanoparticles was initiated after the synthesis of the PLGA-ALN conjugate. It was optimized by using PLGA-ALN conjugate (10 mg) with varying amounts of surfactant (Kolliphor P-188).

Physicochemical characterization of optimized formulation

The PLGA-ALN conjugate: surfactant ratio 1:1 was found to be optimum, and therefore, the same ratio was selected. The RSV amount selected for the optimization includes 1,2,4,6,8 and 10 mg. The consideration was given to obtain minimum particle size, optimum PDI, and stable ZP. Along with it, the maximum percent entrapment efficiency (%EE) and percent drug loading (%DL) were taken into consideration to achieve a stable formulation.

Stability Studies

Temperature-dependent stability studies of optimized PLGA-RSV- ALN NPs were carried at two different temperature conditions, viz. refrigerated 2-8°C and ambient 25°C ±2°C/ with the relative humidity of 60 % ± 5% RH in humidity -cum- photostability chamber for 21 days

Bone targeting efficiency by in vivo imaging system

The IVIS Imaging System (Perkin Elmer - Caliper Life Sciences, USA) was used to analyze the distribution of nanoformulations after intravenous administration. The bone targeting efficiency of ALN anchored NPs towards bone tissue was investigated using Fluorescein isothiocyanate (FITC) as a fluorescent agent. The bone uptake of PLGA-ALN based NPs was studied in one-month-old male BALB/C mice (weight 20-25 g) as at this age bone growth rate is highest as reported by Mizrahi et al. [16]

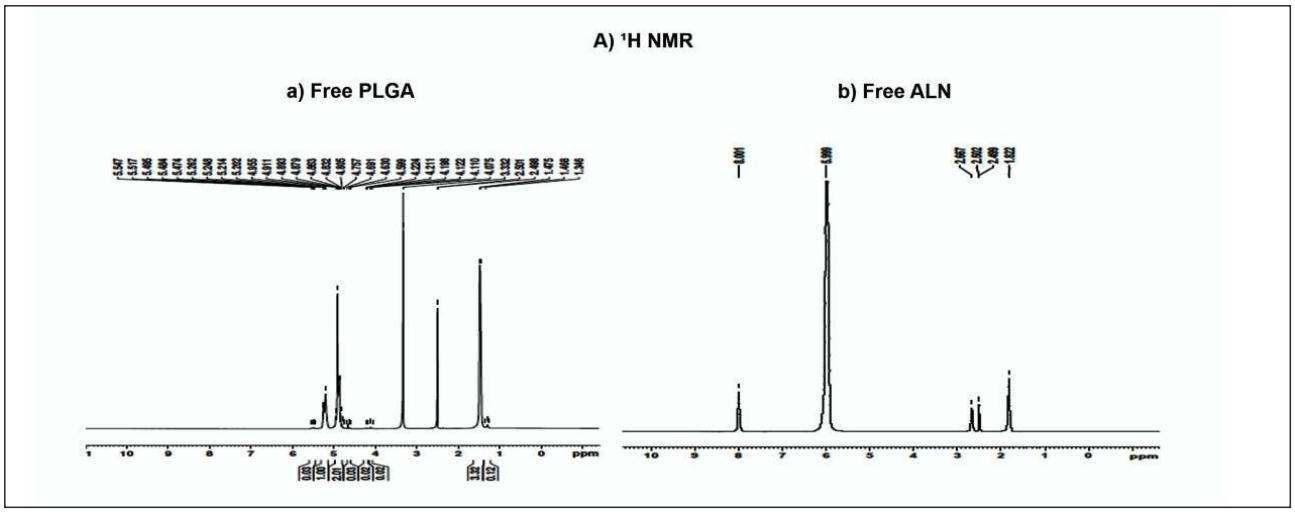
Efficacy studies for antiosteoporosis activity

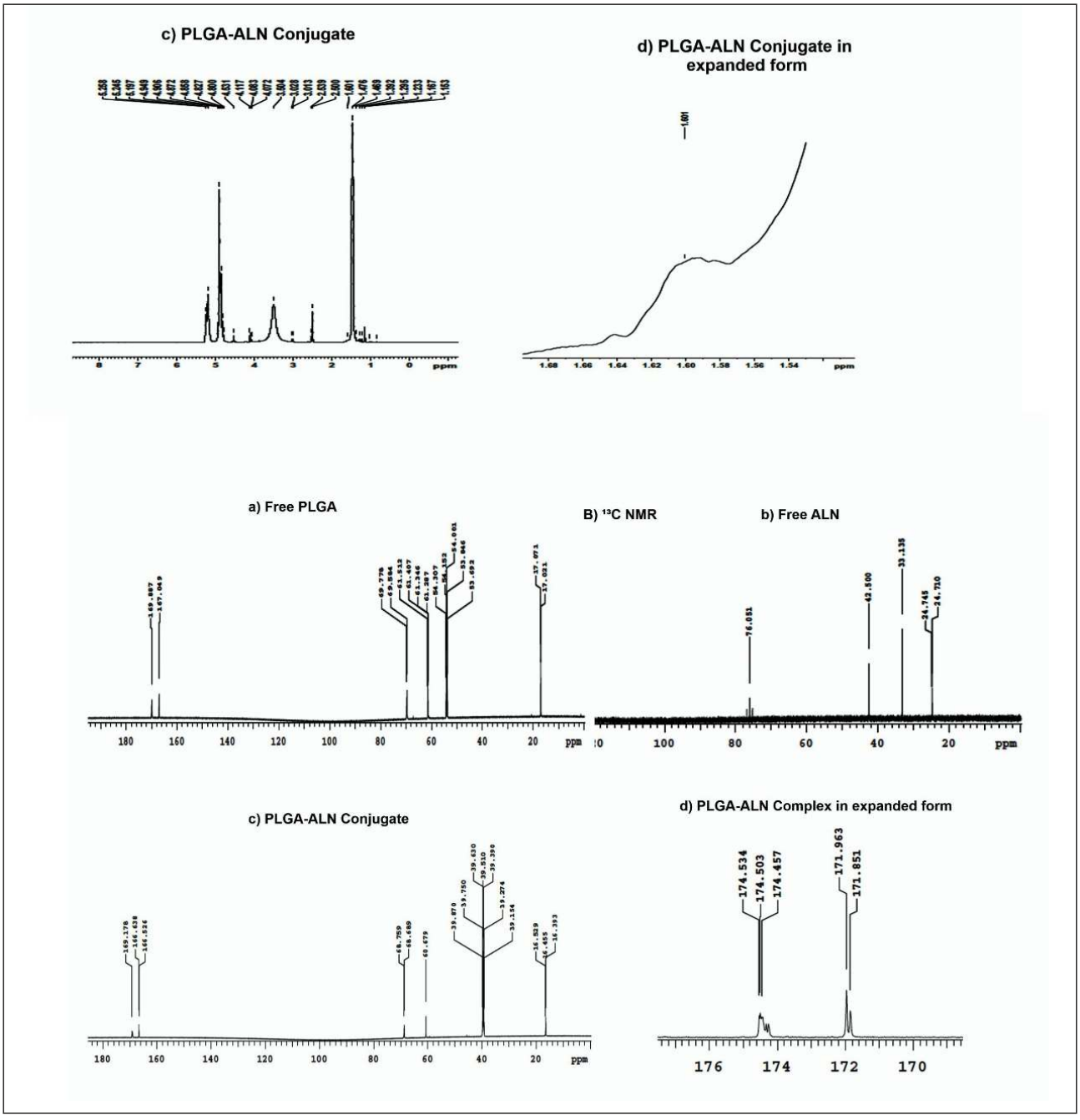
Female wistar rats (three months old) were used to investigate the efficacy study of nanoformulation in postmenopausal osteoporosis. Rats were ovariectomized (Ovx) and left untreated for the induction of postmenopausal osteoporosis. As the nanoparticles were prepared in PBS (pH 7.4), the normal control, sham and Ovx groups were administered intravenously with PBS. The NPs treatment was administered once a week for three months. 17 β-Estradiol (17β-E) and human recombinant parathyroid hormone (1-34 hPTH) were used as a reference standard and administered subcutaneously daily. [17,18]

3. Results

Characterization of PLGA-ALN conjugate

In PLGA-ALN conjugate synthesis, the free carboxylic group of PLGA interacts with the amine group of Alendronate to form an amide bond as reported by Rosario Pignatello et al; (2009)[19]. The formation of the amide bond was further demonstrated by 13C NMR, ^{1}H NMR, FTIR, and XRD analytical techniques.




c) PLGA-ALN Conjugate
d) PLGA-ALN Conjugate in expanded form
a) Free PLGA
B) ¹³C NMR
b) Free ALN
c) PLGA-ALN Conjugate
d) PLGA-ALN Complex in expanded form
ppm

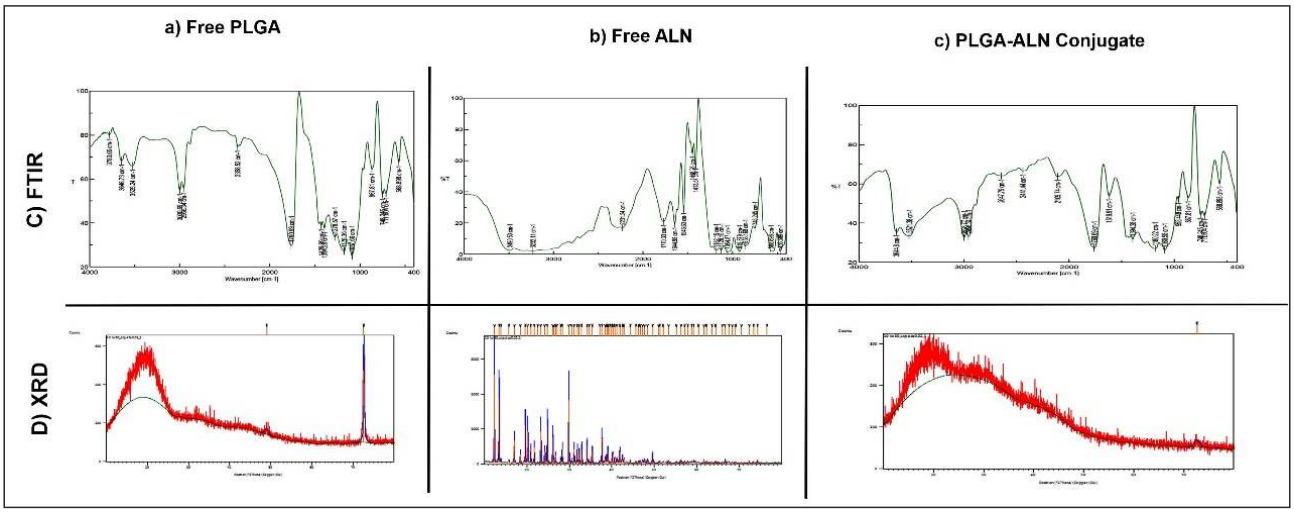

a) Free PLGA
b) Free ALN
c) PLGA-ALN Conjugate
C) FTIR
D) XRD

Figure 2: A) ^{1}H NMR of a) Free PLGA b) Free ALN c) PLGA-ALN conjugate in and d) Expanded version of PLGA-ALN conjugate (All in DMSO solvent). B)13C NMR of a) Free PLGA in deuterated Dichloromethane b) Free ALN in deuterated water c) PLGA-ALN conjugate in DMSO and d) Expanded version of PLGA-ALN conjugate in the range of 150 to 180 ppm. C) FTIR Spectra and D) X-ray diffractogram of a) Free PLGA b) Free ALN c) PLGA-ALN conjugate

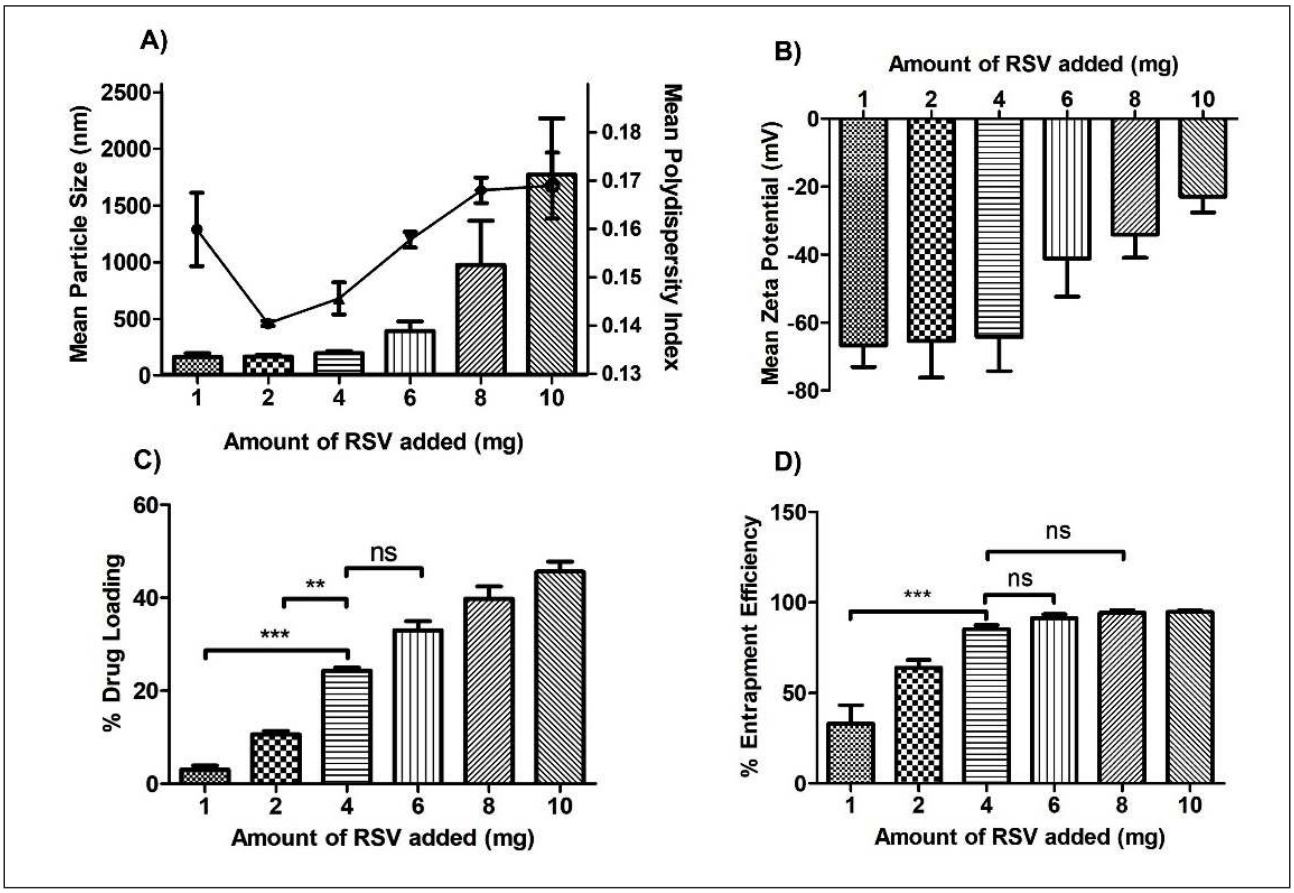
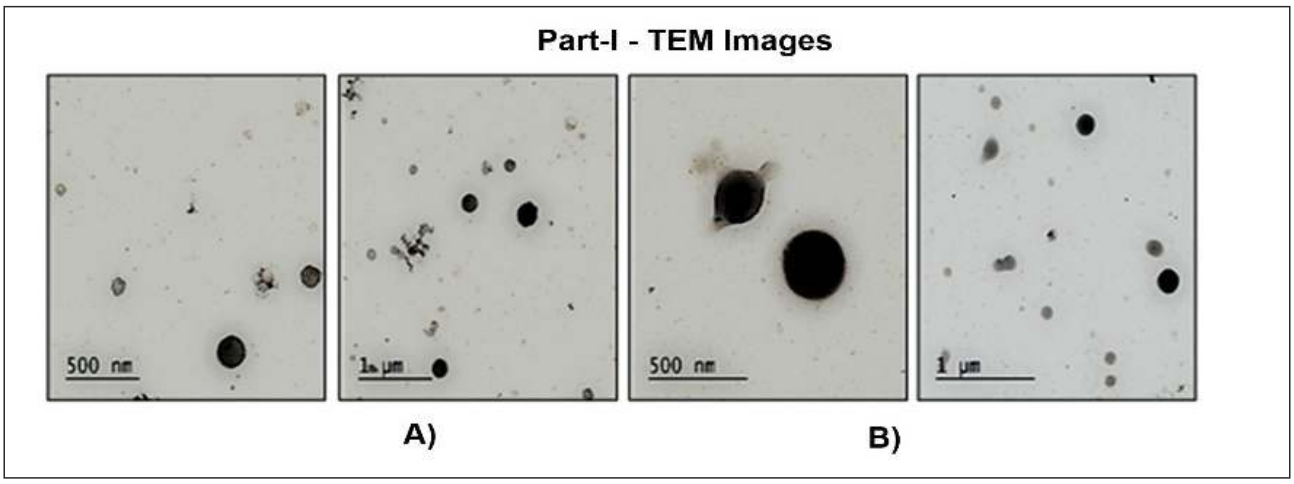


Figure 3: Particle Size, PDI, ZP Distribution, %EE and %DL of Conjugate: Surfactant: RSV ratio A) 10:10:1 B) 10:10: 2 C) 10:10:4 D) 10:10:6 E) 10:10:8 F) 10:10:10.



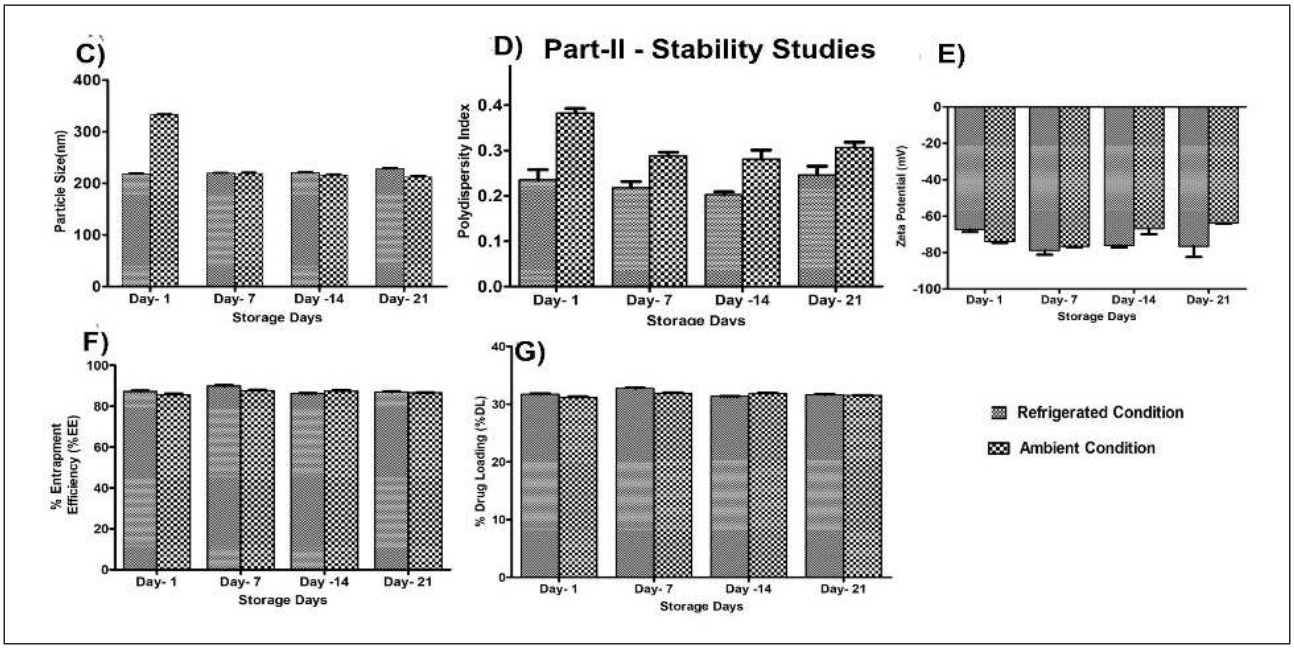


Figure 4: Part I – TEM imaging - Morphology and droplet size of A) blank PLGA-ALN NPs B) PLGA-RSV-ALN NPs at 500 nm and 1µm scale respectively. (Only one TEM image (one scale bar) is sufficient, one with the best clarity. Rest one in which with lot of debris and less clear image of nanoparticles can be removed or moved to supplementary section)

Part II- Stability assessment of the nanoformulation at refrigerated and ambient conditions on storage of 21 days. The effect on C) particle Size D) PDI E) ZP F) %EE and G) %DL were evaluated.

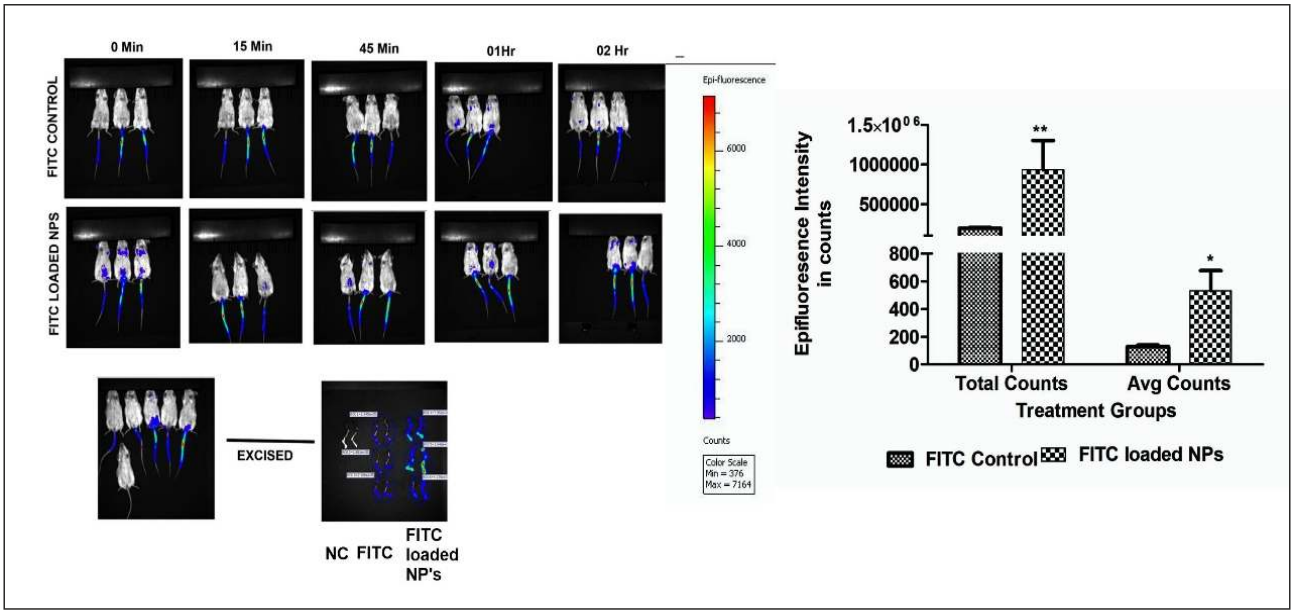


Figure 5: Epifluorescence intensity at whole-body imaging in FITC alone and FITC loaded NPs – The treated mice at 0 min (immediately after injection), 15, 45 min, 1, 2, and 24 hr. The mice were sacrificed after 24 hr, and the epifluorescence intensity in terms of count in an excised bone proved the retention of NPs in the hind limb region.

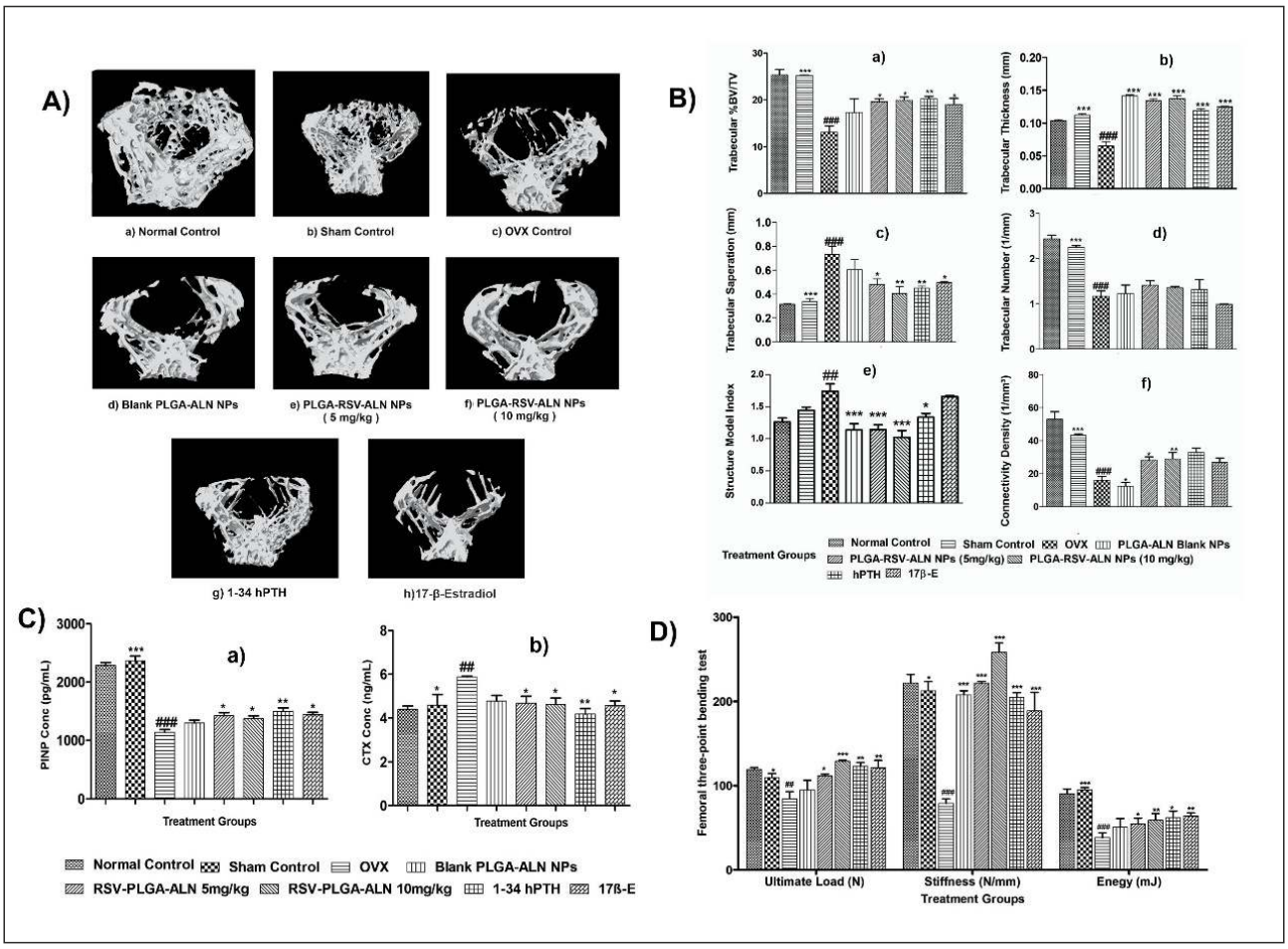


Figure 6 A). Effect of PLGA-ALN NPs on trabecular microarchitecture in an isolated femur epiphysis bone- representative μCT-3D images of isolated bones in different experimental groups and compared with standards 1-34 hPTH and 17β-E.

B). Quantification of bone morphometric parameters in femur epiphysis region representing a) Bone Volume/Tissue Volume (BV/TV), b) Trabecular Thickness (Tb. Th) c) Trabecular Number (Tb. N) d) Trabecular Separation (Tb. Sp) e) SMI (Structure Model Index) f) Connectivity Density (Conn.Den.).

C). Serum PINP and CTX levels

D). Biomechanical analysis of femur bone in the treatment groups –Parameters as ultimate load, stiffness and energy was analysed

4. Conclusion

In this work, we have explored the therapeutic potential of ALN anchored RSV-loaded PLGA NPs as a bone-targeted drug delivery system for postmenopausal osteoporosis. The bone targeting efficiency confirms the ligand-ALN specificity towards the mineralized region of bone. The intravenous administration of the nanoformulation once a week significantly improved the femur trabecular microarchitectural deterioration induced by ovariectomy and also enhanced serum osteogenic markers. In conclusion, the results of the present study demonstrate that, alendronate-linked RSV-loaded PLGA NPs an attractive anabolic strategy for prolonged skeletal retention and reduced dose frequency in osteoporosis

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Development of Epigallocatechin 3-gallate NanoCubes Loaded Mucoadhesive Hydrogel for the Treatment of Oral Submucous Fibrosis

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Purpose

The people habituated to eat the areca nut, betel quid, and gutka often suffer from various oral related diseases such as oral submucous fibrosis (OSF), oral cancer and many more. Among all, OSF is one of the dangerous and chronic disease which causes due to areca nut chewing and it globally accepted as an Indian disease. It leads to activation of various pathological parameters such as TGF-beta1, TIMP, PAI, LOX and Smad which also characterized by connective tissue accumulation in middle most layer of oral mucosa (lamina propria layer) and leads to decrease in mouth opening and burning sensation due to epithelial atrophy caused by inflammatory cell infiltration [1]. Eventhough different treatment strategies has been explored for OSF therapy, very less successful results were observed which indicates the gap in the knowledge and need the improvement. There is a high need of identification of an effective OSF treatment strategy which can gives the symptomatic relief to cure the disease and also alternative to currently used therapy. Based on the literature survey, it was found that the compounds having anti-inflammatory, oxygen radical scavenging properties and anti-fibrotic activity can be considered as beneficial in the OSF treatment. Epigallocatechin 3-gallate (EGCG), a phytomolecule exhibited an anti-fibrotic and anti-inflammatory activity [2], therefore it is selected for the formulation development in the form of EGCG NanoCubes loaded mucoadhesive hydrogel.

Methodology

The EGCG loaded NanoCubes were prepared using hot melt emulsification technique and the optimized formulation was used for the mucoadhesive hydrogel. The optimized EGCG NanoCubes formulation were treated with stearylamine to get positive charge on its surface. The prepared optimized NanoCubosomal dispersion and NanoCubes loaded mucoadhesive hydrogel were evaluated and characterized for various parameters [3,4].

Results and Discussion

OFAT (one factor at a time) design was used for optimization of the formulation by considering the zeta potential, particle size, PDI and encapsulation efficiency as responses. The particle size, PDI, zeta potential of plain and cationic NanoCubes were found to be 131.7 ± 0.69 nm, 0.155 ± 0.06, - 40.5 ± 1.23

mV and 121.6 ± 3.69 nm, 0.240 ± 0.01, 63.6 ± 4.65 mV, respectively while encapsulation efficiency was found to be in range of 65-75 %. Fourier Transform Infrared Spectroscopy (FTIR) spectrum of the formulation showed the pure drug EGCG characteristic peaks retention which indicates the stability and compatibility of drug with the excipients used in the formulation. Differential scanning calorimetry (DSC) analysis showed the disappearance of the drug peak in both optimized formulations which indicates the conversion of its crystalline to the amorphous nature and suggesting that uniform dispersion of EGCG within the NanoCubosomal matrix while X-ray diffractometry (XRD) results showed the decrease in peak intensity in case of formulation when compared to EGCG which indicates the presence of drug in the molecular dispersion with increased solubility. Transmission electron microscopy proved the formation of cubic shaped lipidic nanoparticles, and the size was comparable as suggested by the Malvern particle size analyzer. EGCG solution showed in-vitro drug release of almost 100% in 4 h while plain and cationic NanoCubes showed 90.18 ± 2.98 % and 28.07 ± 1.19 % at the end of 8 h respectively which could be due to the narrow size of channels and limited diffusion of EGCG from lipidic nanoparticles towards the aqueous media.

The prepared EGCG NanoCubes loaded mucoadhesive hydrogel was found to be white in color, smooth and homogenous overall while the pH between 6.0 to 7.0. The drug content was found to be in the range of 85 – 95 %. The prepared hydrogel was found to be mucoadhesive (0.080 ± 0.0002 N) with required viscosity (9253 ± 112 cps) and spreadability (0.024 ± 0.003 g-cm/sec.) which indicates the formulation has ability to spread uniformly with application of little pressure with good contact to the mucosal layer. The formulations were found be stable afterthermodynamic stability studies such as centrifugation and freeze thaw study. In vitro drug release results showed that the EGCG loaded hydrogel (64.12 ± 1.58%) showed faster EGCG release when compared to the plain NanoCubes (60.69 ± 3.42%) and cationic (27.58 ±0.97 %) NanoCubes loaded hydrogel. Ex-vivo drug permeation studies showed that cationic NanoCubes loaded hydrogel [853.42 ± 11.74 µg (85.34 ± 1.17%)] showed faster and higher permeation of EGCG when compared to the EGCG loaded hydrogel [460.71 ± 8.51 µg (46.07 ± 0.85%)] and plain NanoCubes loaded hydrogel [581.26 ± 7.31 µg (58.13 ± 0.73%)] which may be due to higher affinity of positively charged NanoCubes towards the negatively charged buccal mucosal membrane and which formed the higher interactions between them as compared to plain NanoCubes and EGCG loaded hydrogel.The data obtained for in-vitro drug release data of NanoCubes, hydrogel and ex-vivo studies followed Higuchi model as it showed higher r2 values thus indicates controlled and continuous EGCG release from the hydrogel matrix. As per Korsmeyer-Peppas model, n values found to be between 0.45-1.0 which indicates the superimposition of both non-Fickian diffusion-controlled and anomalous transport mechanism of drug release from optimized hydrogel.One-way ANOVA multiple comparison analysis was performed for the obtained data and the results showed the statistical a significant difference ($p<0.05$) between various groups. Ex-vivo retention studies of the fluorescent probe (Rhodamine B) tagged NanoCubes which showed that the

faster permeation of cationic NanoCubes as compared to plain NanoCubes which may be due presence of positive charge on the cationic NanoCubes and negatively charged buccal mucosa, thus proving the penetration of NanoCubes across the mucosal membrane. The research work done by Roblegg, and his team proved that the nanoparticle having positive charge (cationic NanoCubes) with particle size 200 nm and negative charge with particle size of 20 nm (anionic NanoCubes) helps to permeate the buccal mucosal membrane easily through the buccal mucosa. The optimized formulation was found to be stable during the period of accelerated stability studies for 3 months as there were no or negligible sign of change in the texture (appearance), pH, loss of weight, drug content and viscosity of the stability samples.

In-vivo studies were performed using Sprague Dawley rats. The sub-buccal injection of areca nut extract was given every alternate day to induce the OSF for 45 days and buccal mucosa was dissected to confirm the disease induction using histopathology. Once the disease was induced, animals were divided into different groups and started with the treatment for 3 months of duration and samples were collected for the histopathology and other parameters. Based on the histopathological results, the treatment group with EGCG NanoCubes loaded hydrogel showed improvement in the disease condition such as presence of loosely arranged collagen fibres and presence of stratified squamous keratinized epithelium with 6-8 layers thickness without rete ridges when compared with the standard treatment group and other groups [3,4].

Conclusion

Therefore, the optimized formulation showed multifunctional potential benefit in treating OSF and can be considered as the effective and safer substitute therapy to available treatment options.

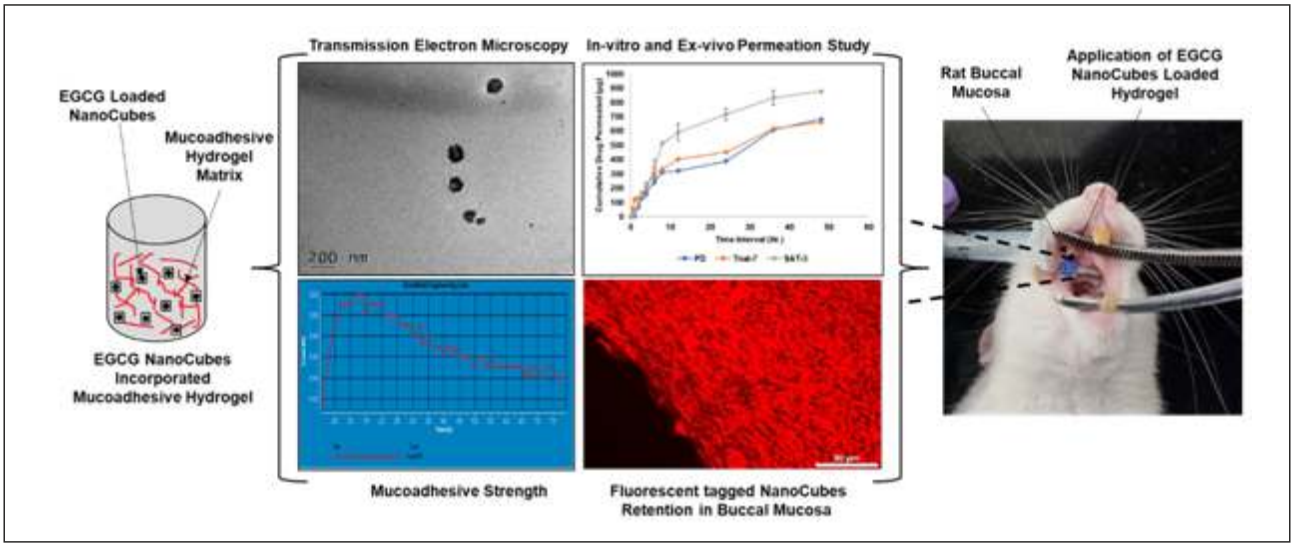

Figure 1. Graphical representation of formulation development and evaluation and application of formulation in disease induced rat model

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Engineering multifunctional biomaterials for stimulating remyelination of Schwann Cells in Peripheral demyelinating diseases

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Introduction

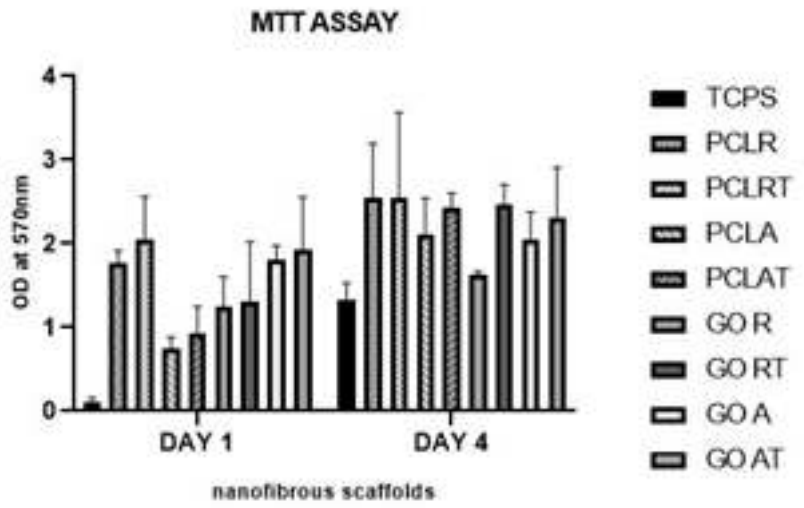
Peripheral demyelinating diseases (PDD) are a group of diseases in which axons, glial cells, and specifically Schwann cells (SC) of the peripheral nervous system (PNS) are damaged. The main cause of these diseases is due to demyelination, that is lack of SC's function. In recent decades extensive research is in the direction of SC focussing on their physiological and neuroprotective effect on the PNS. Using tissue-engineered synthetic biomaterials that can stimulate the biological behaviour of SCs could be a potential treatment strategy for PDD. Biomaterials can regulate the biological behaviour of SC and can be beneficial for functional recovery.

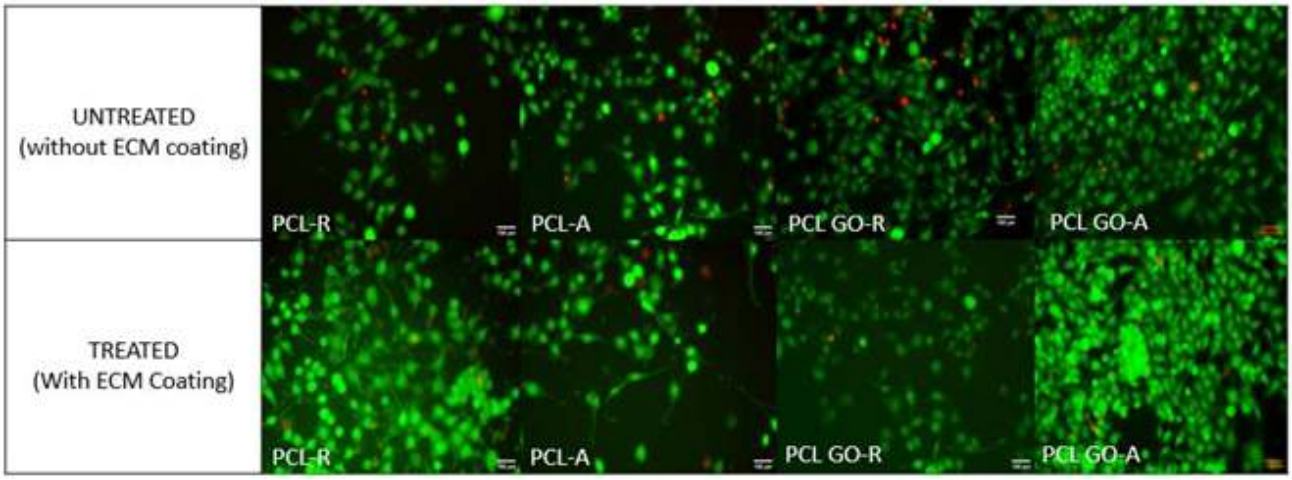
Graphene oxide (GO) is a bioactive nanomaterial, it has a unique nanostructure and exceptional physicochemical properties, it has hydrophilic oxide functional groups, superior in mechanical, thermal, and conductive property, and is also proven to promote adhesion, proliferation, and growth of neuronal cells, therefore intensive research has been done on GO for tissue engineering. Despite the recognized potential of GO in nerve tissue engineering, the poor implantable properties of pure GO make it difficult to fabricate scaffolds by pure GO via conventional techniques such as electrospinning. GO combined with polycaprolactone (PCL) polymer makes the scaffold more hydrophilic with increased mechanical strength and promotes cellular growth.

Methods

In order to mimic the microenvironment for the Schwann cells, decellularized matrix derived from SCs were coated using the spin coating method on the electrospun GO-PCL based nanofibrous scaffolds which will assist in remyelination. In this study, we aim to develop a nanofiber scaffold and do a comparative study of both scaffolds with and without decellularized matrix derived from SCs coating with Schwann cellculture. The protein expression of the ECM was evaluated using western blotting. Biocompatibility assessments were done by cultivating SC cells on both the scaffolds and compared their cellular cytotoxicity through live/dead assay and quantification of cell proliferation using MTT assay. Using F-Actin staining cell morphology and cellular adherence are observed. To investigate the SC's myelin secretion levels on coated scaffolds, gene expression of peripheral myelin protein 22 (PMP22) was observed.

Methods





(Fig 1) Represents MTT Assay for 1st and 4th day points of both random (R) and aligned (A) nanofibrous scaffolds with treatment (T) and without treatment

(Fig 2) Live Dead assay on random (R) and aligned (A) treated and untreated PCL and GO-PCL nanofibrous scaffolds

Conclusion

In (Fig 1) the cell proliferation rate on the scaffolds was compared among the scaffolds in the four-day intervals. The rate of proliferation was found to continue, but no statistical difference was found. From this, we can conclude that all the scaffolds with or with coating showed no cytotoxic effect. From (Fig 2), live Schwann cells are displayed in green fluorescence by calcein staining. The treated samples showed almost no dead cells. This result concludes that cells were alive and well attached on all the scaffolds but showed extended morphology in treated scaffolds which proves that cells in the treated scaffolds have a higher cellular affinity.Thus,this SC matrix coated nanofibrous scaffolds could be used as potential biomaterial substrates for treating peripheral nerve disorders.

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Economic production of human feeders to develop non-xenogeneic cultured human epidermis

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Background & Objectives:

Recently, the cultured human epidermis (CHE) has been considered as a standard regenerative approach in life-threatening burns due to limited donor sites. Although US-FDA approved the exclusive clinical use of CHE in burns patients as lifesaving treatment, there are xenogeneic concerns. Conventionally, the human epidermal stem cells (keratinocytes) are cultured in vitro over growth-arrested murine 3T3 feeder cells prepared through an expensive irradiation technique. Although a cheaper method of generating murine feeders is through the pulse exposure of Mitomycin C (MMC) some studies have indicated the inconsistencies of such feeders which accounts for the xenogeneic effect on the cultured human epidermis. This study is aimed at replacing the murine feeders and employing MMC to develop various subtypes of human fetal dermal fibroblast (HFF) feeders to test their suitability to generate non-xenogenic human epidermis

Methods

Human fetal fibroblast cells (HFF- Genlantis, USA) were subjected to four series of subculture protocols depending on differing initial seeding densities maintained under constant incubation period to derive the following subtypes 3K4D, 5K4D, 10K4D & 20K4D. Each subtype was then characterized and evaluated for its in vitro transformation ability. All the subtypes were then pulse exposed to Mitomycin C (MMC) at six concentrations (1.0, 2.5, 5.0, 7.5, 10.0 & 15.0 µg/mL) to generate feeder cells. Initially, the feeders were evaluated for their acute MMC toxicity and then for the optimal growth arrest employing short-term (20 days) and long-term (>100 days) cell extinction. Based on the cell extinctions, the best-suited HFF feeder was shortlisted and then utilized to test their suitability within the co-culture with human adult epidermal keratinocytes (KC-Genlantis, USA). Another set of 4-150 feeders of a sub-type of Swiss 3T3 (Chugh et al 2017; established in our laboratory as ideal feeders to produce transplantable cultured epidermal sheets) were used as controls for comparison. To find out the optimal keratinocyte seeding density needed for a successful epidermal culture, three different densities of keratinocytes, viz., 3000, 5000 & 10000 cells/cm2, were employed. The co-cultures were incubated at standard culture conditions in our formula of Keratinocyte medium (Yerneni & Chugh 2015).

Results

Each subtype of HFF cells exhibited distinct cellular characteristics as evident from the cell characterization. In the in vitro transformation experiment, the 10K4D subtype developed the least possible spheres in comparison to other HFF subtypes suggesting their suitability as feeders. After pulseexposure of MMC, there was concentration-dependent initial acute MMC toxicity only with the 10K4D subtype. Later, assessing the short-term cell extinction it was observed that only the 10K4D subtype had a statistically significant concentration-dependent optimal growth arrest in comparison to the other subtypes where spurts of growth revival were observed intermittently during the extinction period. However, in the 3K4D subtype, at5µg/mL, 7.5µg/mL, and 15µg/mL of MMC exposure there was optimal growth arrest. Similarly, evaluating the long-term cell extinction, it was observed that only 10K4D maintained growth arrest at all concentrations except for 1µg/mL of MMC. But, the other subtypes exhibited growth revival in succeeding periods of cell extinction. The co-cultures were initiated with 3K4D feeder cells (5µg/mL) at a high density (because 3K4D feeders at low seeding density assumed a much narrow shape compared with broader 3T3 feeders) resulted in numerous KC colonies with stunted growth.A broader feeder cell morphology (required for keratinocyte growth) was observed among 10K4D feeders (7.5µg/mL) in reduced cell seeding densities. Therefore, the co-cultures using 10K4D cells were performed at a much-reduced density but spiked the keratinocyte cells at varying seeding densities(3000, 5000 & 10000 cells/cm2) to analyze which combination would be ideal for satisfactory growth of keratinocytes. The keratinocyte confluence resulted in 90% in 9 days and 7 days with HFF and 3T3 feeders respectively. Cultures with 3000, 5000 & 10000 cells/cm2 of KC + Human feeders formed the sheets until 18, 15, and 12 days of incubation, respectively, while those co-cultured with 3T3 feeders formed the transplantable epidermal sheets by 10 days.All confluent co-cultures employed with 10K4D feeders on the day of lifting as epidermal sheets exhibited characteristic cobbled-stone appearance with desmosomal junctions with several dividing cells indicating the ability to sustain stemness).

Conclusions

Each HFF subtype generated in the laboratory had an independent cellular behavior and responses to MMC at various concentrations. Studies reveal that human fibroblasts have the innate ability to undergo transformation when suspended in methylcellulose, unlike 3T3 cells. Hence, in the transformation assay, only the 10K4D subtype formed the least possible transformed spheres indicating its suitability to irreversibly growth arrestwith MMC. To perform the co-culture with keratinocytes and feeders, the optimal growth-arrested feeder with the lowest possible concentration of MMC needs to be segregated. The feeders generated with the higher concentrations of MMC may render MMC toxicity within the co-culture system. Hence, based on the short-term and long-term cell extinction profiling, 3K4D cells exposed to 5µg/mL and 10K4D cells exposed to 7.5 µg/mL of MMC were chosen as feeders

along with the control murine feeders (3T3 4-150 MMC). By redefining the seeding densities of feeders and keratinocytes, the cultured human epidermis (CHE) could be generated utilizing human feeders of the 10K4D subtype. Surprisingly, a notable feature was that the HFF feeder cells do not require differential removal from the epidermal sheets, unlike the murine 3T3 feeders. The texture of sheets from 3000 KC cultures showed more gaps than the other two groups which perhaps suggest the cut-offrequired for optimal seeding density of KC. The cultured human epidermal sheets thus generatedrequire further evaluation and characterization to prove their potential in the therapeutic application for burns.

Keywords: Human fetal dermal fibroblast, epidermal stem cells, keratinocytes, feeders, mitomycin c, growth arrest, non-xenogeneic

3D printing of ceramic-clay composite for cost effective bioresorbable scaffold for bone regenerative applications

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3D printing is one of the additive manufacturing technologies which has opened additional possibilities for tissue regeneration. 3D printed ceramic scaffolds are used for hard tissue regeneration, especially in regenerating defective or damaged bone tissues. The bioresorbable characteristics of ceramic scaffolds plays a vital role in replacement of defective bone regions. They are also used as an implant for recovery of critical bone defects, replacement of tumour region, and congenital abnormality.

In this study, we attempted 3D printing of Hydroxyapatite-Bentonite (HB) composites for bone scaffold. 30:30 wt% of hydroxyapatite and Bentonite were mixed as paste in addition to carboxymethyl cellulose, as a binder to improve the viscosity of the prepared slurry. The print model was designed using Autodesk and sliced using simplify 3D, the dimension of the 3D printed structures was 10×10×10mm which are then sintered at different temperatures from 400 ^{0}C, 600^{0}C, 800^{0}C and 1000^{0}C. The sintered samples are taken for mechanical studies, It was observed that the printed scaffolds exhibited different mechanical properties and the highest compressive strength of 49.6 MPa was recorded at 1000 ^{0}C, and 47.1 MPa was recorded at 800 ^{0}C, 29.7 MPa was recorded at 600 ^{0}C, and 29.4 MPa was recorded at 600 ^{0}C.

The surface morphology of the scaffolds was observed using inverted microscope and reportedly has a rough surface that can promote cell adhesion and proliferation. The printed scaffolds were further characterized using FTIRto identify the presence and response of functional groups present in the scaffold with respective temperatures. The XRD characterization allows to identify the crystallinity of the scaffolds in respect to different temperatures.

Based on these basic studies it is believed that it can be 3D printed and optimised according to different shapes with different properties. Using 3D ceramic printing technology, this material can be printed and used as an ideal bone scaffold for bone regeneration.

Results

3D printing and sintering

Figure 1. 3D printed scaffold

The 3D printed scaffolds were dried as shown in the fig 1, then observed in inverted microscope for the morphological characteristics.

Figure 2. 3D printed scaffold (dimension 10×10×10mm)

The 3D printed samples with dimension 10×10×10mm were sintered at different temperatures (400 ^{0}C, 600 ^{0}C, 800 ^{0}C and 1000 ^{0}C). Shrinkage of the samples were absorbed depending on increase in the temperature.

XRD and FTIR characterization

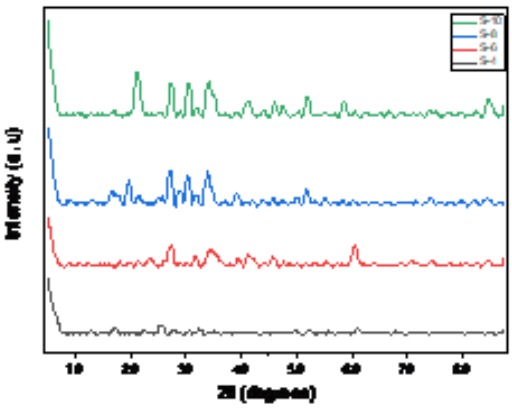

Figure 3. XRD data of samples with different temperature

The XRD of the Bentonite and HAp composites are displayed in Fig. 3. The crystal phase acquired by XRD data shows an increment in crystallinity for the BH composite at 1000 ^{0}C, contrasted with BH at 400 ^{0}C, 600 ^{0}C and 800 ^{0}C. This outcome exhibited the higher crystalline structure of BH-S-10. The sharp and significant peaks related to HAp were seen at 25.94, 29.02, 31.89, 32.28, 33.0, 34.15, 39.93, 49.6 and 53.3 at 2θ degrees. The positions and d-values coordinated with well with JCPDS no. 09-0432. The peaks at 25.3, 24.5, 34.7 and 63.2 confirmed the presence of bentonite in the composite.

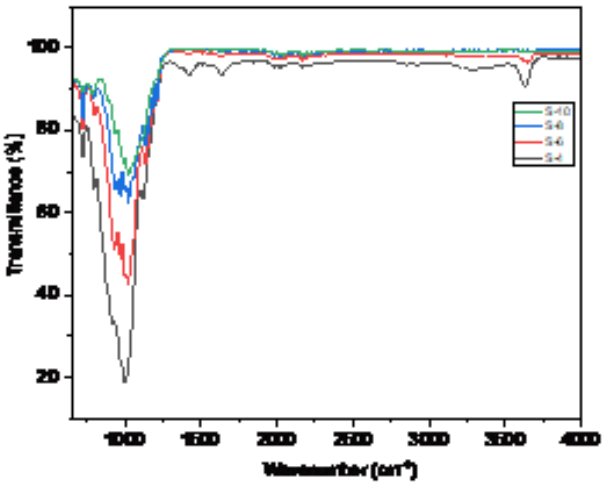

Figure 4. FTIR data of samples with different temperature

The functional group of the composite material were available in the previously mentioned composite. The absorbed band at 3627-3630 cm-1 were doled out to the hydroxyl bunch (OH). The wide absorption groups at 3434 and 1633 cm-1 might be attributed to the OH extending and bending, individually for the adsorption of water atoms on the bentonite and hydroxyapatite surfaces.Absorption groups at 1040-1044 cm-1 mean the presence of Si-O-Si bonds in BH. The PO_4group were assigned out to the absorption band at 1036-1043 cm^{-1} which confirms the presence of hydroxyapatite in the BH nanocomposite. Also, the event of hydroxyapatite in the nanocomposite might be verified by its ingestion band in the FTIR spectra.

Mechanical strength

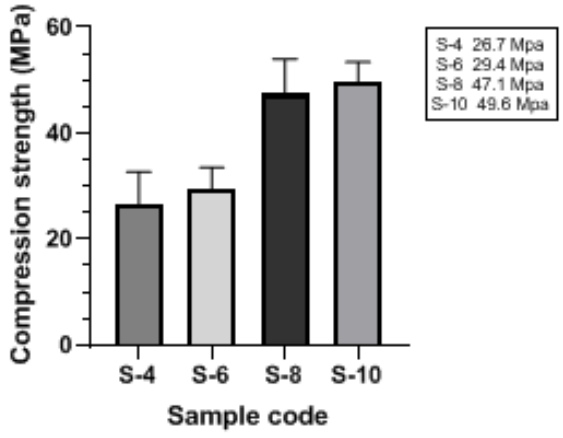

Figure 4. Compression study of sintered scaffold

The compression study data shown in fig. 4 represents the compression strength of the scaffold sintered with different temperatures (400 ^{0}C, 600 ^{0}C, 800 ^{0}C and 1000 ^{0}C). 5000 KN weight was applied to all scaffolds with the dimension 10×10×5mm. BH-S-10 shows the highest compression strength (49.6 Mpa) when compared to other sintered scaffolds.

Discussion

The Bentonite and Hydroxyapatite composite shown good results in printing. The shrinkage of the sample after sintering shows the densification of bentonite and hydroxyapatite which results in increasing compressive strength of the scaffold.

Fabrication of Extracellular matrix based nanoscaffolds to support functional hepatocytes

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AIM

To fabricate novel nanofiber scaffolds (dLEM-PLA) using liver extracellular matrix that shall promote long term culture of primary hepatocytes.

MATERIALS & METHODS

Polymer preparation: PLA (Poly Lactic Acid) was dissolved in HFIP (Hexafluroisopropanol) 10% (w/v) under constant stirring overnight at room temperature

LEM Preparation: 8-week old Sprague Dawley rat liver was perfused through the portal vein and decellularized with detergents 1% Triton X-100 + 0.1% NH_4OH and 1% SDS + 0.1% NH_4OH at a flow rate of 5ml/min , further the detergents were washed with distilled water overnight at the same flow rate. The decellularized liver was then removed and powdered with liquid nitrogen. The powdered LEM was then stored in liquid nitrogen until use.

Electrospinning: Electrospinning solutions were prepared by mixing PLA (Poly Lactic Acid) (10% w/v) and LEM (10% w/v) in the ratio (1:1) and was kept at 4ºC under constant stirring overnight. The solution was then loaded into a 5ml syringe and was allowed to flow through a 24G blunted needle at a distance of 12 cm and at 15KV high voltage, the flow rate was maintained at 1.5ml/hr. The scaffolds were collected on 13mm cover slips in a random orientation which was further dried overnight and sterilized with 70% ethanol to utilize them for invitro cultures.

Hepatocyte isolation: 8-week old Sprague Dawley rat liver was cannulated through portal vein and digested by non-recirculating collagenase perfusion method. After which, the liver was excised from the animal, minced and centrifuged at 50G for 8min to separate out the hepatocytes from the non parenchymal cell population. The viability of the isolated hepatocytes was assessed with Trypan Blue staining and was also characterized with immunostaining for Albumin after 24 hrs of plating.

In vitro culture of isolated hepatocytes on the electrospun scaffolds: The isolated primary rat hepatocytes were seeded onto the scaffolds at a density of 11* 10^4 cells/well in a 24-well plate. The

cells were assessed for viability at different time points with Calcein AM staining and to assess the functionality of the seeded hepatocytes on the nanoscaffolds immunostaining with Albumin was performed and to further validate their functionality , the conditioned media from these cells at different time points was collected and was tested for Albumin and Urea secretion.

RESULTS AND DISCUSSION

Characterization of decellularized liver: Characterization of the decellularized liver was performed in terms of Histology to assess the presence of remnant cells. H& E staining was performed to confirm the absence of nuclei in the decellularized tissue samples and MT staining confirmed the presence of the major ECM component collagen intact after decellularization. DNA content analysis showed complete nuclei removal and significant DNA decrease in the decellularized liver in comparison to the control liver ($P<0.0001$)

Characterization of the Electrospun scaffolds: Scanning Electron Microscopy of the electrospund LEM-PLA scaffolds showed proper fiber formed without any bead on string structures at all concentrations of LEM used. The fiber diameter was calculated using Image J by taking an average of 50 different areas (with 69 pixels um^{-1}). Porosity of these nanoscaffolds scaffolds was analysed with the particle analysis feature of Image J. The pore size of the scaffold (44 + 2.5um) with 10% wt of both the polymer and the LEM (ratio being 1:1) was found out to be closer to that of native human liver (30-40um) and thus was chosen for *in vitro* cultures. Water contact angle measurement showed improved hydrophilicity of dLEM-PLA scaffolds in comparison to that in PLA scaffolds. Protein release from the dLEM-PLA scaffolds at 37ºC was less than 2% showing the stability of these scaffolds under in vitro culture conditions.

Characterization of the isolated primary rat hepatocytes: Trypan blue assay was used to determine the viability of the isolated hepatocytes which was found out to be >90%.To further validate the isolated cells, characteristic marker of the hepatocytes Albumin was stained after 24 hrs of plating. The Albumin expression was visualized with a confocal microscope.

Assessment of hepatocytes on the electrospun scaffolds: The viability of the cells seeded onto the nanoscaffolds were assessed for viability at Day4, 10 and 20. Primary hepatocyte viability on dLEM-PLA could be maintained till day 20, although there was a slight decline in cell functions at day 20 as compared to day 10. Hepatocytes appeared to be in rounded morphology on PLA scaffolds while their hexagonal shape was better maintained in dLEM-PLA scaffolds. Functionally, both albumin gene expression and secreted levels were increased in cells plated on dLEM-PLA scaffolds as compared to cells on PLA scaffolds on day 4 and 10.

CONCLUSION: Primary hepatocytes seeded on novel dLEM based nanofibrous electrospun scaffolds provides a valuable technique in prolonging hepatocyte viability and functionality. These scaffolds may serve as an excellent platform for varied applications such as ex vivo drug testing.

Design and optimization of 3D bioprinting of PVA-Schwann cells based bioink for peripheral nerve tissue engineering

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Peripheral nerve injury is a very common neurological disorder that can hamper the quality of life causing sensory and motor dysfunction. Owing to their regenerative potential, small peripheral nerve defects get repaired by themselves, while larger defects require tissue engineering substitutes to bridge the nerve gap. One of the recent technologies and strategies to address the peripheral nerve regeneration is through 3D bioprinting. 3D bioprinting is a technique to generate sophisticated structures of precise dimensions with suitable printer and bioinks. While the bioprinters are of various types, extrusion based bioprinter is widely used as it can create constructs with high cell densities. It allows the use of multiple print heads for printing different materials within a single structure. The major disadvantage of this bioprinting technique is that the cells undergo shear stress while passing through the nozzle during the printing procedure and the availability of appropriate materials to be used as bioinks. Bioink is combination of cells and hydrogels which have appropriate properties that make them printable. To design an optimum bioink, an equilibrium must be achieved between the rheological properties of the bioink to maintain shape fidelity of the printed structure and also the cell viability in the printed structure. The bioink should exhibit proper gelation during extrusion and should become mechanically strong to support the next printed layer and closely represent the original CAD design. This property of the bioink is called the printability. Shape fidelity has always been determined by visual inspection and to achieve a well-structured 3D construct using a hydrogel bioink various parameters have to be optimized

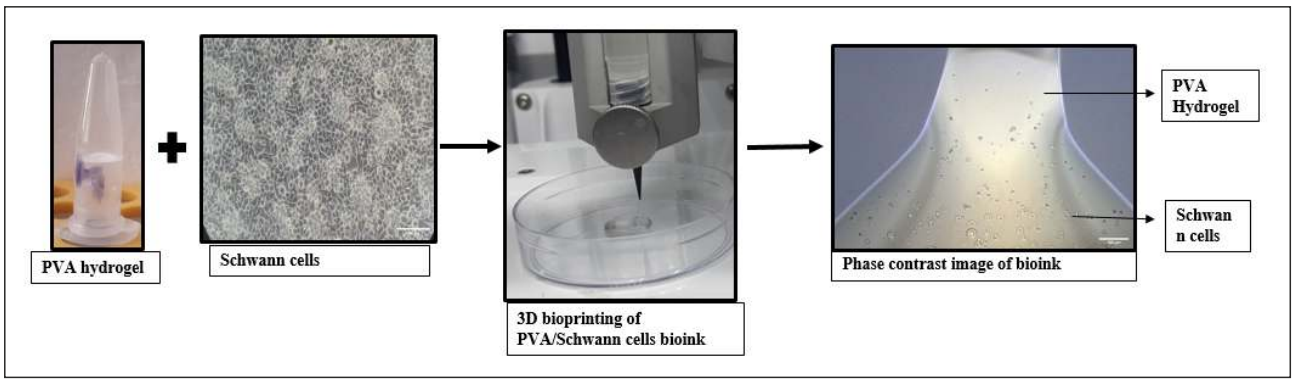

Figure: 1 D Bioprinting process of PVA/Schwann cells bioink

Therefore, in the present study, we optimized Poly vinyl alcohol (PVA) bioink prepared using Rat Schwann cells and assessed various printing parameters like pressure, nozzle diameter, temperature, crosslinking method and evaluation of shape fidelity of bioink. The concentration of PVA and citric acid was optimized by evaluating the non-flowing behaviour of the gel. It was observed that at 25% w/v concentration, optimum printing was achieved. Dual stage crosslinking was optimized which included pre-print crosslinking with citric acid and post-print crosslinking with sodium hydroxide. The rheological properties of the crosslinked gel was compared with that of uncross-linked PVA gel. Swelling and degradability tests were done for samples with single and dual crosslinking. Results indicated that the swelling ratio is more with single crosslinking than when dual crosslinking was done indicating the increase in crosslinking degree (Figure 2). The Degradation test also showed that dual crosslinked scaffold presented less mass loss when compared to single crosslinked scaffold over a period of time (Figure 3).

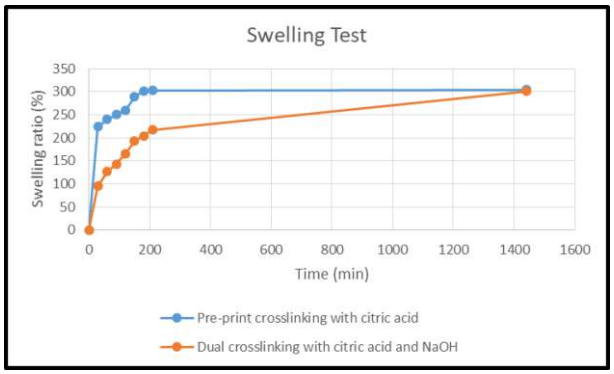

Figure 2: Swelling test

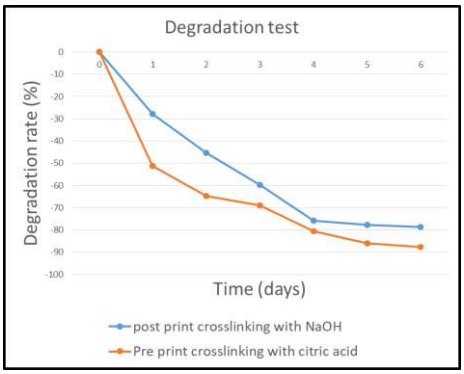

Figure 3: Degradation test

Biocompatibility was assessed using live/dead assay and MTT assay of cells printed using 25 G nozzle and with two crosslinking methods. Our data showed that optimum print was achieved with 25G nozzle at 50 KPa pressure while maintaining adequate cell viability.

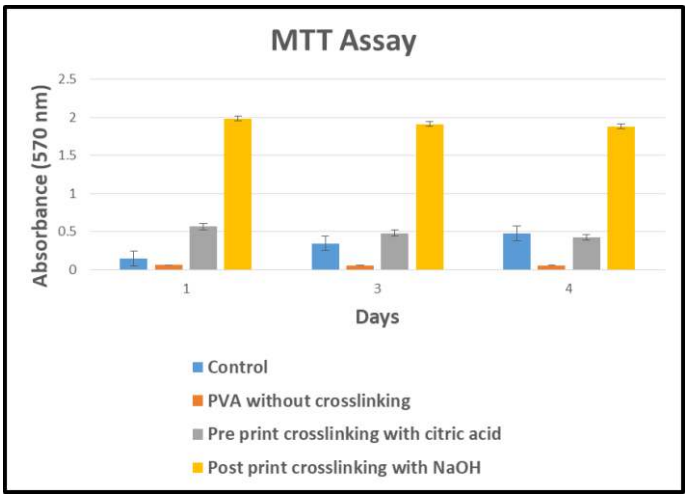

Figure 4: MTT Assay

Cell seeding efficiency was also evaluated in comparison with cells seeded on the casted film. The printability was optimized by evaluating printability of the bioink printed with 25 G nozzle and various printing parameters like printability, filament fusion test and filament collapse test. As shown in the graph below, printability was obtained in the range of 0.9-1.1 which indicated that the 3D printed structure demonstrated sound filament morphology and stability.

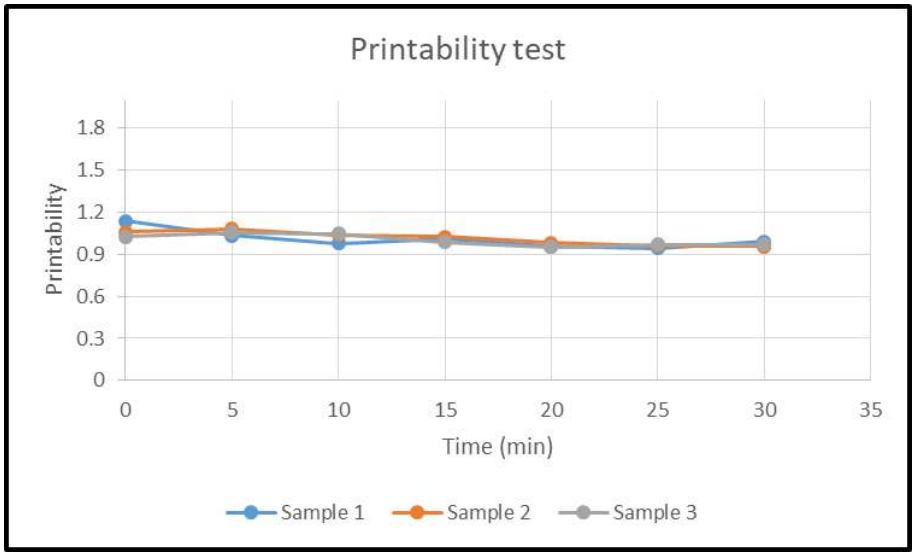

Figure 5: Printability test

It was concluded that PVA/Schwann cell bioink was could provide optimum printability and could be used in peripheral nerve tissue engineering applications.

Keywords: Peripheral nerve regeneration, 3D bioprinting, bioink, printability, polyvinyl alcohol, Schwann cells

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Deciphering the role of miR-499a-5p in the generation of cardiomyocytes from Wharton's jelly mesenchymal stem cells

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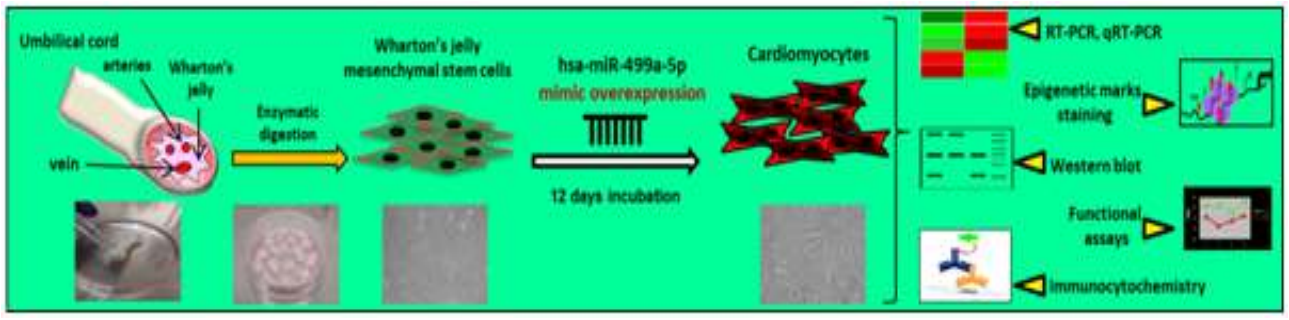

Background: Cardiovascular diseases (CVDs) remain the leading cause of global death[1]. The full-fledged function of the heart is executed by the cardiomyocytes (CMs). Most of the pathological conditions associated with heart diseases result in cardiomyocytes death. An available therapeutic agent only reduces the death of CMs but does not regenerate or replace them [1]. Eventually, stem cell-based regenerationhas emerged as a promising therapeutic strategy to repair the damaged heart tissue. Generation of cardiomyocytes from stem cells and transplanting them into the heart is among well-studied approaches.Distinct methods like direct reprogramming or transdifferentiation have also started gaining attention for therapeutic purposes. It is a process of converting cells into different cell types directly without going through the pluripotent stage. miRNAs are small non-coding Ribonucleic Acid (RNAs) that regulates gene expression by either targeting mRNA or repressing translation. Growing evidence manifested that microRNAs (miRNAs) havea profound role in heart diseases and developmental processes [2, 3]. Many reports showed that miR-499 in combination with other miRNAs or transcriptional factors involved in cardiac differentiation, apoptosis, and homeostasis [4, 5]. In this study, wedemonstrated that overexpression of a single miRNA, miR-499a-5p induces cardiomyocytes differentiation in Wharton's jelly mesenchymal stem cells and the Wnt/β-catenin pathway played a crucial role.

Methods: Wharton's jelly derived mesenchymal stem cells (WJMSCs) were isolated using an enzymatic method and were maintained and passaged consecutively. WJMSCs were characterized and Passage 3 to 5cells was used for the study. First, WJMSCs overexpressed with miR-499a-5p mimic, and overexpressed cells were maintained for 12 days. The cell viability was assessed by (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) (MTT) assay. After 12 days post-transfection, the miR-499a-5p was confirmed by Quantitative Real-time Polymerase Chain Reaction

(qRT-PCR) analysis. The cardiac genes (Nkx2.5, Troponin I, MHC-alpha, MLC2v, MYL6, and ACTC1) and Wnt/β-catenin pathway regulators (Wnt3a, sFRP4, DKK1, GSK-3β, and β-catenin) expression wereanalyzed by reverse-transcriptase Polymerase Chain Reaction (RT-PCR), qRT-PCR, and western blot. The mitochondrial potential, calcium flux, adenosine triphosphate (ATP), and Nitric Oxide (NO) levels were measured using TMRE, Fura 2-AM, ATP, and Griess assay. The changes in epigenetic mark (H3K27me3 and H3K27Ac) and structural regulator (Troponin I and alpha-actinin) were estimated by immunocytochemistry.

Results:The flow cytometry analysis found that isolated WJMSCs were expressing key positive stem cells markers CD73, CD90, and CD105 while having minimal expression for negative marker CD34. Then, we overexpressed WJMSCs with a concentration of 10, 20, and 50nM of miR-499a-5p mimic and negative control to understand the cytotoxicity. After 48hr overexpression, first,we assessed the effect of overexpression on the viability of the cells. We found there is no significant difference in cell viability after overexpression. The overexpressed cells were maintained for another 12 days. For the optimal miRNA concentration, Troponin I (Trop I) expression was analyzed using qRT-PCR. The obtained results described that Trop I expression increased by almost 2-fold in 50nM concentration of miR-499a-5p overexpression which was used for further study. While, except for a slight increase in 20nM, there was no change in trop I expression in 10nM of concentration. The western blot analysis supported qRT-PCR resultsfor Trop I expression which increased upon miR-499a-5p overexpression. Additionally, we evaluated the miR-499a-5p overexpression stability using qRT-PCR. After, overexpressing WJMSC with 50nM mimic, we analyzed miR-499a-5p expression at day 2, day 7, and day 12. The analysis revealed that at day 2, miR-499a-5p expression increased drastically by almost 30-fold, after that gradual decrease in expression was observed at day 7 while at day 12, expression was around 3-fold compared to control. Then, we investigated cardiac genes in miR-499a-5p overexpressed cells by reverse-transcriptase (RT-PCR) and qRT-PCR, the data demonstrated an increase in cardiac genes expression, Nkx2.5, Troponin I, MHC-alpha, MLC2v, MYL6, and ACTC1. The differentiated cardiomyocytes generated from the standard method were used as a positive control for comparison. In addition, we observed a positive signal for Trop I and alpha-actinin in miR-499a-5p overexpressed cells in immunocytochemistry expression demonstrating cardiomyocytes. Further, TMRE, Fura 2-AM, ATP, and Griess assays have established the functionality of the cardiomyocytes. We noted that the mitochondrial activity, Calcium flux, ATP generation, and Nitric oxide production were higher in miR-99a-5p overexpressed WJMSCs in comparison to control. Interestingly, the obtained results were almost similar to positive control. To decipher the Wnt pathway signaling in the process of miR-499a-p induced cardiomyocytes differentiation, we evaluated the Wnt/β-catenin pathway regulators using qRT-PCR and western blot. We found that the β-catenin level got upregulatedindicating activation of theWnt/β-catenin pathway. In addition, qRT-PCR data showed an increase in expression of Wnt3a,

GSK-3β, and β-catenin and a decrease in sFRP4 expression in comparison to control affirming Wnt/β-catenin pathway activation. Also, Immunocytochemistry indicateda decrease in H3K27me3 expression while an increase in H3K27ac expression indicated the involvement of epigenetic modifications.

Inference: A miRNA playsa very crucial role in cardiac differentiation, proliferation, apoptosis, hypertrophy, and excitation-contraction coupling (ECC).miR-499 overexpression has promoted cardiac differentiation in embryonic stem cells (ESCs) [5, 6, 7] and rat mesenchymal stem cells [8]. Similarly, miR-499 in combination with miR-133 has induced cardiac differentiation in embryonic stem cells [3]. Furthermore, a cocktail of miRNAs includesmiR-499 has directly reprogrammed fibroblast into cardiomyocytes [9].In this study, we found that the transient transfection of a single miRNA, miR-499a-5p induces differentiation of WJMSCs to cardiomyocytes. An increase in expression of cardiac markers has confirmed the cardiomyocytes differentiation. In cardiomyocytes, calcium involves in electric activity and contractility function which controls excitation-contraction coupling (ECC)[10]. We determined that miR-499a-5p induced cardiomyocytes have increased intracellular calcium levels. The heart requires a high amount of energy to carry out its physiological function therefore mitochondria is rich in cardiomyocytes[11]. Our study showed that miR-499a-5p overexpressed cardiomyocytes have more active mitochondria and high ATP production. NO acts as an effector molecule of cardiomyocytes which regulates cardiomyocytes proliferation, maturation, and contractility [12, 13]. The data revealed that the NO production improved in miR-499a-5p overexpressed cells compared to control which signifies its involvement in cardiomyocytes regulation. In heart development, the Wnt pathway plays a biphasic role. We observed Wntpathway activation in miR-499a-5p induced cardiac differentiation. Our study providesa dual approach to address the challenges associated with cardiovascular diseases. First, with this method, we can generate cardiomyocytes from mesenchymal stem cells which can be transplanted into the injured heart for cardiac regeneration. Second, Intracardiac injection of miR-499a-5p overexpression could reprogram cardiac fibroblast which is responsible for cardiac fibrosis into cardiomyocytes to achieve cardiac output.

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Characterization of economically developed lab-grown human skin intended for burns therapy

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Background and objective: Burns isa global health problem, more people die due to burns than Malaria and TB, on an average 180,000 deaths/year, mostly observed in low and middle-income countries. At present, cell culture-based therapies are becoming more and more popular and the future for treating incurable diseases appears to be rapidly heading in the direction of adopting stem cell-based therapeutics. The human keratinocytes culture for application in burns was one of the earliest recognized cell-based therapeutic approaches using adult epidermal stem cells dermis for application in burns. These products are generated by adopting the Rheinwald-Green technique, which is used gamma-irradiated murine fibroblast as a feeder (xenogeneic) expensive. Due to the high production costs involved with equipment, infrastructure, and technical expertise for the γ-irradiation growth arresting technique, Mitomycin C is the preferred alternative to develop ideal cultured epidermis The safe sub-type population was generated by adopting a specific subculture scheme that prevented accumulation of resistant variants/transformants. Subsequently, an arithmetically derived dosing strategy was devised that ensured employment of low concentration of Mitomycin C to produce an ideal batch of feeder cells possessing maximal growth-stimulating influence on human epidermal keratinocytes. The validated sub-type was thereafter utilized as feeder cells that promoted keratinocyte growth into transplantable epithelia. The final product was characterized for cytokeratins, feeder contamination, genetic stability, no traces of Mitomycin C and no tumorigenesis in nude mice. However, the latest cellular therapy guidance stipulated evaluation of certain stem cell markers, Bovine serum albumin (BSA) in the final product. Hence, this study is aimed at reproducing the standardized technology of generating the feeder cells, keratinocyte-feeder co-cultures and cultured epidermal sheets and to test for traces of BSA and keratinocytes stem cell markers.

Aim: The aim of the study was to developed the cost effective human culturedepidermal sheets and characterization adopting a lab-based technique.

Materials and methods: The Mouse embryonic dermal fibroblast (Swiss 3T3 cells) 3K3D banking performed by Chugh et al method was validated several times for its optimal generate feeder cells, human keratinocyte banking was performed their Human Keratinocytes are grown over3T3 feeders in a 1:3 ratio produced by a combination of MMC concentration derived as dose per cell was shown to be equivalent to irradiated for producing cultured epithelial autografts without the traces of MMC. Whole cellular extract was prepared from keratinocyte and BSA-ELISA against BSA standards was prepared to construct a standard curve and sample test were performed.

Results: The cultured epidermis was produced several attempt of feeder combination 4-150 was found to be ideal validated 4-150 concentration to produce for epidermal sheet development these sheets validated, Bovine serum albumin (BSA) ELISA kit its competitive ELISA, to perform were cultured epidermal sheet validation for how much concentration of albumin present medium what we were used in epidermal cultured sheet and the main purpose to validate the regulatory point of view for skin grafting in patients. Along with immuno-histochemical localization of markers in both keratinocyte-feeder co-cultures and a cultured epidermal sheet to find out stemness of cultured epidermis.

Conclusion: In conclusion the final product CEA will be subjected to the detection of xenogeneic elements as per of ICMR-DBT Stem cell guidelines.

Keywords: Stem cell, Swiss 3T3 cells, Keratinocyte, mitomycin-C, γ-irradiation,Culture epithelial autografts.

Design, optimization and characterization of γ-methacry loxypropyltrimethoxysilane doped halloysite clay nanotubes using ultra turrax homogenizer

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Introduction: The inclusion of organic moieties on the surface of HNTs has peaked attention, as it allows in fabricating multifaceted compounds which results in significant increase for drug loading capacity, mechanical strength and also for the enhancement of dispersion of HNTs into polymer matrix. Naturally sourced HNTs are composed of double layered aluminosilicate minerals with an ultra tiny hollow nanotubular structure, having a molecular formula $Al_2Si_2O_5(OH_4).2H_2O$ with their length ranging from 400-1000 nm, the inner and outer diameter varying from 10-40 nm and 40-80 nm. HNTs are mainly constituted by siloxane (Si-O-Si) groups on the outer surface and the inner lumen is composed of aluminol (Al-OH) groups which makes them highly hydrophilic exhibiting gibbsite like order and the edges of HNTs consists of Al-OH and Si-O-Si groups. HNTs are natural in origin, biocompatible, biodegradable, has remarkable thermal stability and high aspect ratio. An alternative to these advantages, HNTs have some shortfalls such as insufficient mechanical strength, less drug polymer dispersion ability and lack of drug loading capacity. To overcome these shortfalls, the assemblage between the nanotubes and polymer must be engineered by doping process. There are alternative ways to dope the surface of HNTs like surfactant modification, organosilanes coupling agents, intercalation modification and acid etching method. Among these methods, organosilanes modification has proven to be the most efficient and gifted technique to dope the surface of HNTs. Doping of halloysite nanotubes (HNTs) with γ-methacryloxypropyltrimethoxysilane (γ-MPS) as a silane coupling agent has sparked the interest of researchers. HNTs have a tendency to agglomerate due to the impact of van der Waals forces and in-homogeneity and agglomeration characteristics of HNTs results in deterioration of eventual properties of nanocomposites and homogenous mixtures of HNTs. The ideal strategy to achieve homogenous mixtures and uniform dispersion of clay into the polymeric matrix is the application of severe shear stress such as ultra turrax homogenizer, which results in disruption of agglomerates and accomplishes homogenous mixtures and uniform dispersions of HNTs in the polymer nanocomposites. In addition to this, surface doping using organosilanes empowers the enlargement of basal spacing by facilitating the intercalation of organic and inorganic moieties within the interface of HNTs and thereby opening a window to exfoliate distinctive layers. Thus, doping of HNTs using γ-MPS by the impact of homogenization technique proves to be a significant strategy to intensify the properties of halloysite nanotubes.

Methodology:

The objective of the present study was to design, optimize and characterize a homogenous mixture of doped halloysite nanotubes with γ-methacryloxypropyltrimethoxysilane by using ultra turrax homogenizer. Optimization of doped halloysite nanotubes was performed by applying Custom Design using JMP software 16.1 by considering 2 levels and 3 factors, to determine the impact of independent variables such as amount of γ-MPS (X1), HNTs (X2) and ethanol (X3) on the response variables i.e., angle (Y1) and zeta potential (Y2). The association between the independent and dependent variables was investigated by using the JMP software generated quadratic polynomial equations and 3D surface plots. The doped HNTs were characterized for fourier transform infrared spectroscopy, thermogravimetric analysis, x-ray diffraction, scanning electron microscopy, transmission electron microscopy and zeta potential.

Results and Discussion: Doping of HNTs (DHNTs) with γ-MPS was confirmed by the presence of functional groups characterized by FT-IR analysis. Spectrum of pristine HNT revealed the absorption peaks at 910cm^{-1} and 1031cm^{-1} signifying the presence of Al-OH vibrations and Si-O groups. Some peaks were also observed at 437cm^{-1} and 542cm^{-1} as a result of deformation of Si-O, Si-O-Si and Al-O-Si groups. Another peak was found at 3565cm^{-1} representing the interlayer water molecule. Two new peaks were observed at 1496.96cm^{-1} and 29 25cm^{-1} attributed to deformation (scissoring) of CH_2 and symmetric stretching of C-H_2. Presence of two new peaks confirms the successful doping of HNTs. Absence of a peak at 1700cm^{-1} and the emergence of peaks at 911.38cm^{-1}, 3621.42cm^{-1} and 3694.25cm^{-1} implies the scarcity of freely available hydroxyl groups of HNTs and unable the formation of hydrogen bond between HNTs and γ-MPS. Hence, the efficiency of HNTs modification was slightly decreased in DHNT F4, DHNT F5 and DHNT F8 sample. Another peak was observed at the frequency of 1031cm^{-1} in the spectrum of MHNTs emphasizing the formation of Si-O-Si bonds as Si groups of γ-MPS were linked to the surface of HNTs. In comparison with the spectra of pristine HNT, a sharp intensified peak was observed at 912cm^{-1} in modified HNT emphasizing the potentiality of RSi-O-Si and RSi-O-Al bonds between RSi-OCH_3 and RSi-OH groups of γ-MPS with Al-OH groups present at the edges of HNTs and Si-OH groups present on the surface resulting in HNT modification. These findings authenticate the successful doping of γ-MPS on the surface of HNTs. Pristine HNT revealed a sharp narrow peak at 2θ of 11.36º representing a basal spacing of 7.47 Å (determined by using Bragg's law), indicating that halloysite clay nanotubes belongs to the state of hydration (7 Å hydration). Upon doping, the diffraction peak of DHNT F1 sample showed a slight shift in the interlayer distance of 7.52 Å at 11.39º, indicating slight intercalation of γ-MPS into the layers of HNTs. Increase in basal spacing of DHNT F2 and DHNT F3 samples to 7.71 and 7.75 Å at the 2θ of 11.87º and 12.04º suggest better doping of HNTs. the intensity and sharpness of diffraction peaks in both DHNT F4 and DHNT F5 samples were drastically decreased to 2θ values of 11.67º and 11.41º, equal to d-spacing of 7.62 Å and

7.58 Å. This could be possible as a result of existence of strong hydrogen bonds between the layers and thereby assisting the inhibition of Al-OH groups present in the lumen and making them unavailable for doping of HNTs. Furthermore, the XRD pattern of DHNT F6 and F7 sample presented a sharp peak and the basal reflection of this sample shifted to higher 2θ value of 12.07º, indicating the successful doping of HNTs using γ-MPS as silane. This is achievable by the influence of high speed and temperature generated during homogenization and thereby culturing the frame work to materialize the intercalation within the layers of clay nanotubes. Transmission electron microscopy is a widely used analytical tool for exploring the surface morphology and topography of clay nanotubes. Pristine HNTs are identically characterized by hollow tubular multilayered structure with an open ended lumen, having an outer diameter of 40-70 nm, inner diameter of 10-30 nm and the length of HNT nanotube ranged from 400-800 nm. After silylation of γ-MPS on the surface of HNTs, the outer diameter of DHNT F1 sample was slightly increased to 36.83 nm and the surface texture was observed to be rough in nature, indicating the deposition of thin layer of silane moieties on the surface of HNTs. Micrographs of DHNT F2 and F3 sample reveal that the formation of covalent bond with γ-MPS on the surface of HNT resulted in disentanglement of HNTs. Thus doping of HNTs with γ-MPS lead to an improvisation of entanglement of HNTs and thereby facilitating the dispersibility of HNTs. From TEM image of DHNT F4 and F8, it is clearly observed that the nanotubes were thin walled and exhibited smooth morphology with irregular diameter, indicating that the nano tubes were of low tubular quality. Morphology of DHNT F5 sample is observed to be in the form of aggregation, such aggregation morphologies were formed under the influence of wander Waals forces. The TEM image of DHNT F6 sample showed that the outer diameter was enlarged to 54.49 nm, while the inner diameter was reduced to 23.04 nm, signifying that a layer of γ-MPS was coated on the outer surface of HNT and also a part of lumen was stuffed with γ-MPS moieties. The surface morphology of DHNT F7 sample was found to be extensively uniform with an increased diameter and high tubular integrity, this is achievable because of increased concentration of γ-MPS, resulting in formation of siloxane groups on the surface and thereby enhancing the hydrophobicity of HNTs and maintaining the integrity of nanotube. Pristine HNT exhibited a negative zeta potential value of -33.64 mV at pH of 7.0. This negative charge is mainly attributed to the silica groups present on the surface of halloysite nanotubes. After doping, the surface potential of doped HNTs was notably increased. The zeta potential value of DHNT F1 sample was -58.15 mV, indicating the moderate stability of formulation. In comparison to DHNT F1 sample, the zeta potential values for both DHNT F2 and DHNT F6 sample was found to be -79.23 mV and -87.15 mV suggesting the good stability and homogeneity of the formulation. Whereas, DHNT F4, DHNT F5 and DHNT F8 sample exhibited the surface potential values of -66.2 mV,-60.45 mV and -73.61 mV. This reduction in zeta potential is mainly attributed to the scarcity of –OH groups on the surface of HNTs. Similarly, DHNT F3 and DHNT F7 sample showed an increased zeta potential value of -90.38 mV and -95.7 mV. The

exhibition of higher zeta potential value corresponds to excellent stability and dispersibility of the sample.

Experimental Design Analysis

Statistical analysis for angle (2θ) and zeta potential (mV): The model F-value of 50.57 implies that the model is significant for Angle (Y1) and there are 0.12% chances that a model F-value seems to be higher due to the noise for each case. From the data obtained, it is crystal clear that, the variable X1 (amt of γ-MPS) and X3 (amt of Ethanol) were statistically significant for the response Y1, as the ($p<0.05$). Similarly, another variable X2 (amt of HNT) was found to be statistically non-significant for response Y1, as ($p>0.05$). The model F-value of 182.68 implies that the model is significant for Zeta Potential (Y2) and there are 0.10% chances that a model F-value seems to be higher due to the noise for each case. From the data obtained, it is crystal clear that, the variable X1 (amt of γ-MPS), X2(amt of HNT) and X3 (amt of Ethanol) were statistically significant for the response Y2, as the ($p<0.05$).The results of ANOVA analysis indicate that the influence of independent variables on the response variables was found to be statistically significant ($p<0.05$). The result of % error for both the responses was found to be below 5%, signifying that the optimized sample was reliable and reproducible.

Conclusion: Halloysite nanotubes were successfully doped with γ-MPS by using ultra turrax homogenizer. The results of statistical analysis indicate that the application of custom design proves to be an ideal tool for optimizing the doping of halloysite nanotubes.

Key words: Halloysite nanotubes, γ-methacryloxypropyltrimethoxysilane, Optimization, Custom design.

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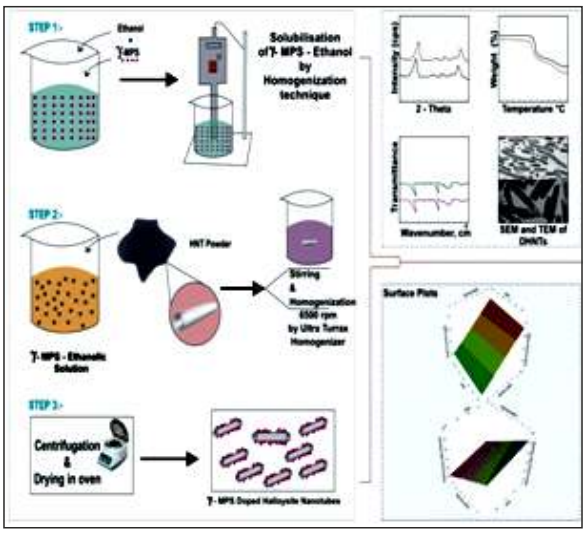
Graphical Abstract



Hydrothermal synthesis of Hydroxyapatite-Graphitic Carbon Nitride Composites doped with Magnesium and their Characterization

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Bioceramics can be defined as biocompatible ceramic materials that are used for bone repair and reconstruction of diseased or damaged parts of tissues. Calcium phosphate based bioceramics are the alternate material available for the bone tissue replacement and regeneration therapies due to their excellent biocompatibility and osteoconductivity. The most widely used member of the calcium phosphate family is hydroxyapatite (HAP) with a Ca/P ratio of 1.67. HAP is an osteogenic, osteoconductive, osteoinductive, bioactive, non-toxic, biocompatible, bioceramic commonly used for bone tissue engineering and as a drug carrier of chemotherapeutics. The flexibility of its apatite structure makes HAP to accept metal substitutions. The high ion-exchange and sorption capacities enable substituted HAPs as promising adsorbent for removal of toxic heavy metals. Magnesium (Mg) plays a vital role in muscle activity, nervous system, membrane transport, cell proliferation, mineral metabolism, and it also regulates osteoclast functions. When compared to other metal ions, doping of Mg in the HAP lattice offers numerous advantages for bone tissue engineering. Mg also plays an important role in widening the electron–hole pair separation and extending the range of light response, thus improving the photocatalytic activity. Mg-doped HAP is very essential for the better bone development with higher antibacterial activity and expected to have a high biocompatibility. Graphitic carbon nitride (GCN), the most stable allotrope of carbon possesses good chemical and thermal stability, nontoxic in nature, inexpensive and makes it applicable along with the hydroxyapatite for photocatalytic degradation of pollutants, bone regeneration and adsorption studies. The present work aims to synthesize HAP-GCN composites by hydrothermal treatment and dope the composites with varying concentrations of Mg^{2+} ions (0.01 M, 0.05 M, 0.10 M, and 0.50 M). Calcium nitrate tetrahydrate (1.00 M) and ammonium dihydrogen phosphate (0.06 M) are used as precursors for preparing pure HAP. Magnesium nitrate hexahydrate was used as the precursor for Mg doping. Melamine was used as the precursor for the synthesis of GCN. For the synthesis of pure HAP, the ammonium dihydrogen phosphate solution is added drop-wise to the calcium nitrate tetrahydrate solution with stirring. For the synthesis of HAP-GCN composite, melamine was added to the calcium nitrate tetrahydrate solution, stirred for 2 h to ensure complete mixing followed by drop-wise addition of ammonium dihydrogen phosphate solution. For Mg doping, varying concentrations of magnesium nitrate hexahydrate was

added to the calcium nitrate tetrahydrate solution with suitable adjustments in the Ca^{2+} ions concentration. The reaction mixture was subjected to hydrothermal treatment at 150 C for 2 h, dried in oven at 110 ^{0}C followed by calcination at 550 ^{0}C for 3 h. The samples were characterized further for their functional groups by Fourier transform infrared spectroscopy (FT-IR) and for their phase purity and crystallinity by X-Ray diffraction (XRD) measurement. The morphology of HAP, HAP/GCN and Mg-HAP/GCN was assessed using a scanning electron microscope (SEM) and the elemental composition was analyzed using energy dispersive X-ray analysis (EDAX).

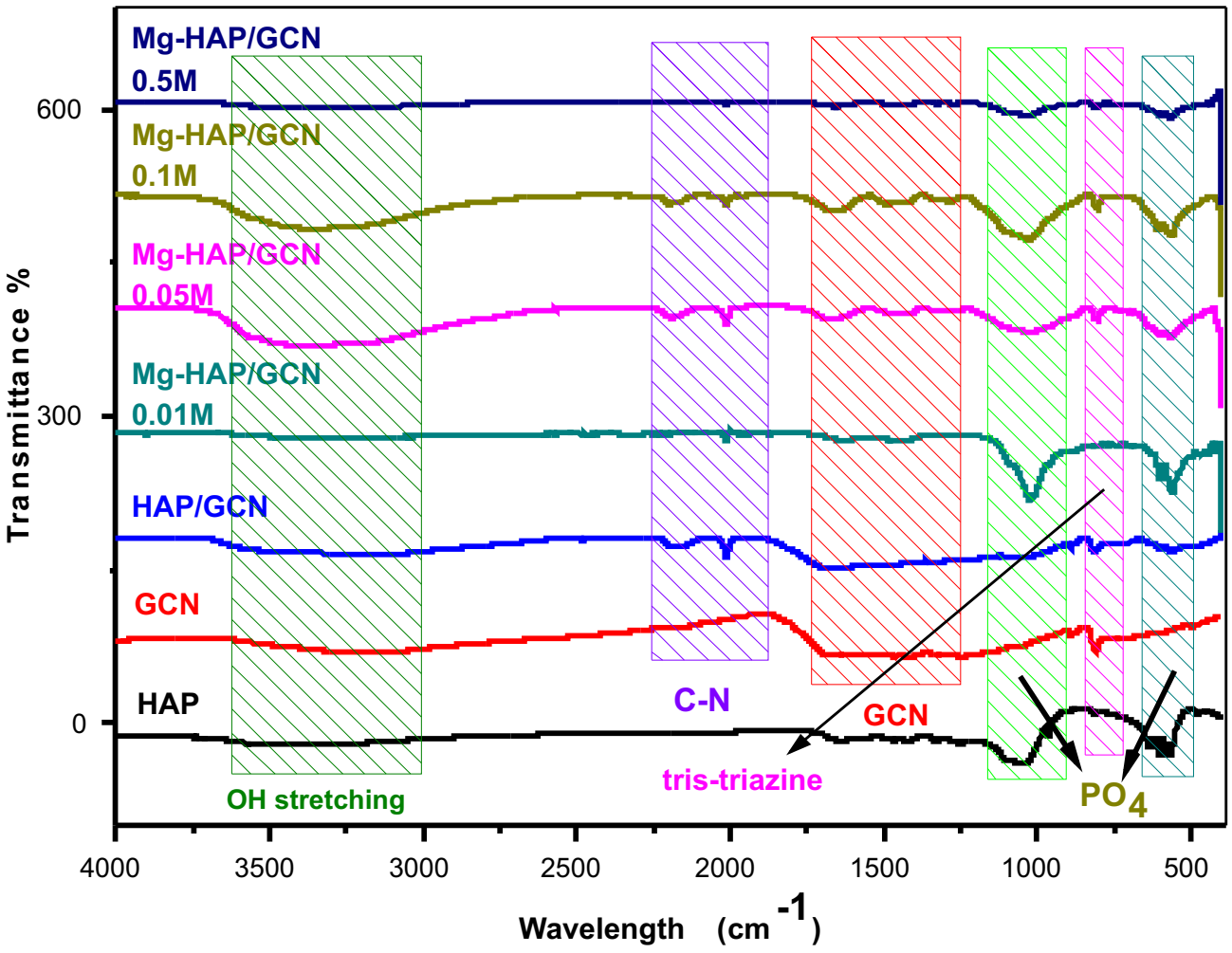

Figure 1: FT-IR spectra of HAP, HAP/GCN and Mg-HAP/GCN composites

The FT-IR spectra of HAP, HAP/GCN and Mg-HAP/GCN composites are shown in Figure 1. The IR bands in the region between 1020 cm^{-1} and 1030 cm^{-1} can be assigned to the PO_4^{3-} group of the HAP/GCN and Mg-HAP/GCN composites. The broad peak around 3178 cm^{-1} can be correlated to the stretching modes of CN heterocycles of GCN while the bands observed in the region between 1200 cm^{-1} to 1650 cm^{-1} can be ascribed due to the C-N/C-C stretching vibrations. The IR band at 799 cm^{-1} and at 808 cm^{-1} are due to the triazine cycles of GCN. The better biocompatibility of GCN combined with the bioactivity of HAP is likely to make HAP-GCN composite a useful alternative for HAP in terms of improved strength and better solubility. Mg-doping is likely to improve the antibacterial properties of the Mg-HAP/GCN composites.

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In-silico Analysis of Thymoquinone as Anti-cancer Agent against Chemoresistance Associated Proteins in Ovarian Cancer

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Results

Thymoquinone (TQ) plays an important role in the prevention and treatment of ovarian cancer (OvCa). The screening of structure-based designs is essential for drug discovery and understanding the role of proteins in cancer and cisplatin resistance. In the present study, we provide illustrations for the interaction between chemoresistance proteins such as Bcl-2, Bax, STAT3, p53, and caspase-3/9 with TQ for a probable anti-cancer activity. The initial data information about the ligand (TQ) such as IUPAC name, CID number, molecular formula, and canonical SMILES ID was collected using PubChem. The canonical SMILES were subjected to an online SMILES translator for structure generation and the structure was saved in .pdb format with 3D coordinates. Further, energy optimization of TQ was evaluated using Avogadro's Software. The optimization was to build a computational model and satisfy the valency. After evaluation, the optimized energy obtained was TQ=16.99 kJ/mol. The receptor (proteins- Bcl-2, Bax, STAT3, p53, and caspase-3/9) sequence was collected with the help of UniProt. The receptor sequence was subjected to homology modeling using Phyre2 and SWISS-MODEL. The models generated from SWISS-MODEL and Phyre2 were analyzed for corresponding sequence match, match percentage, and human origin along with structure resolution. We used AutoDock Tools to remove water molecules and add polar hydrogen. PatchDock was used for molecular docking of TQ and proteins with root mean square deviation (RMSD) the cluster at ≤1.5Å. Atomic Contact Energy (ACE) was used as a parameter to analyze the solutions. We visualized the ligand and receptors using Discovery Studio. SWISS-MODEL also gave validation of docked solution through Ramachandran Plot in Discovery Studio. The docking results for Bax showed binding of TQ was significantly strong at Trp158 with ACE -87.32. Similarly, Bcl-2 amino acid residues were docked at Arg127, Gly155, Ser105, and His20 at BH1, BH3, and BH4 (not seen at BH2) domains. p53 binding was, obtained at Tyr234, Met237, Ala161, Arg174 at DNA binding domain. The amino acid residues in the SH2 domain showed strong binding for Arg609, Pro669, and Gln644 for STAT3. TQ interacts with Caspase-3 subunits p12 and p17 several positions through hydrogen bonds. TQ also binds to active sites within the subunit chains Arg165, His121, Gln162, and Ser151. TQ also binds to the CARD domain strongly at position Gln21.

Discussion

TQ has been studied for its anti-cancer properties in various cancers. However, specific expressions of apoptotic markers in OvCa and its cisplatin-resistant cells upon TQ treatment have not been elaborated before. Complementing our in-vitro studies, we have carried out in-silico analysis of TQ molecular docking with proteins of interest in OvCa as well as the ones contributing to cisplatin resistance. PubChem was used to retrieve all the relevant information and SMILES. 3D structure and pdb coordinates of TQ were generated using NCI/CADD group Online SMILES translator and structure file generator. After deleting water molecules and adding polar hydrogens to balance the valency in AutoDock tools, the geometry was optimized in Avogadro software to achieve the lowest binding energy during molecular docking. UniProt is a protein database that has all the available data on different proteins of various organisms. Bax, Bcl-2, STAT3, P53, Caspase-3/9 for Homo sapiens were looked for sequences, relevant domains, and regions involved in cancer activities. Whole protein, as well as specific domain sequences, were retrieved and used for homology modeling to achieve structures and pdb files. Phyre2 and SWISS-MODEL are two servers used for building 3D models of the proteins. Phyre does this by aligning the hidden Markov models and gives scores for a structure match within databases like PDB (Protein Data Bank). We got better models from the SWISS-MODEL ExPASy web server. After aligning the sequences using BLAST algorithm templates, it builds the model for the specific sequence and optimizes the structure by energy minimization. Moreover, it was convenient to select appropriate models using SWISS-MODEL as it comes with the quality check and Ramachandran Plot validation for each model. In cases of dock failures with a couple of SWISS-MODEL structures (which may be due to reasons like low structure resolution or the absence of appropriate binding sites), Phyre2 structures were used for molecular docking with TQ. Due to a large number of protein sequences and blind docks at all the available binding sites within the sequence, we opted for an online docking software PatchDock. The top ten best results were downloaded and visualized using Discovery Studio. The docking solutions of TQ and the proteins with conventional and Carbon-Hydrogen bonds were selected. Other parameters like bond length and atomic contact energy (ACE) were also used to assess their affinity. Discovery Studio also gave post-docking structure validation through Ramachandran Plots. The whole structure and specific sequences within the protein gave some interesting dockings with TQ which were analyzed with reference to the sequence information on UniProt. These include interactions with amino acid residues within domains responsible for pro-apoptotic activities. TQ interacts with amino acids Arg127, Gly155 of BH1 domain, Ser105 of BH3 domain, and His20 of BH4 domain. The strong interactions with BH3 and BH4 domains suggest a modulatory role of TQ in Bcl-2's anti-apoptotic activity. Therefore, in the case of TQ treatment, the anti-apoptotic activity of Bcl-2 may be downregulated, to ensure the apoptosis of OvCa cells. Although the pro-apoptotic domain in Bax did not show any interaction with TQ, it did bind to other amino acids which might have some regulatory effect on Bax. Similarly, TQ showed interactions with the proteins STAT3, Caspase-3/9 that take part in apoptotic activities in OvCa. Since these proteins are also involved in the cisplatin-resistance mechanisms, their interaction with TQ is relevant for its anti-cancer activities in this scenario. Corresponding work in the wet lab which is currently ongoing in our studies will further confirm these interactions and modulation in protein expression levels.

Influence of Iron doping in Hydroxyapatite-Graphitic carbon nitride composite towards the physiochemical characteristics

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Hydroxyapatite (HAP) is the most studied material as a bone substituent due to its similarities with the mineral part of bone and it has a Ca/P ratio of 1.67. The key properties of HAP include bioactivity, osteoconductivity and biocompatibility. To improve the characteristic properties of HAP, formation of composites with HAP and doping are suggested as viable options. Graphitic carbon nitride (GCN) is a polymeric material composed of tris-triazine-based patterns with the C/N ratio of 3/4. GCN based composites possess fluorescent, electroluminescent, biocompatibility and antibacterial properties, which opens up new avenues for its use in biomedical application such as wound healing application, bone regeneration and fracture healing, photodynamic therapy (PDT) and bio-imaging an drug delivery. Doping of HAP with iron (Fe) improved the cytocompatibility, hemolysis and antibacterial properties. Fe-doped HAP assumed significance in controlled drug delivery, magnetic resonance imaging (MRI), and hyperthermia therapy. The present study aims at to synthesize HAP-GCN composite and to dope it with Fe so that the desired characteristics can be imparted. The HAP was synthesized by chemical precipitation method using 1.0 M $Ca(NO_3)_2 \cdot 4H_2O$ and 0.60 M $(NH_4)H_2PO_4$ as precursors. Melamine was used as the precursor for the synthesis of GCN. For preparing HAP/GCN composite, 4 g of melamine was added to the $Ca(NO_3)_2 \cdot 4H_2O$ solution, stirred vigorously for 2 h followed by drop-wise addition of $(NH_4)H_2PO_4$. The resultant precipitate was aged overnight at 25 C, filtered, washed and dried overnight at 100 ºC. Subsequently, the precipitate was sintered in a muffle furnace at 550 ^{0}C for 2 h. For the synthesis of Fe-HAP/GCN composites, the concentration of Fe was varied (0.01, 0.05, 0.10 and 0.50 M). The required amount of Fe was added to the $Ca(NO_3)_2 \cdot 4H_2O$ solution so as to adjust the total concentration of Ca^+ Fe is 1.0 M. A similar protocol was employed for the synthesis of HAP/GCN and Fe-HAP/GCN. The HAP, HAP/GCN and Fe-HAP/GCN samples were characterized by X-ray diffraction (XRD) measurement, Fourier-transform infrared (FT-IR) spectroscopy, scanning electron microscopy (SEM) and energy-dispersive X-ray (EDS) analysis. The XRD patterns confirm the formation of HAP, HAP/GCN and Fe-HAP/GCN composites (Figure 1). There is a considerable reduction in peak intensity and broadening of the peaks are observed upon formation of HAP/GCN composite. Doping of higher concentration of Fe (0.50 M) changes the crystallinity of Fe-HAP/GCN composites. The FT-IR spectra indicate the presence of peaks pertaining

to the hydroxyl and phosphate groups of HAP along with the peaks pertaining to GCN, validating the formation of HAP/GCN and Fe-HAP/GCN composites. The morphological features reveal that the pure HAP is rod-shaped, which is transformed to a fluffy sponge-like structure when HAP is formed a composite with GCN. The EDS analysis indicates the presence of Ca, P and O as major elements for HAP while presence of additional peaks corresponding to Fe, C and N are noticed for HAP/GCN and Fe-HAP/GCN composites, validating the formation of composites and doping of Fe. Pure HAP lacks antibacterial activity whereas the HAP/GCN due the presence of GCN imparts better antibacterial activity. Fe-HAP/GCN can be effectively used for hyperthermia therapy. Further studies are currently under progress.

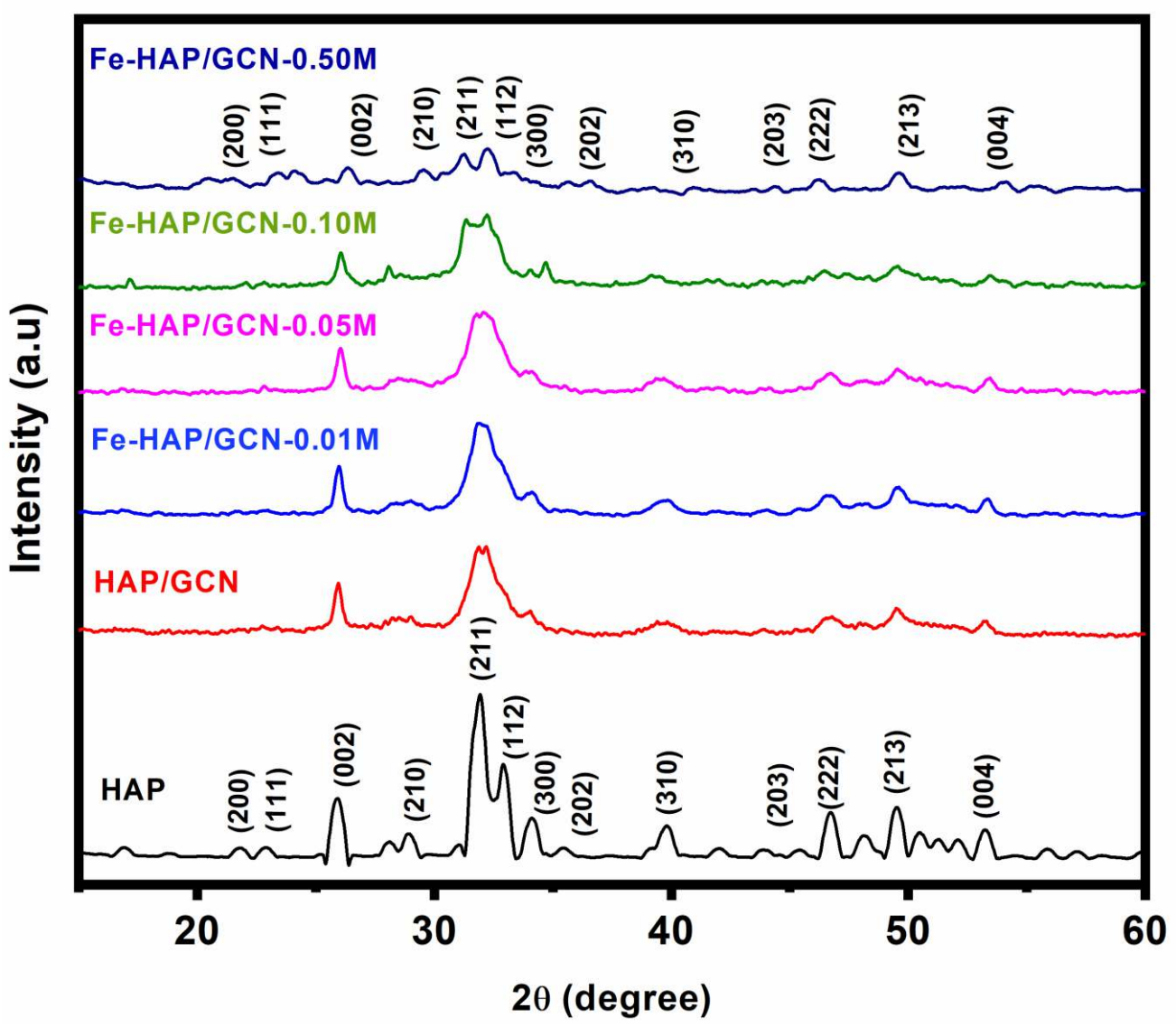

Figure 1: X-ray diffraction pattern of HAP, HAP/GCN and Fe-HAP/GCN composites synthesized using varying concentrations of Fe (0.01 M, 0.05 M, 0.10 M and 0.50 M).

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Synthesis, Characterization of Novel Quaternary Ammonium Based Antimicrobial Monomer for Dental Applications

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Background of the study: A novel antimicrobial monomercan be used as antimicrobial agent to reduce the colonization of Candida albicanson the denturebaseprosthesis.These monomer having a unique property of being copolymerizing with PMMA denture base resin and provide long term antimicrobial efficacy without being released [1].

Objectives: Aim of the present study was to synthesize and characterize quaternary ammonium based antimicrobial monomer such as quaternary ammonium dimethyl-hexadecyl-methacryloxyethyl-ammonium iodide (DHMAI) and assess its cytotoxicity and antimicrobial propertyfor prosthetic applications for the treatment of denture induced stomatitis (DS).

Methods: DHMAI monomer were synthesized through a Menschutkin reaction and its chemical structure was characterized using FTIR, 1H-NMR. The cytotoxicity and antimicrobial activity was assessed using Methyl Thiazolyl Tetrazolium (MTT) assay and Minimum Inhibitory Concentration (MIC) test respectively [2].

Results: FT-IR and 1H-NMR results confirmed the structure of DHMAI monomer. MIC result revealed that DHMAI exhibited better antimicrobial activity(DHMAI at 1 µg/mL) and are found to be cytocompatible with mouse fibroblast cells up to a concentration of 5 µg/mL.

Significance: The results of the present study indicates DHMAI improved the amicrobial activity and found to be cytocompatible hence can be effectively used as a promising antimicrobial agent for dental applications in preventing DS.

Keywords: Denture stomatitis, C. albicans, antimicrobial monomer, PMMA denture base resin.

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Nanotized Praseodymium Oxide Stabilized Collagen Biomatrix for Soft Tissue Engineering Application

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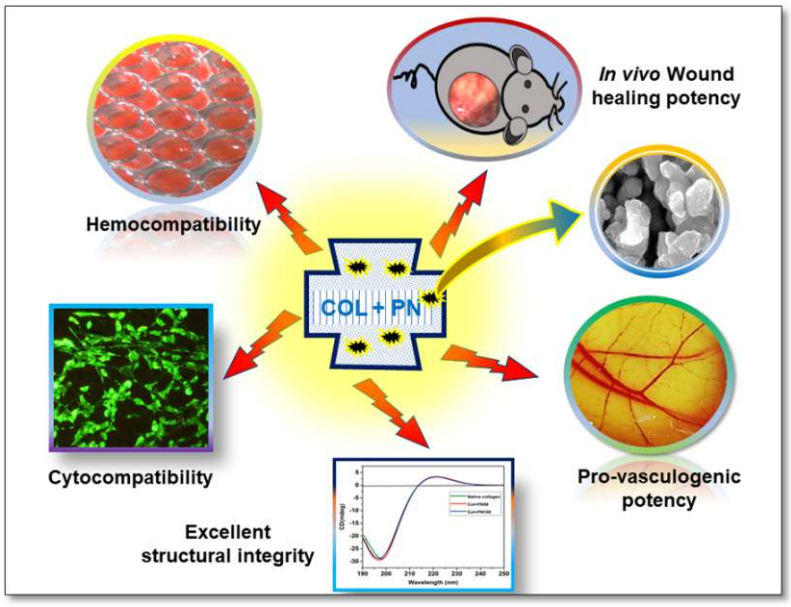
The study involves the development of a highly vascularisable collagen biomatrix scaffold containing rare-earth metal Praseodymium oxide nanoadditives for angiogenic and soft tissue regenerative applications. The therapeutic potential of Praseodymium oxide nanoparticles rendered pro angiogenic microenvironment by upregulating VE-Cadherin expression in the scaffold. The incorporation of praseodymium oxide nanoparticles into collagen induced the stabilization of collagen without compromising the structural integrity of collagen. The nanoparticle stabilized scaffolds possess less susceptibility towards protease enzymes, high cyto-compatibility and high hemo-compatibility which are the desired properties of a biomaterial. The scaffold provided necessary micro-environments for the proliferation of endothelial cells and fibroblast cells eliciting the wound healing process *in vivo*. Biological signal modulatory property of rare earth metals remains an unexplored domain that can bring significant therapeutic improvement in developing advanced biomaterials. This study opens up the path for exploring the potential use of nano-scaled rare earth metals in biomaterial application for tissue engineering applications by modulating the pro-angiogenesis effect. (*V. Vijayan, et al., Nanomedicine, 2021, 33, 102364*)



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Supramolecular Nanostructures mediated Bioglass Composite as Bone Matrix Mimick

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The remarkable paradigm shift from tissue replacement to tissue regeneration in the last decade focuses on designing smart artificial scaffolds that replicate the structural and functional characteristics of natural tissue thereby, inducing a positive response in the body of self-healing development. Bone tissue forms biologically inspired materials that have been a continuous field of regenerative medicine and biomedical engineering and bioactive glasses (BG) have evolved as precursor for bone regeneration thereby bringing a revolution in healthcare in the context of modern biomaterial-driven regenerative medicine. However, the development of such materials at stringent high-temperature synthetic protocol and lack of high fidelity structure-functional understanding has so far been limiting its clinical application. The templates used for designing the BG materials have a pivotal role in directing some of the crucial parameters such as ease of synthesis, 3-D network, mechanical property, biocompatibility and biodegradability. Thus, changing from conventional templates such as chitosan, gelatin to supramolecular peptide fibers enables us with the above advantages to eventually achieve an efficient biomimetic mineralization pathway. Such peptide-based supramolecular biomaterials are intriguing owing to their de novo design at molecular level to hierarchical self-assembly to eventually mimic the natural biopolymers present in ECM. [1]

For the first time, we discuss the role of living supramolecular polymerization assemblies in controlling structure-property of peptide-BG composite materials, a strategy hitherto unexplored in this field. We postulate the mineralization of the BG materials to promote hydroxyapatite formation utilizing the positively charged lysine moieties of biomimetic peptide nanostructures and subsequent improvement in the mechanical properties and stability of the composite hydrogel.[2] These nanocomposites were tested for osteogenic activities and the results endorse development of a sustainable nanocomposite with high load bearing ability and profound bioactivity which can be employed for bone tissue engineering application.

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BIOTEM-2021

Poster Student

Bioenhancement of antipsychotic drug by enzyme inhibition

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Asenapine maleate, an antipsychotic drugs used in the management of schizophrenia, both these drugs have extremely poor bioavailability due to rapid first pause metabolism mediated by the CYP and UGT family of enzymes. Oral route of drug delivery remains to date the safest and most patient compliant route of drug administration, in this study we have attempted to increase the oral bioavailability of asenapine maleate by administering it in conjunction with certain bioenhancers. With extensive literature survey it has come to our attention that the current method of bioavailability improvement adopted by us has not been tried and tested for asenapine maleate[1].

Molecular modelling platform by Maestro, *Schrödinger* was used to screen a list of bioenhancer. Bioenhancers that showed the greatest docking score and ideal interactions in MD simulations were selected for *in-vivo* pharmacokinetic studies. Male wistar rats were divided into groups, following which the drugs and bioenhancers were administered orally in different administration regimes. At predetermined time intervals, blood was collected from retro orbital plexus and amount of drug was quantified using HPLC. Pharmacokinetic parameters were estimated using Phoenix Winnonlin software, PkSim software use then use to generate a physiology based pharmacokinetic model with which human pharmacokinetic parameters were predicted. It was seen that the co-administration of asenapine with bioenhancer increased the pharmacokinetic properties of the drugs significantly, in the PBPK model as well a similar increase was seen.

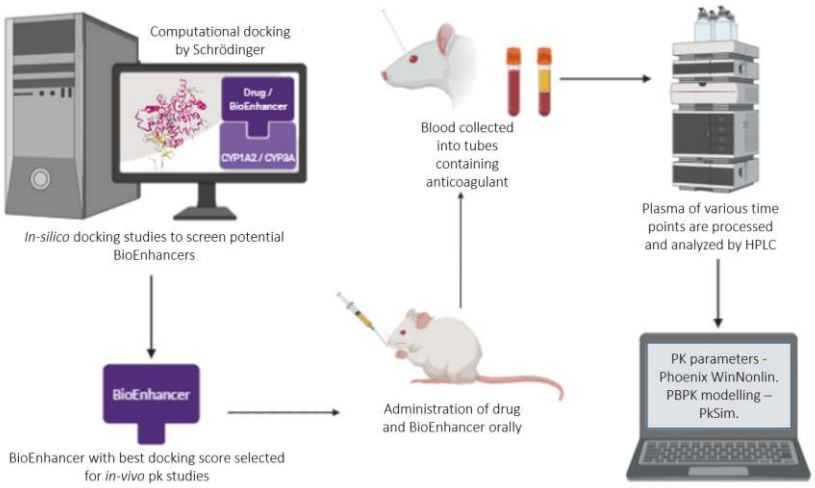

Figure: Graphical Abstract

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Biomimetic Surface Patterning of Honey Embedded Silk Fibroin Porous Scaffold Improves Mesenchymal Stem Cell Proliferation, Differentiation, Epithelial Transition, and Restrain Senescence

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Premature cell ageing and irreversible arrest of cellular growth due to impaired proliferation and replicative senescence are major challenges associated with maintenance of mesenchymal stem cells in regenerative medicine [1]. To circumvent these, we developed a hierarchically patterned porous honey loaded silk fibroin scaffold using a combination of soft lithography and freeze-drying technique. Soft lithographically embossed biomimetic microdome arrays on 2% honey incorporated silk fibroin porous scaffold (PHSF2) was the most comparable to native environment required for stem cell adhesion and proliferation among all the studied variants as parametric variations showed enhanced surface roughness, swelling, and degradation rate with good interconnective porosity and mechanical strength for this particular substrate. PHSF2 also depicted sustained release of honey eventually contributing to remarkable antibacterial efficacy against methicillin resistant *Staphylococcus aureus* (MRSA). A frugal approach by simple replication of rose petal surface structures provided sticky hydrophobicity which allowed cellular pseudopods to anchor on the substrate surface by altering their cytoskeletal rearrangement and thereby increased cellular spreading area and cell sheet formation. Both Nitro blue tetrazolium assay and DCFDA fluorescence spectroscopy revealed limited free radical generation within stem cells followed by molecular expression studies showing decreased p53 and p21 expression and a correlation with decreased senescence-associated β galactosidase activity assured synergistic effect of biophysical cues (patterns) and biochemical cues (honey) on preventing untimely halt of stem cell growth. Traits of underpinning mesenchymal to epithelial transition was showed by PHSF2 as an increase in the molecular expressions of CDH1, CK19, SOX9, RUNX2, and PPARγ was observed. This work highlights thrifty fabrication of a potential stand-alone smart stem cell delivering regenerative healing implant.

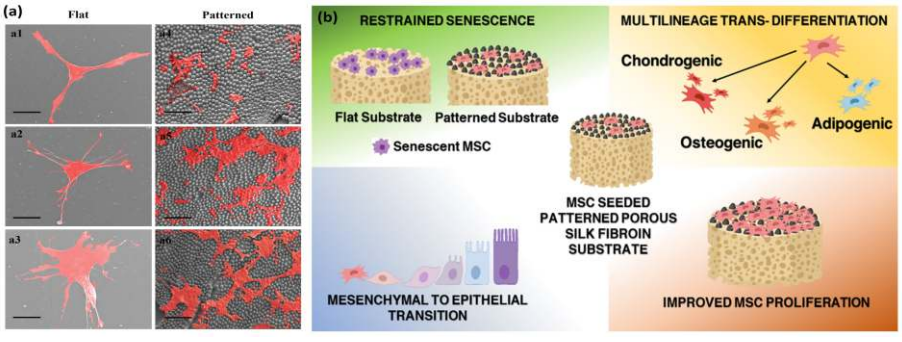

Figure 1: (a) SEM micrographs of mesenchymal stem cells growing on flat and patterned scaffold surfaces (b) schematic showing single scaffold with multiple effects on mesenchymal stem cells

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Chitosan microspheres of quercetin and selenium to treat dimethylhydrazine induced colon cancer in rats

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Chitosan is a natural polysaccharide with biomedical applications. In pharmaceutical industries, chitosan has multiple applications, especially in drug delivery technology. Another natural product, quercetin, is known for its biological activity, such as anti-cancer activity. Selenium was reported to enhance anti-cancer activity. Hence, the purpose of the current work was to assess the combined effect of quercetin and sodium selenite loaded chitosan microspheres in Wistar rats having 1,2-dimethylhydrazine (DMH)-induced colon cancer. Microspheres were prepared by emulsification technique and characterized by DSC, FTIR and SEM. The encapsulation efficiency was 74.30 and 55.12% for quercetin and selenium microspheres, respectively. Colon cancer was induced in rats by DMH (30 mg/kg/week, i.p.) for 16-weeks. After confirming colon carcinogenesis, the rats were divided into eight groups and treated with microspheres for four weeks. The results are compared to those of normal and disease controls. A reduction in the number of aberrant crypt foci (ACF) and cancerous polyps were observed upon treatment with quercetin and selenium microspheres. The combined effect revealed a significant reduction in the ACFs and polyps, but it did not show advantages over the quercetin (10 mg/kg, p.o) and sodium selenite (0.03 mg/kg, p.o.) pure and combination as well as individual microspheres. The oxidative stress markers and inflammatory markers in colon tissue were modulated upon treatment with microspheres. However, there was a cause of concern on haematological and biochemical toxicity of sodium selenite microspheres.

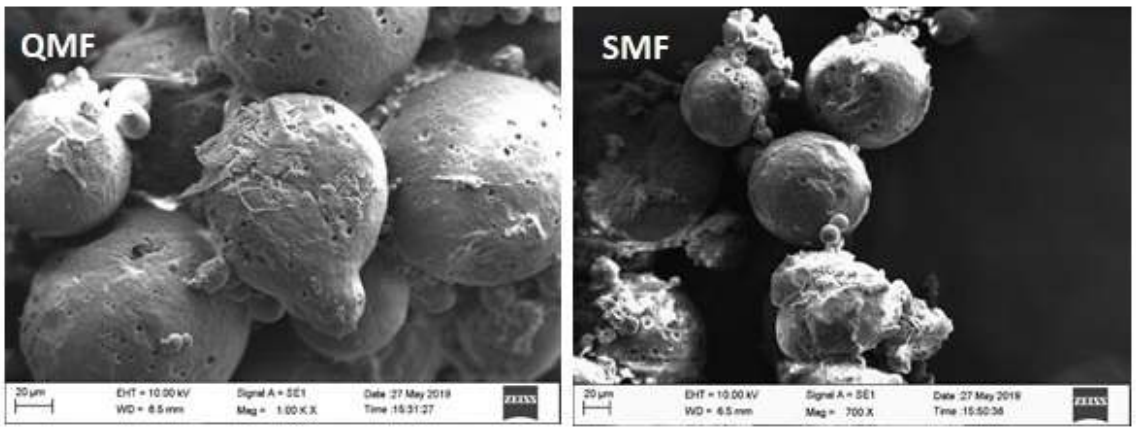

Figure 1: SEM images of Quercetin and selenium microspheres. QMF: Quercetin microsphere formulation; SMF: Sodium selenite microsphere formulation

Development of the polymer-induced molybdenum disulfide nanocomposition and its antibacterial activity

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Microbial diseases are a major concern to public health all around the world. Excessive use of antibiotics and failure of conventional antibiotic treatments is the biggest challenge in the biomedical field. With this regard, researchers are developing novel metal-based nanomaterials as antimicrobial agents. Hence, in this study, the hydrothermal technique followed by the liquid exfoliation approach was used to produce a polymer-induced MoS_2 nanocomposite. A developed nanomaterial was characterized by using several analytical techniques. The UV-visible spectrum confirms the formation of hydrothermally developed MoS_2 nanosheets and polymer-induced MoS_2 nanocomposite. a Physico-chemical property of the MoS_2 nanosheets and polymer-induced MoS_2 nanocomposite were studied by Fourier-Transform Infrared (FT-IR) spectroscopy, X-ray diffraction (XRD) analysis, and Raman analysis. Dynamic light scattering (DLS) analysis shows that after exfoliation diameter of the MoS_2 nanosheets has reduced. Atomic force microscopy (AFM) analysis suggests that we succeeded to develop few-layered MoS_2 nanosheets. Furthermore, the antimicrobial assays reveal that developed nanocomposite has remarkable antibacterial activity against *Staphylococcus aureus* (*S. aureus*) and *Streptococcus mutans* (*S. mutans*). Hence, developed nanocomposite has promising applications in the biomedical field.

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Decellularized plant tissues as natural 3D cellulosic scaffolds for tissue engineering applications

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In this study, *Borassus flabellifer* (Linn.) (BF) immature endosperm was decellularized to produce three dimensional (3D) cellulose scaffolds that can support mammalian 3D cell culture. To this regard, we first evaluated the chemical composition, nutritive profile and pharmacological activities of BF endosperm. The results demonstrated that the BF tissue represented a complex concoction of polysaccharides with intrinsic phyto-ingredients which provide excellent pharmacological properties. Furthermore cellulosic scaffolds (CS) obtained from BF was treated with chitosan to produce cellulose-chitosan (CS/CHI) hybrid scaffolds. The comparative investigation on both scaffolds exhibited adequate swelling with controlled porosity and pore-size distribution. The physiochemical characterization showed reduced biodegradation, improved thermal stability and enhanced compressive strength in CS/CHI group. Biological studies reported favorable adhesion and proliferation of fibroblasts with evident cellular penetration and colonization on the both scaffolds. Taken together, plant derived cellulosic scaffolds could be used as an alternative scaffolding material in regenerative medicine.

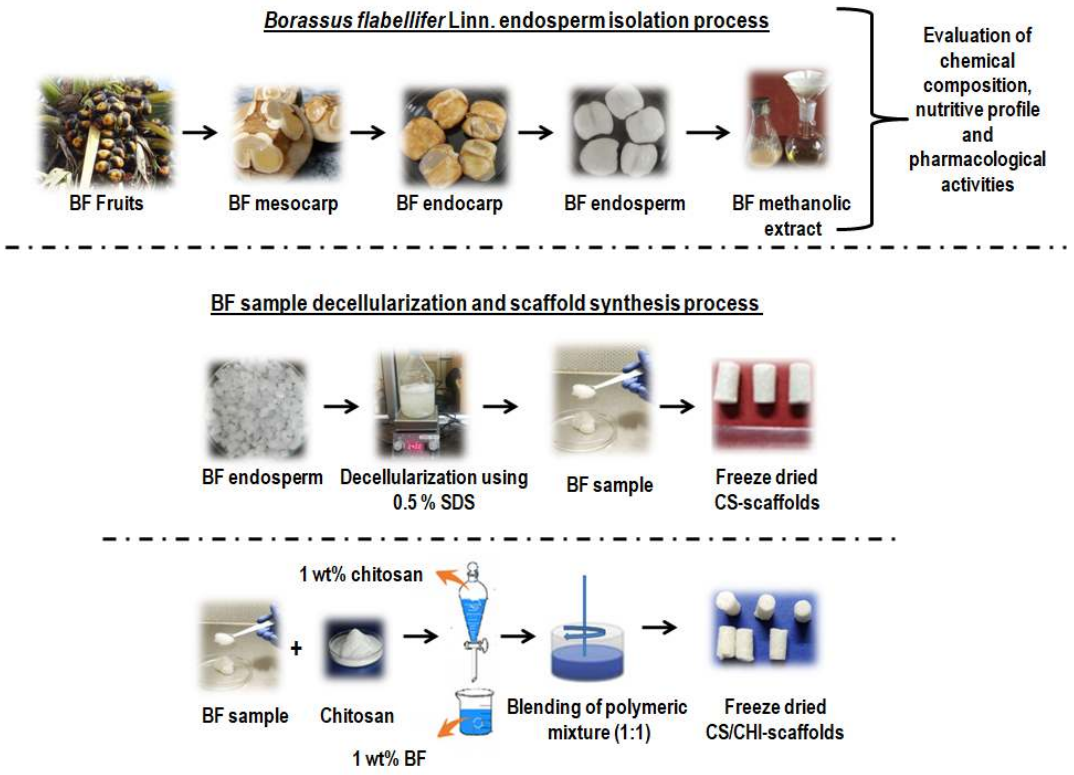

Figure 1: Pictorial step-wise representation of BF endosperm isolation, nutritional and pharmacological profiling, decellularization and scaffold synthesis process

Hydroxyapatite nanophases augmented with selenium and manganese ions for bone regeneration: Physiochemical, microstructural and biological characterization

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Hydroxyapatite (HAP) nanopowders with different manganese (Mn) and selenium (Se) contents with Mn/Ca and Se/P molar ratio of 1 mol%, 2.5 mol% and 5 mol% were synthesized by wet-co-chemical precipitation method. The results revealed that with either Mn or Se doping, ion-substituted apatite phase was achieved with good crystallographic features. The combined evidence obtained from spectrometric techniques revealed that nanocrystalline HAP was effectively doped with Mn and Se ions, where Se in form of $SeO3^{2-}$ replaced $PO4^{3-}$ and Mn^{2+} replaced Ca^{2+}. Mn and Se doped HAP samples exhibited rod-like and needle-like morphology with strong tendency to form agglomerates. HAP enriched with Mn and Se represented a strong antibacterial effect and also showed prominent blood compatibility. From the biocompatibility testing, it was evident that Mn and Se doped HAP augmented the osteoblasts adhesion, migration and proliferation in a dose-dependent manner. To conclude from this study, it is clearly evident that the doping amount of both Mn and Se ions can determine the size and morphology of the final HAP product. Therefore, Mn and Se HAP nanopowders with molar ratio less than 5 mol% without any heat treatment can provide good crystallographic features to HAP with satisfying micro-structural, thermal and biological properties.

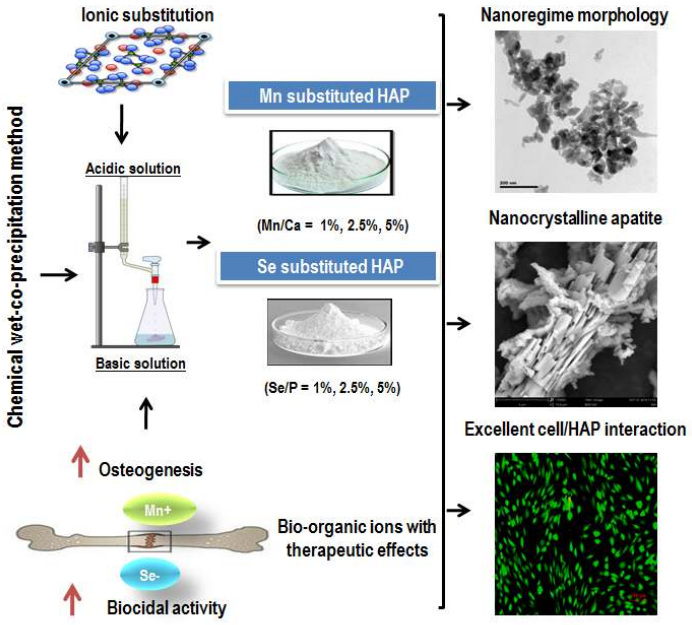

Figure 1: Pictorial step-wise representation of chemical-co-precipitation of HAP synthesis with substitution of Mn and Se ions in the crystal lattice.

Role of Fiber Thickness and Surface Treatment of Electrospun Polycaprolactone Matrices on the Growth of Different Breast Cancer-Associated Cells

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Cancer models mimicking the tumor microenvironment are necessary to successfully develop and predict responses of oncological drugs. In this study, electrospun polycaprolactone (PCL) matrices were tested for the development of an in vitro breast cancer model. The effects of fiber thickness and plasma-treatment of the matrices on *in vitro* growth of breast cancer-associated cells, namely breast cancer cells MDA-MB-231, primary adipose-derived stem cells (ADSC) and primary endothelial progenitor cells (EPC) were evaluated. PCL was electrospun in random-orientation into nanofibers (125 ± 32 nm) and microfibers (8801 ± 716 nm) and aligned-nanofibers (865 ± 104 nm) matrices and characterized by scanning electron microsocopy (SEM). Surface treatment of the matrices by air-plasma led to increased oxygen/carbon ratio and hydrophilicity, characterized by x-ray photoelectron spectroscopy (XPS) and water contact angle measurements respectively. WST-8 analysis revealed that the metabolic activity of all three cell types increased exponentially over 12 days on all matrices. MDA-MB-231 and ADSC showed a higher metabolic activity on nanofibers due to enhanced cellular adhesion compared to microfibers, and grew similarly on hydrophobic and hydrophilic matrices. In contrast, EPC showed a significantly higher metabolic activity on microfibers than on nanofibers at day 12 and had further significantly improved growth of hydrophilic matrices. Cross-sectioning analysis showed that cells grew on the surface of nanofibers (< 20 µm), while microfibers had considerable cellular infiltration (> 200 µm). Fluorescent ubiquitination cell cycle indicator (FUCCI)- transfected MDA-MB-231 cells indicated the cells in growth (G1) and mitotic (S/G2/M) phases, while mammosphere formation assay indicated the enhancement of cancer stem cell population (CSC) within the MDA-MB-231 cells when cultured on PCL matrices. These findings suggest that the electrospun PCL matrices are a suitable tool for the development of breast cancer models containing several cell types, which could ultimately lead to designing novel tumor therapies.

Oxaliplatin Pt (IV) prodrugs conjugated to Human serum albumin as potential antitumor agents

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Cancer is a leading cause of mortality worldwide, accounting for almost 10 million deaths in 2020 (World Health Organization). Nanomedicine has emerged as a promising strategy for effective cancer treatment. In this work, reductive microenvironment-sensitive long-circulating human serum albumin conjugated oxaliplatin nanoparticles were prepared. Compared to the normal cells, cancer cells show a 100-1000-fold upsurge in the redox potential and presence of glutathione. The disulfide bonds are reduced into sulfhydryl groups in the presence of glutathione, which leads to faster drug release.Here, oxaliplatin is conjugated with dithiodiglycolic acid and conjugated to HSA. The formation of product was confirmed at every step by ^{1}H NMR and change in zeta potential. The NPs were Characterized using particle size analyzer, loading efficiency, powder X-ray diffractometry, scanning electron microscope, stability studies, and CD spectra. The NPs were evaluated *in vitro* using murine and human breast cancer cells, 4T1, MDA MB 231 cell lines, respectively.The MTT assay demonstrated that the NPs showed a marked increase in the OXA mediated cytotoxicity. The *in vivo* experiments using 4T1 tumor-bearing mice confirmed that the nanoparticles efficiently suppressed tumor growth without eliciting systemic toxicity. The NPs showed no sign of nephrotoxicity as observed with conventional oxaliplatin treatment.

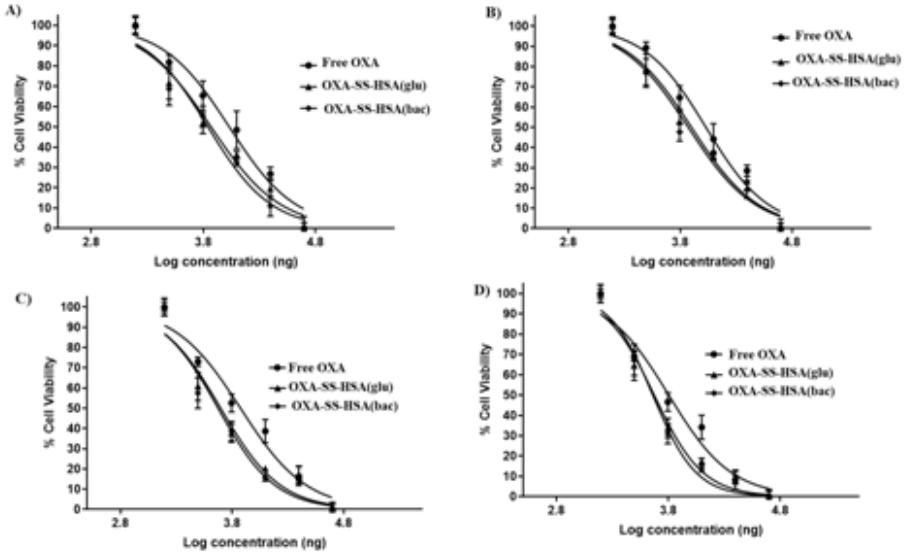

Figure 1: MTT assay

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Retinoic acid-conjugated poly (d, l-lactide)-based micelles as a nanocarrier system for effective delivery of doxorubicin in cancer

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Cancer is the second most life-threatening disease affecting most of population worldwide. The delivery of the chemotherapeutic agents, doxorubicin as well as retinoic acid are challenging due to its poor biopharmaceutical properties. The purpose of the present study is to overcome the limitations of conventional chemotherapy and to improve therapeutic efficacy via development of nanomedicines and providing combination chemotherapy. The aim was to synthesize block copolymeric micelles, methoxy poly (ethylene glycol)-poly (D, L lactide) (mPP) in conjugation with retinoic acid acid which assembles to form the polymeric micelles that encapsulate doxorubicin. mPP-RA was synthesized by ring opening polymerization reaction. Conjugation with RA tends to enhance the solubility and the cytotoxic effect of RA in cancer cells and it was characterized by ^{1}H NMR and FTIR. Doxorubicin was loaded into micelles, and they were prepared using thin film hydration method and physicochemically characterized for encapsulation efficiency (EE), drug loading (DL), particle size, zeta potential and critical micelle concentration (CMC). The Dox loaded micelles were evaluated *in-vitro* by using 4T1 and MCF-7 cell line. *In-vivo* anti-tumor efficacy and biodistribution studies were performed in 4T1 xenografted mice model. The EE % and DL % of the Dox loaded micelles was 45.50 ± 0.06 % and 7.58 ± 0.01% respectively. The polymer exhibited low CMC of 50 µg/mL. The Dox loaded micelles showed a controlled release with over 72h. Uptake study have showed that Dox@mPP-RA micelles showed higher intensity compared to Dox, mPP-RAmicelles and Dox@mPP micelles in 4T1 and MCF-7 cell line. Cytotoxicity of Dox@mPP-RA to the cells was more compared with Dox and Dox@mPP micelles. Dox@mPP-RAinduced total apoptosis of 58.58% and 52.15% in 4T1 and MCF-7 cell line. Further *in-vivo* efficacy study results showed that Dox@mPP-RA increased suppression of tumor growth compared to the Dox in 4T1 xenografted mice model.

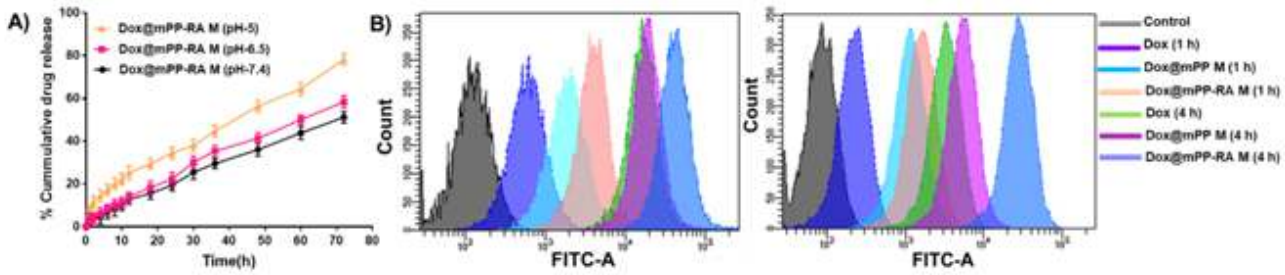

Figure 1: In-vitro drug release study of Dox@mPP-RA micelles at Ph-5, 6.5 & 7.4 (A) Cellular uptake study. 4T1 (left) and MCF-7 (right) cells were treated with Dox, Dox@mPP and Dox@mPP-RA micelles (B).

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Chitosan Oligosaccharide Lactate conjugated pluronic F127 micelles for the treatment of Bacterial keratitis

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Bacterial keratitis (BK) is a vision-threatening ocular infection caused by both gram-positive and gram-negative bacteria, including *Pseudomonas aeruginosa, Staphylococcus aureus and Streptococcus pneumoniae*.BK is highly prevalent in developing countries due to poor hygiene and in developed countries due to the improper use of contact lenses. The standard therapy for BK is fluoroquinolone antibiotics as an eye drop, which suffers from frequent dosing, poor corneal penetration, and sub-optimal killing of bacteria. This work used antibacterial and mucoadhesive chitosan oligosaccharide lactate (COL) conjugated pluronic F127 polymer to form a self-assembled nanomicellar structure to load gatifloxacin. The micelles were prepared with two different mole ratios of F127 and COL (1:1, and 1:2, referred to as FCOL1 & FCOL2). ^{1}H NMR and FTIR confirmed the synthesis of the product. The micelles were characterized for particle size, drug loading efficiency, and zeta potential. Minimum Inhibitory concentration (MIC) was determined by the microbroth dilution method. The corneal mucoadhesive property of the synthesized polymeric micelles was evaluated on Balb/c female mice. The results showed better contact time with the ocular surface, and their small size allowed for improved tissue penetration. The micelles exhibited no signs of ocular irritancy. The developed formulation showed significantly increased bacterial killing ability compared to the conventional gatifloxacin eye drop formulation.

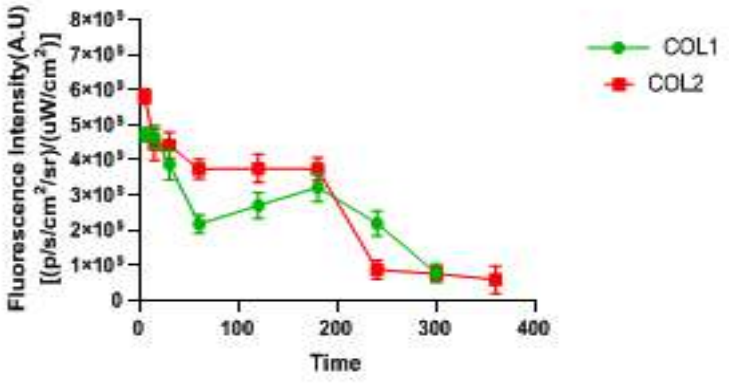

Figure 1: Retension of micelles in mice' eye. Mean ocular fluorescenceintensity analyzed by IVIS Lumina *in vivo* imaging system

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Scrutinizing the structural influence of sodium monovalent cation in traditional bioactive glass network – A systematic exploration

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Bioactive glass, one of the important classes of Biomaterials, finding its inevitable place in the mounting Bio-medical technology. Being capable of repairing and regenerating the damaged bone and teeth, Hench developed 45S5® bioactive glass with composition 45SiO_2, 24.55 CaO, 24.5% Na_2O and 6% P_2O_5 is a well-known commercial product under trade worldwide [1]. Even still, researchers are working on different composition of bioactive glass to overcome the weak mechanical stability of 45S5®, but by retaining the compatibility and bioactivity properties. One such study is presented here by eliminating the one of the network modifying cations i.e., Na_2O source and comparing the results with traditional bioactive glass.

Sol-gel mediated bioactive glass of above mentioned composition [Na^+ BG] and another without sodium source [No Na^+ BG] were synthesized and annealed at 700°C for 3 hours to achieve phase stabilization and to remove nitrates. XRD structural analysis confirms the presence of $Na_2CaSi_2O_6$ [Sodium calcium silicate] and $Na_2Ca_4(PO_4)_2SiO_4$ [Silicorhenanite] in Na^+ BG where apatite-like phase is formed in No Na^+ BG[2]. Raman and FTIR analysis confirms the availability of non-bridging oxygen (NBOs) that weakens the network in case of Na^+BG, but not in No Na^+ BG. FE-SEM analysis showed the mesoporous structure with large pore size in Na^+ BG than reduced porous structure found in No Na^+ BG.

Bioactivity is studied by soaking the material in Simulated Body fluid that forms hydroxycarbonate (HCA) apatite layer on the surface, later crystallizes to bone. XRD , FTIR and Raman analysis showed the formation of hydroxyapatite peaks, reduction in non- bridging oxygens and Si-O-P linkage evolution respectively in case of the bioactive glass devoid of sodium. SEM micrographs on the Day7 evidently displays the precipitation of HCA on the surface. Thus, it is predicted that sodium free bioactive glass can also play a better role in certain biomedical application.

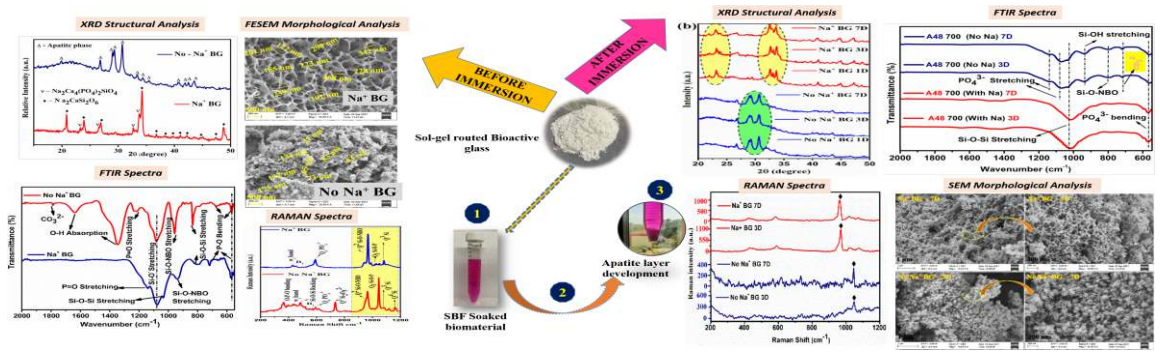

Figure 1: XRD, FTIR, RAMAN, FESEM and SEM results of bioactive glass with and without sodium monovalent cation.

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pH-Responsive Pro-drug Nanoparticles of Gemcitabine for Cancer Treatment

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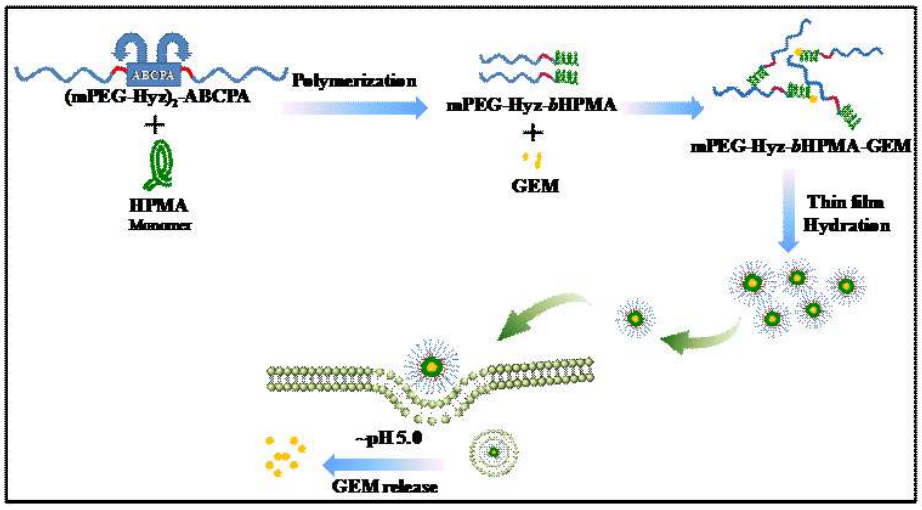
Gemcitabine (GEM) is a nucleoside analog used to treat breast, lung, ovarian, and pancreatic cancers. It is a BCS class III drug (high solubility, low permeability). In addition to poor absorption, GEM suffers from poor bioavailability due to its short half-life. Herein, we developed $mPEG_{5k}$-*b*-*N*-(2-hydroxypropyl) methacrylamide (HPMA)-gemcitabine (GEM) polymer conjugate with pH-sensitive hydrazone linker between PEG and *b*-HPMA. The conjugates were structurally characterized by UV, IR, NMR, and GPC analysis. The self-assembled nanoparticles were physicochemically characterized for their particle size, zeta potential, drug conjugation, stability by DSC, surface tension, and pH-dependent drug release studies. The nanoparticles were stable under physiological pH (7.4) but degraded at mildly acidic conditions to disassemble and release Gem. The *in-vitro* cytotoxicity and cellular uptake of gemcitabine conjugated nanocarriers were evaluated in MDA-MB-231 and MCF-7 human breast cancer cell lines. The results exhibited significant cytotoxicity in both the cell lines than the free gemcitabine with time-dependent internalization. The results indicated this biodegradable amphiphilic pH-sensitive gemcitabine hybrid system could be employed as a potent nanomedicine for Gem-mediated cancer treatment.

Keywords: Cancer, gemcitabine, block-HPMA, pH, hydrazone.



Clinophosinaite based Bioceramics Glass- A systematic investigation

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One of the most prominent bio-materials with extensive applications include silicate based bioactive glasses, developed with the varying composition of SiO_2, CaO, Na_2O and P_2O_5 in-order to enhance the desired multiple properties like anti-bacterial, bioactivity, anti-inflammatory etc., It is obvious that calcium and phosphate ions from the bioactive glass network results in the precipitation of hydroxycarbonate apatite layer followed by crystallization and regeneration of bone or teeth. In this study, bioactive glasses with equal molar ratio of Ca:P phases were developed and investigated on the influence of phase evolution and its effect in morphology and properties.

Bioactive glasses with equal molar ratio of Ca:P were achieved stoichiometrically through sol-gel wet chemical method. Different sintering temperatures i.e., 700°C, 800°C, 900°C, 1000°C were followed to stabilize the biomaterials and to identify phase transition. XRD results proved the evolution of equal Ca:P molar ratio phases such as Rhenanite [$NaCaPO_4$] and Clinophosinate [$Na_3CaPSiO_7$]. Clinophosinate is found to be one of the rarest silicate mineral phases, marks its major role in hard tissue engineering [1] is being evolved highly at 1000°C in our case. The quantifying evolution of clinophosinate with Rhenanite over increasing annealing temperature also results with the major morphological modifications. Phosphate band widening were observed by FTIR.

Important property of bioactivity to be shown by biocompatible glasses were studied by soaking the biomaterial in simulated body fluid (SBF) whose results astonishes that within 12 hours of immersion, appreciable apatite precipitation was noticed and were confirmed through XRD and FTIR. SEM results also imaged the precipitated HCA layer over the surface of the soaked bio-materials. Hemo-compatibility seems to be enhanced by the prepared bio-active glasses on contact with simulated body fluid.

Thus, it is predicted that equal Ca:P molar ratio based bioactive glasses can show good bioactivity and turn to be hemocompatible once in contact with body fluid.

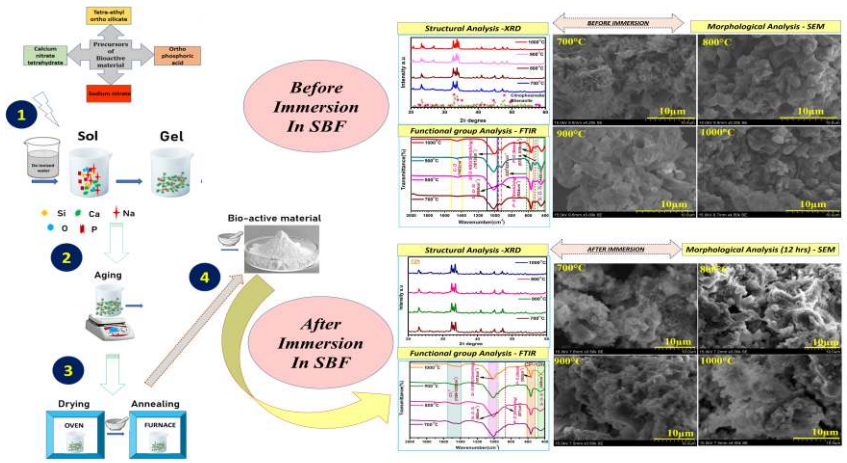

Figure 1: XRD, FTIR and SEM results of equal Ca: P molar ratio phase evolved bioactive glass.

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Impact of Process Variables, Architecture and Properties of Nano-Hydroxyapatite

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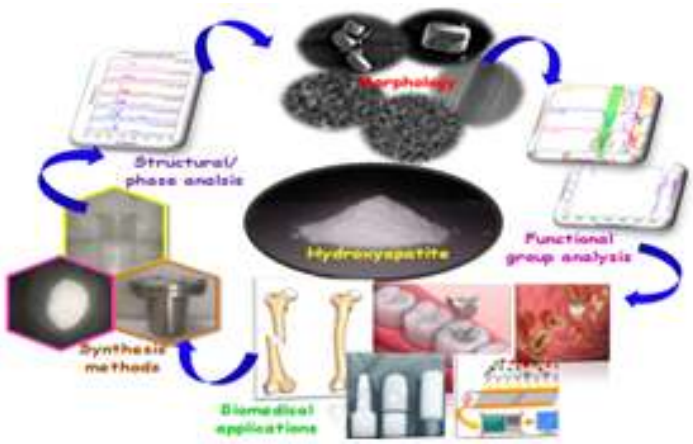
Hydroxyapatite, a bio-ceramic with compositional stoichiometric of $Ca_{10}(PO_4)_6(OH)_2$ is broadly used in the field of orthopaedic and dentistry due to its resemblance in the structural composition of natural bone apatite. Synthetic Hydroxyapatite holds the essential inorganic component of natural bone calcium and phosphate with a ratio of 1.67.

Owing to its similar mineral component with the same ratio and unique biological properties like osteoconductivity, bioactivity and biocompatibility it has been largely utilized by the current researchersaround biomaterials [1].

In the present study, fabrication of HAP via hydrothermal method is systemically examined by varying pH as well as reaction time and are presented here. The reaction time of 24 hours indicates the pure phase of HAP that is evident by XRD studies. Further, the increase in the reaction time denotes the appearance of the secondary phase Monetite along with the HAP parent phase. Morphological evaluation using SEM and TEM reveals rod-like shapes with different dimensions. Subsequent Functional group and vibrational modes analyses of HAP are studied by FTIR and RAMAN spectroscopy. The Biosuitability of hydroxyapatite is confirmed by a hemolytic assay that demonstrates considerable compatibility according to ASTM standards.

Keywords: Hydroxyapatite, hydrothermal, monetite, biocompatibility.

Graphical abstract



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Influence of sintering temperature over 53S bioactive glass and their imprints in *in- vitro* bio mineralization

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Bioactive glasses are very promising materials for soft and hard tissue repair. The single crystalline phase $NaCaPO_4$ in 53S bioactive glass obtained through sol–gel method. The bioactive glass sintered at 700 ^{0}C revealed $NaCaPO_4$ crystalline phase. Dominance of bridging oxygen is observed in 53S-700 BG through high resolution XPS spectroscopy which supports the XRD results in terms of exact crystal structure formation ($NaCaPO_4$). The dominant Q_4 Si–O–Si stretching in the 700 ^{0}C heat treated bioactive glass exhibits bonding with bridged oxygen confirmed through functional group analysis.

A comparatively elevated mechanical stability is achieved in the 700 ^{0}C sintered bioactive glass with respect to compactness in the crystal structure. The spiky rod-like apatite precipitation and dominant $Ca_5(PO_4)_3(OH)$ phase symbolize the prominent mineralization behavior of the bioactive glass heat treated at 750 ^{0}C due to the rapid ionic release from the material. On the whole, development of 53S bioactive glass matrix encourages researchers to analyze the bio-chemical features of this material focusing on bone regeneration.

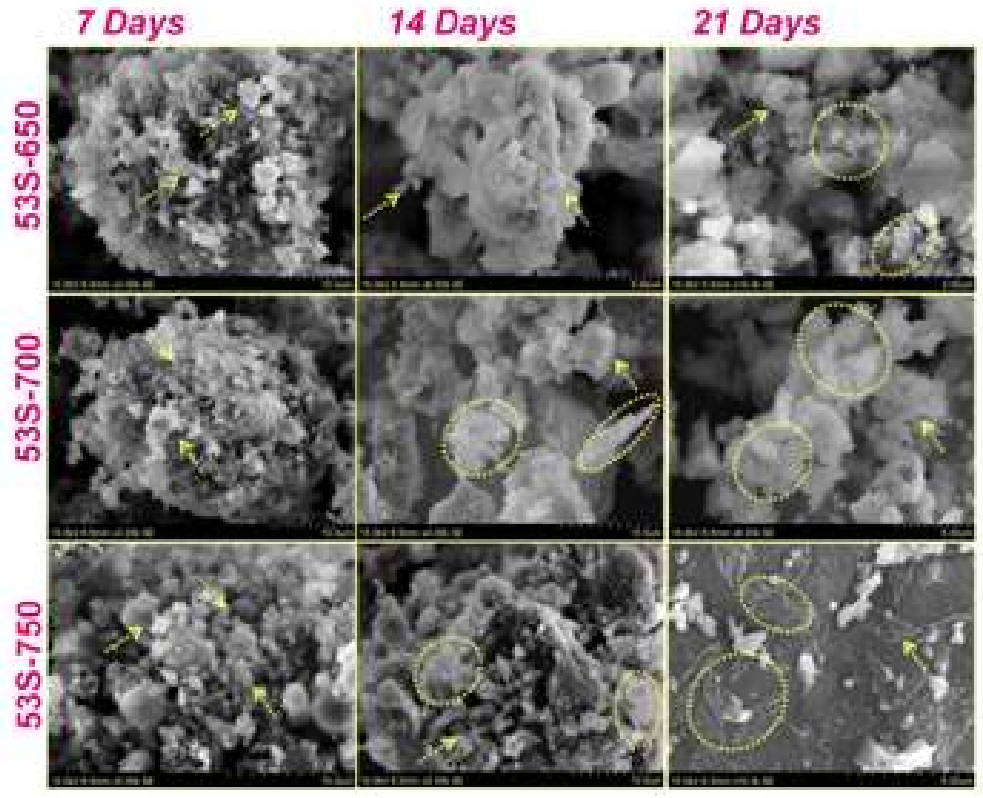

Figure.1. Surface morphology of mineralized 53S bioactive glasses.

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Glycosylated Mesoporous Silica Nanoparticles Loaded with Lapatinib for the Treatment of Breast Cancer

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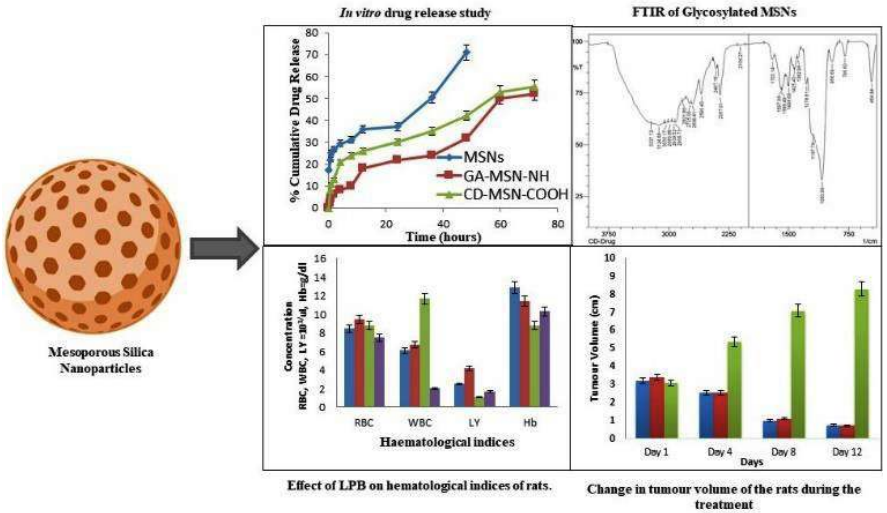
The purpose of this study is to develop glycosylated Mesoporous Silica Nanoparticles (MSNs) of Lapatinib (LPB) to target breast cancer. Glycosylated nanoparticles are a deep-rooted promise of breast cancer therapy which has specificity to lectin receptors and have a massive influence on every cellular progression. With this rational the glycosylated MSNs loaded with Lapatinib was prepared and evaluated for various parameters which confirm maximum drug loading into the MSNs with improved bioavailability at target site. Lapatinib was encapsulated within the mesopores by utilizing three different techniques such as solvent immersion, impregnation and incipient wetness impregnation. The amine-functionalized MSNs were glycosylated with D-Glucuronic acid sugars while the carboxylic acid functionalized MSNs were glycosylated with β-Cyclodextrin sugars where EDC-NHS chemistry is applied for both the methods. The influence of MSNs functionalization and type of functionalization on the shape and particle size of the MSNs was investigated. Further, a drug release study showed almost the same percentage of drug release in both the types of glycosylated MSNs which was better when compared to the pure drug loaded into the plain MSNs. The glycosylated nanoparticles revealed reduction in the tumour size and the survival of the rats are determinants of the safety and the efficacy of the anticancer drug-delivery system. The results suggest that when the glycosylated MSNs loaded with Lapatinib have a great potential to inhibit the development of breast cancer.



Effect of LPB on hematological indices of rats.

Change in tumour volume of the rats during the treatment

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Moxifloxacin HCl delivery via thermo-responsive mixed micelles in bacterial keratitis

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Bacterial keratitis (BK) is a corneal inflammation mainly caused by Gram +ve & -ve bacteria such as *Pseudomonas Aeruginosa*, *Pseudomonas pneumoniae,* and *Staphylococcus Aureus*. BK leads to loss of vision if left untreated. The most successful way to treat the infective keratitis is to maintain the adequate amount of drug on the corneal surface for an extended period and by increasing the penetration ability of the drug into the corneal tissue. Here, mixed micelles of different chitosan-PLGA and poloxamer (F68 and F127) polymer ratios were prepared and moxifloxacin was incorporated. The conjugation of chitosan-PLGA was confirmed by ^{1}H NMR, FTIR spectroscopy. The micelles were characterised by CMC, particle size, zeta potential, drug loading, encapsulation efficiency. Further, the mucoadhesive and thermoresponsive properties were assessed. The MIC& MBC of the micelles was determined by micro-dilution method and MTT assay. The anti-bacterial efficacy of micelles was determined by performing a live/dead assay on bacterial biofilms and planktonic bacteria. The results indicated that the micelles were nanosize (101±2&111±2.1 nm for F68 1:5 & 1:10 respectively and 121±1.9, & 127±1.75 nm for F127 1:5 & 1:10 respectively), and have the self-assembling property (CMC 1.698 µM for F68 1:5 & 1:10 respectively and 1.397µM for F127 1:5 & 1:10 respectively). The mixed micelles (F68&127 of 1:10) showed ocular retention for a longer time than other tested micelles (F68 & 127 1:5). In conclusion, the optimized mixed micelles has offered substantial therapeutic benefit compared to conventional eye drop treatment with moxifloxacin in BK.

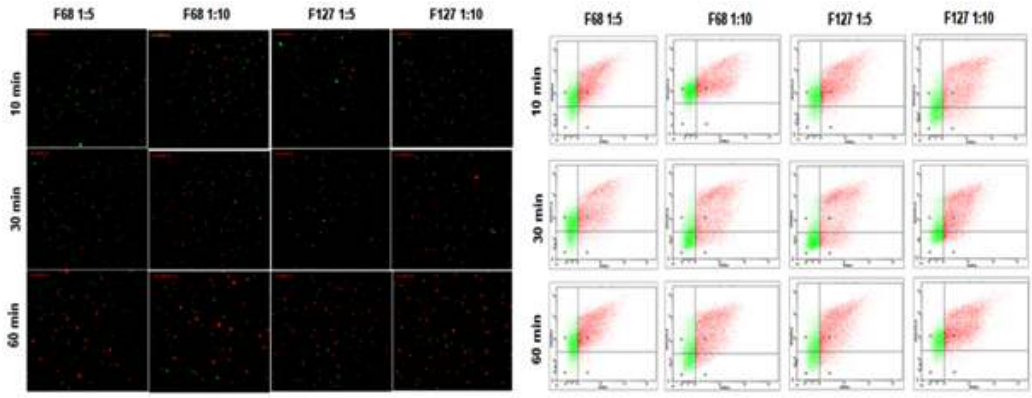

Figure 1: Live/dead assay of the *P aeruginosa* after the treatment with micelles. The fluorescence images (left).The flow cytometric quadratic dot plot diagram displaying the SYTO-9 and PI-stained cells populations (right).

References:

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3D Culture Model for Studying Cellular Senescence

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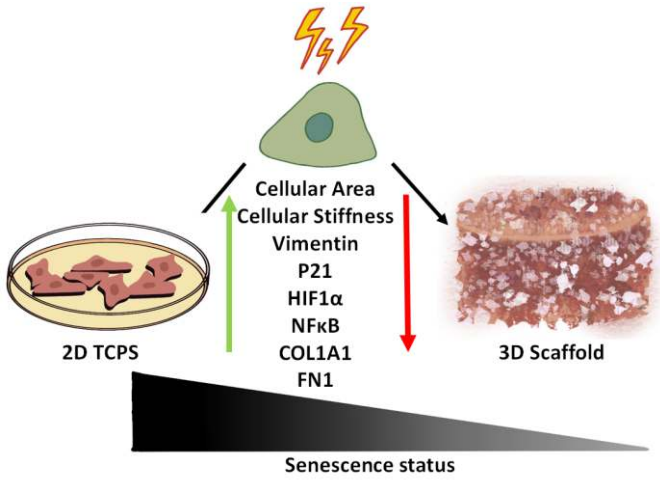
Cellular senescence is a process in which cells are growth-arrested and undergo distinctive phenotypic alterations when exposed to high but sub-lethal DNA damage. This phenomenon is implicated in several age-associated diseases and is a hallmark of aging. Aging studies have conventionally been performed on two-dimensional (2D) culture systems that poorly represent the native cellular microenvironment. It is now widely recognized that three-dimensional (3D) culture systems better mimic *in-vivo* physiology. Given the limitations of 2D culture systems, the cost and time required for animal studies, we aim to recapitulate the tissue environment better using 3D polymeric scaffolds, thereby offering better insights into the molecular mechanisms of aging. We utilized PCL (polycaprolactone) to fabricate porous 3D scaffolds using salt-leaching technique. Ionizing radiation was used as the source to induce senescence in HeLa cells. Non-irradiated cells were used as controls. We show that the senescent cells display large flattened morphology on 2D substrate; however, cells in 3D scaffolds do not display extreme modulation in shape and size. Actin arrangement varied between senescent and non-senescent cells and between substrates (2D vs. 3D). We also looked at motility and division between cells *via* live-cell imaging. We characterized the nanomechanical properties of live cells using a Bio-AFM wherein higher stiffness was observed in senescent cells. When cells were retrieved from 3D scaffolds and re-plated on 2D substrates, senescent cells displayed mechanical memory retention for up to 24 hours. We also probed vimentin levels using immunofluorescence and observed that senescent cells on 2D substrate had the highest levels compared to 3D groups. Collagen 1 and fibronectin 1 were also investigated to look at changes in extracellular matrix components and observed that the levels were significantly reduced in 3D cultured cells. We then investigated senescent-associated and inflammation-related genes using RT-PCR and found that the levels of p21, HIF1α, IL6, IL8, and NFκB were decreased in senescent cells cultured on 3D scaffolds. Our work demonstrates that the senescent cellular physiology significantly varies between culture platforms, leading to differences in cellular division, cytoskeletal organization, nanomechanical properties, and senescence signatures.



Synthesis and Characterization of Biocompatible Bimetallic-Semi-Aromatic Polyester Hybrid Nanocomposite

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Nanocomposites have been broadly used in bioelectronic, biosensing, photocatalytic, and bioimaging. Moreover, its use in bioengineering field is emerging continuously. The present study reports first-time the synthesis of a novel bimetallic-semi-aromatic polyester hybrid nanocomposite. The obtained $MnFe_2O_4$-poly(*t*BGE-*alt*-PA) hybrid nanocomposite was physicochemically characterized. FTIR analysis confirmed the synthesis of hybrid nanocomposite. XRD data showed the crystal nature of hybrid nanocomposite due to $MnFe_2O_4$ nanoparticles (NPs). TGA study presented the thermostable nature of hybrid nanocomposite and DSC analysis exhibited the absence of chemical interactions between the copolymer and $MnFe_2O_4$ NPs in hybrid nanocomposite. Further, the net negative charge was measured on the surface of this almost spherical hybrid nanocomposite. Later, we observed the biocompatible and hemocompatible nature of nanocomposite and in future, it may open many novel avenues in various fields of biomedical science.

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2. Gupta PK, Pappuru S, Chakraborty D and Verma RS. "Enhanced anti-cancerous activity of dual drug loaded core-shell nanoparticles composed of metal-free fully alternating copolymer, *Journal of Pharmaceutics & Drug Delivery Research* 2018, 7, DOI: 10.4172/2325-9604-C1-027

3. Semi-aromatic polyester nanocomposite and method for preparation thereof, Inventors: Piyush Kumar Gupta, Soumya Pandit, Shaily Chauhan, Rohit Kumar, Rekha Gahtori, Siva Chander Chabattula, Sunny Dholpuria, Sharad Agrawal, Bableen Flora, Patent no. 202111040352, Filing Date: 06.09.2021, Publication Date: 01.10.2021

Synthesis and characterization of novel bimetallic-semi-aromatic polyester nanocomposite for possible biomedical use

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Nanocomposites are hybrid nanomaterials that have been widely used in bioelectronic, photocatalytic, biosensing and biomedical applications. The present study synthesizes novel ZnFe2O4@poly(*t*BGE-*alt*-PA) composite. The obtained bimetallic-semi-aromatic polyester composite were physicochemically and biologically characterized. FTIR analysis confirmed the preparation of composite. XRD analysis exhibited crystalline nature of composite.TGA and DSC analysis displayed the thermal stability of composite and no chemical interactions between the zinc ferrite nanoparticles and copolymer respectively. The novel hybrid nanomaterial is found to be biocompatible and hemocompatible nature and it may be used in different biomedical applications.

Reference

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2. Gupta PK, Pappuru S, Chakraborty D and Verma R S. "Enhanced anti-cancerous activity of dual drug loaded core-shell nanoparticles composed of metal-free fully alternating copolymer, *Journal of Pharmaceutics & Drug Delivery Research* 2018, 7, DOI: 10.4172/2325-9604-C1-027
3. Semi-aromatic polyester nanocomposite and method for preparation thereof, Inventors: Piyush Kumar Gupta, Soumya Pandit, Shaily Chauhan, Rohit Kumar, Rekha Gahtori, Siva Chander Chabattula, Sunny Dholpuria, Sharad Agrawal, Bableen Flora, Patent no. 202111040352, Filing Date: 06.09.2021, Publication Date: 01.10.2021

Synthesis and characterization of decellularized extracellular matrix coated gallic acid-containing polyurethane cryogels for cardiac regeneration

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Myocardial infarction refers to the condition which involves blockage of coronary arteries in the heart that are essential for the supply of blood, oxygen, and nutrients to the myocardium. Most tissue-engineered scaffolds face difficulty in controlling inflammation, attenuating oxidative stress, mechanical stability, and regeneration of damaged cardiomyocytes. In this study, we synthesized a highly elastic polyurethane-based scaffold with an antioxidant phenolic compound gallic acid in its backbone, that was designated as PUGA. The successful synthesis of the polymer was checked through Fourier Transform Infrared Spectroscopy and Nuclear Magnetic Resonance. The cryogels fabricated at sub-zero temperature were later tested for their morphology through scanning electron microscopy and antioxidant activity by DPPH (2,2-diphenyl-1-picryl-hydrazyl-hydrate) assay. The scaffolds have a pore diameter of 5 – 10 µm, and porosity, as measured by the cyclohexane method, came out to be 88 ± 2%. PUGA slowly attenuated oxidative stress and could inhibit 50% free radicals in 15 min, and its activity matched that of free gallic acid after 120 min. Decellularized extracellular matrix from goat heart was coated on the surface of the cryogel to make the scaffold more biocompatible. The extracellular matrix was evaluated for proper decellularization by microscopic techniques, nucleic acid, and glycosaminoglycan content. Young's modulus calculated from mechanical testing data was ~300 KPa which depicts the suitable elasticity of the material to be used as a cardiac patch. The cytocompatibility of the scaffold was checked with H9C2 cardiomyoblasts and neonatal cardiomyocytes by MTT assay and fluorescence microscopy. The material was also able to attenuate oxidative stress on cells and maintained significantly higher cell viability (66% in scaffold extract-treated cells compared to 12% in non-treated cells). The scaffolds finally promoted healthy vasculature formation by maintaining viability and release of nitric oxide from endothelial cells. This nitric oxide acts as vasorelaxant and will prevent further blockage in the arteries. Thus, this material could be used as a promising scaffold for cardiac regeneration.

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Preparation and Evaluation of insulin loaded Glucose-responsive Polymeric Nanoparticles

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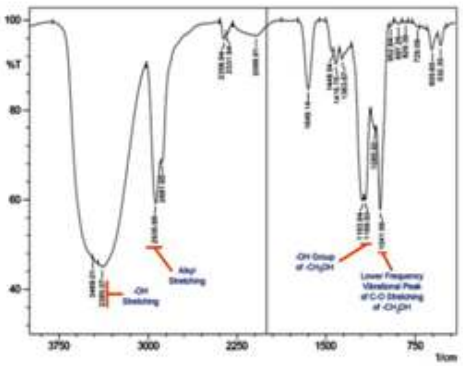
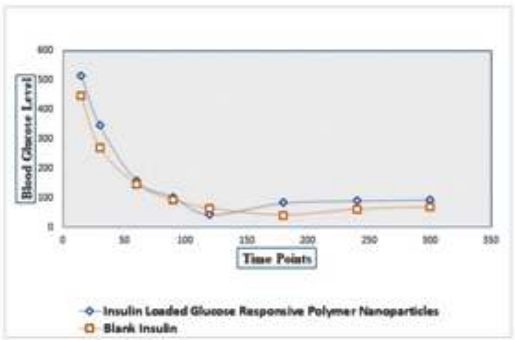
The aim of the study was to develop a transdermal delivery system for delivery of insulin. In the present study, a glucose responsive polymer was synthesised by the conjugation of chitosan with 4-carboxy phenyl boronic acid using carbodiimide chemistry. The glucose responsive polymer was characterized by FTIR, XRD, DSC and NMR. Insulin loaded glucose responsive polymeric nanoparticles were prepared by electrostatic interaction followed by characterization using zeta size, zeta potential, entrapment efficiency and drug loading. The efficacy of the prepared formulation was evaluated by subcutaneous injection of the formulation in streptozotocin induced male Wistar rats. The results of FTIR and NMR confirmed the conjugation of chitosan with 4- carboxy phenyl boronic acid. Entrapment efficiency was found to be 80% indicating insulin was effectively entrapped by glucose-responsive polymer. The size of the Nanoparticles were 400 nm to 450nm and zeta potential 21+2 mv. A significant decrease in the blood glucose level was seen in diabetes-induced rats. The elevated blood glucose was brought to normal level in 90 minutes following administration and was maintained for 300 minutes. Based on the obtained results, insulin loaded glucose responsive polymeric nanoparticles have shown potential to decrease the blood glucose level in diabetic rats and can be probed further for transdermal delivery.

Key words: Insulin, Glucose responsive nanoparticles, Carbodiimide chemistry, Diabetes,



FTIR of conjugate (Glucose responsive polymer)



Blood glucose levels at different time points of insulin loaded glucose responsive polymeric nanoparticles

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"How to conduct clinical trial: An evidence based approach"

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As new biomaterials are developed by in-vitro test in the laboratory; utilization of these materials in human being can not be done straight away. This should be done by a clinical trial of high-level evidence in human being; otherwise it will be unlawful. The purpose of interaction is that dentistry and Orthopedics doctors involve in rehabilitation and restoration of lost tooth/ bony structure with biocompatible substitutes. These substitute range from lost enamel, dentin, bone to dental implant. In this era of interdisciplinary research, there is a need of collaboration between biomaterial scientists, medical specialists and dentists for the better patient care.

This presentation will focus on what are the prerequisites of clinical trial like approval from CDSCO, ethical approval, and clinical trial registry. It also cover how to conduct clinical trial in collaboration.

Statistical optimization for the development and validation of stability indicating RP-HPLC method for quantification of diclofenac sodium in the organogel prepared by employing twin screw processor

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A novel stability indicating RP-HPLC method was developed for estimating diclofenac sodium (DS) in the organogel processed by a twin-screw processor. The inherent stability of DS was evaluated by a forced degradation study. No notable degradation of DS was seen in different stressor conditions. Method validation was done as per ICH Q2(R1) standards by using 2^4 full factorial design employing Design Expert® software. The influence of independent variables on the responses like retention time, peak area, number of theoretical plates, and tailing factor was assessed. The quantification of DS from the organogel was done by separating it on the Phenomenex ODS C18 column (C18, 5 µm, 4.6mm id x 250 mm, 100 Å) using 60:40% v/v acetonitrile and water with 0.3% v/v Triethylamine (TEA) adjusted to pH 3.0. The method was linear between 50 -5000 ng/mL and the R^2 value was 0.9991. The limit of detection (LOD) and limit of quantification (LOQ) were estimated as 19.41 and 58.83 ng/mL. Analysis of variance (ANOVA) revealed the significance of the experimental model ($P<0.001$) in method validation by deliberately changing the independent factors. This method was sensitive in estimating DS in the organogel processed by twin-screw processor showing a mean recovery and %RSD of 97.02% and 0.018%.

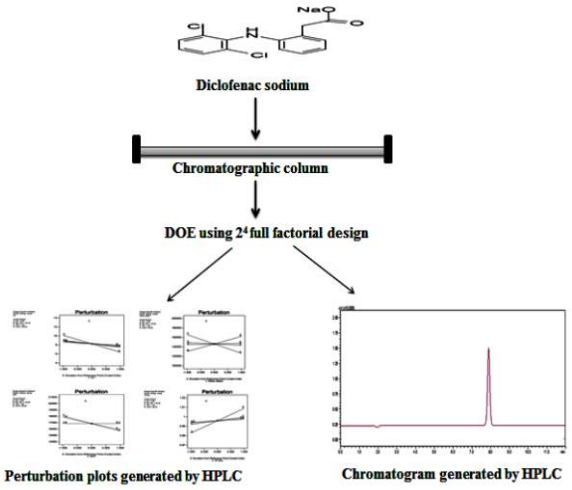

Figure 1: Graphical abstract

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Topology dictates cellular and in-vivo uptake of DNA-based 3D cargos

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Structural DNA nanotechnology involves fabrication of small strands of DNA to create various nano-objects in 1D, 2D and 3D with precise control of shape and size that have been utilized in a multitude of biological and biomedical applications. One of the most studied branches of structures from DNA nanotechnology are various 3D polyhedras of varying sizes and geometries. The main reason why these cages have been the focus of scientific research is their ability to be coupled to external biological targeting entities like peptides, small molecules, antibodies, etc., and their ability to encapsulate various nanoscale cargos within their internal void[1]. Despite such attractive potential, the practical applications of DNA nanodevices in biological systems are limited and not finely tuned. This is primarily due to the lack of in-depth understanding of interactions of DNA nanodevices with biological membranes and the role of the topology of DNA nanostructures in modulating such interactions with the plasma membrane, thereby affecting their cellular internalization. The knowledge of these interactions can be applied to develop *Smart Nanoparticles* for biological and biomedical applications. The correlation between the topology of DNA nanostructure and their internalization efficiency has not been explored much. We have studied the binding and uptake pathways of DNA nanodevices of different geometries and sizes. We have found that of all the geometry tested, only tetrahedral geometry showed maximum internalization in cellular and in-vivo systems. This geometry bias can also be seen in the 3D-spheroid model, where tetrahedral DNA nanostructure showed maximum invasion potential compared to other nanostructures[2].

This work has very high-end applications in rational designing DNA Nanodevices for tissue targeting in vivo and then further applications in the areas of bio-imaging, drug delivery, immune activation, etc.

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Effect of newly designed hybrid threaded tapered Ti6Al4V dental implant in enhancing osseointegration:Validated in rabbit model against a commercial implant

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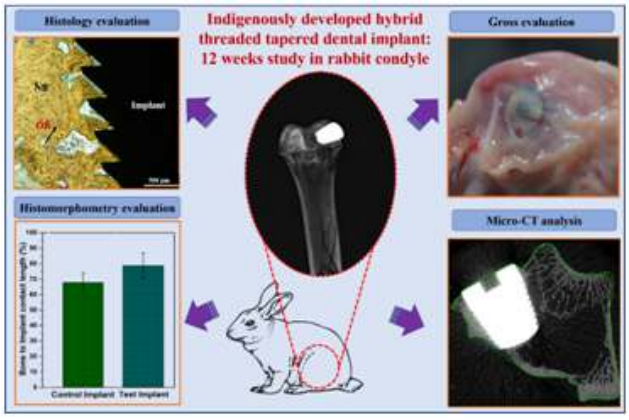
One of the desired requirements of any dental implant system is its long-term stability and bone healing, leading to enhanced osseointegration. Two aspects of the dental implant system are essential and those are surface modification or macro/micro design features in terms of thread geometry or distribution. In the present work, the osseointegration of Ti6Al4V based newly designed hybrid threaded tapered implant without any surface modification have been validated and benchmarked against Straumann® implant (large grit sand blasted acid etched) in the rabbit model for 12 weeks. The test and control implants were implanted in the rabbit condyle on the contralateral limbs. The peri-implant bone interfaces were analysed by staining histological sections of bone-implant interfaces. The overall assessment suggests homogenous and continuous osseointegration around the hybrid threads of the test implants. Superior bone to implant contact percentage (BIC) was observed in the case of hybrid threaded test implants with an average value of 78.7%, compared to 67.8% in the case of control implant. The bone formation and osseointegration on the test implant surface were assessed qualitatively and quantitatively using micro-computed tomography (μ-CT), molecular gene studies and histomorphometric analysis at the end of 12 weeks. All the findings were carefully evaluated to analyse*in vivo* bone healing and osseointegration of the hybrid threaded tapered dental implant. It can be concluded that the extent of neobone formation and expression of the osteogenic genes is positively correlated with optimal design features of the implant, which leads to the contact guidance of the osteoblasts on the implant surface. The study also advocates that the novel tapered multithreaded implant design concept alone (without surface modification) can facilitate osseointegration in a manner better than clinically used surface modified implants.



Extrusion-based 3D printing of gelatin methacryloyl with nanocrystalline hydroxyapatite

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The particle shape and size distribution of inorganic fillers play a crucial role in the scaffold buildability when those are incorporated in the viscoelastic polymer matrix. In order to address this issue, the phase pure rod-shaped nanocrystalline hydroxyapatite (HAp) powders with varying particle sizes and shapes were synthesized by a one-pot hydrothermal method without any regulatory surfactant at an initial solution pH of 9. The hydrothermal treatment parameters were investigated within a wide range of temperature (130-200°C) and duration (6-36 h). As-synthesized nanocrystalline HAp particles (0-5 wt%) were incorporated into pre-crosslinked gelatin methacryloyl (GelMA) hydrogel matrix to fabricate a predesigned scaffold architecture using a custom-made 3D bioprinter. The printing parameters (nozzle diameter, extrusion pressure, printing speed) were optimized for each composition. The biophysical properties (uniaxial compression behaviour, swelling ratio, and *in vitro* degradation) of the composite hydrogel scaffolds were critically analyzed to unravel the role of nano-sized HAp addition.The compression strength and modulus were substantially improved, while the rate of water uptake and bio-enzymatic degradation significantly reduced with HAp content. We propose that the inorganic-organic nanocomposite hydrogel could be efficiently assembled to formulate a potential bioink for 3D bioprinting applications towards bone tissue regeneration.

Histone deacetylase inhibitor overrides the effect substrate stiffness on mesenchymal stem cell behaviour on the soft gel

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Keywords: Mesenchymal stem cells, substrate stiffness, histone deacetylase inhibitor.

Abstract

It has been demonstrated that substrate stiffness may govern various cellular phenotypes such as cell spreading, cytoskeleton tension, focal adhesion and differentiation. For example, when human Mesenchymal cells (hMSCs) are cultured on soft polyacrylamide (PAA) gels, they spread less, forms smaller adhesion points, apply less traction on the substrate, and preferentially differentiate into adipogenic lineage. It is known that during the differentiation process, epigenetic modifications such as acetylation, de- acetylation, methylation take place that changes the chromatin structure. However, how the mechanosensing process and chromatin modification crosstalk with each other is not known. In this work, we wanted to check how one such chromatin structure modifier i.e. Valproic acid (VA) influences the mechanoresponse of hMSCs on soft PAA gels. VA is a histone deacetylase inhibitor (HDACi), that interferes with the histone deacetylation process making the chromatin more loosely wrapped around the histone molecules.

Our finding shows that when hMSCs on the soft gels are treated withVA, they show phenotypes that are typical of stiff substrates cultures. Treatment with VA increases the projected cell spread area, focal adhesion maturation and cellular traction on the soft gel. It inhibits adipogenic and promotes osteogenic differentiation of hMSCs, as opposed to what is observed without VA. Further, it causes higher translocation of mechanosensing transcription factor YAP to the nucleus, as we expectedly see in cells on rigid substrate. We further concluded that VA overrides hMSCs mechanotransduction process on soft gel via phosphorylation of extracellular-signal-regulated kinase (ERK). In summary, our finding for the first time suggests that HDAC inhibitor (valproic acid)can override the mechanotransduction process of hMSCs on soft gels.

Role of chondrocyte derived exosomes and macroporous cryogel scaffolds for cartilage tissue engineering

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Cartilage regeneration has been a long pursued goal wherein phenotype maintenance and retention of properties has remained a challenge. Tissue engineering strategies utilized for regeneration of articular cartilage includes use of cells, scaffolds, bioactive factors and physical cues in different combinations. In the current study we have focussed on the use of exosomes, subclass of extracellular vesicles which were obtained from the goat knee chondrocytes. Articular cartilage was utilized for chondrocytes isolation and subsequent exosomes isolation was carried from these chondrocytes using ultrafiltration method. Size distribution of exosomes was studied which was in range of 45 to 110 nm and visualized for their morphology using electron microscopy and atomic force microscopy. Exosome intake by chondrocytes was tested by fluorescent labelling of the exosomes which came out to be 2 h. Scaffolds were fabricated by crosslinking the polymer solutions at sub-zero temperature using cryogelation. Different types of scaffold (cryogels) were fabricated *viz.* monolayer, aligned cryogels and multi-layered cryogel for osteochondral tissue where chitosan, gelatin, chondroitin sulfate were utilized for the top cartilage layer (CGC) and nano-hydroxyapatite, gelatin fabricated for the underlying bone layer (HG). These cryogels were characterized for their physical, mechanical properties and their potential to support cell growth over them. CGC cryogel was tested as a carrier for exosome which showed exosome release profile of 46% at 24 h, 72% at 48 h and 80% at 72 h, respectively. Chondrocyte proliferation over CGC and pre-osteoblast over HG was evaluated. Imaging using scanning electron microscopy was carried to visualize scaffold microarchitecture as well as the cells growing over the cryogels. Confocal microscopy was carried to visualize the cells growing over the aligned CGC cryogels as native articular cartilage has different zones with alignment. Finally, effect of different exosome concentration and CGC cryogel were assessed in carrying chondrocyte proliferation and migration.

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Co-administration of Paclitaxel and Curcumin in surface functionalized Nano-formulation to create Synergistic effect and targeted delivery for Cancer Treatment

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Increased levels of the transcription factor nuclear factor kappa B (NFƘB) increases drug resistance in cancer cells. Multi-drug delivery utilising a combination of anti-cancer drugs with various action mechanisms has shown synergistic effects and NFƘB inhibition on cancer cells. The polysaccharide, Hyaluronic acid (HA), is a biocompatible polymer used to target CD44 receptors, over expressed in various cancer cells. Limited aqueous solubility of the anticancer drugs and non-targeted delivery limits the therapeutic efficiency of the cancer treatment. Polymeric Nano drug delivery with surface functionalization is a promising way to overcome drawbacks of conventional therapy. The present study focuses on developing PLGA (Polylactide-Co-Glycolic acid) nanoparticles (NPs) and incorporating them with Paclitaxel/Curcumin anti-cancer drugs by single emulsion solvent evaporation method and HA targeted delivery of Paclitaxel/Curcumin through the Interfacial Activity Assisted Surface Functionalization (IAASF) technique. The nanoparticles where characterized for its size, zeta potential, morphology, drug loading and surface modification through, particle size analyser, SEM, RP-HPLC and ^{1}H-NMR. *In vitro* release study showed a slow and sustained release of the drug from the NPs. The formulated targeted NPs as mono or in combination form when treated against cancer cell lines showed significant cytotoxicity, increased cellular uptake, and decreased NFƘB activity compared to free drugs in mono or combination form. The combination of drugs in nano-formulation showed greater cytotoxicity compared to mono drug NPs. Therefore, from the assay results, we can conclude that a combination of drugs in nano-formulation and targeted delivery will be helpful for cancer therapy.

Keywords: Polymeric Nanoparticles, Combination Therapy, NFƘB Activity, PLGA, Cytotoxicity, Receptor mediated endocytosis, Targeted delivery.

Smart Polymer-Based Therapeutic Systemfor Mucosal Healing and Regeneration in Inflammatory Bowel Disease

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Inflammatory bowel disease (IBD) typically includes Crohn's disease and ulcerative colitis, which is a chronic condition characterized by prolonged inflammation of gastrointestinal tract. IBD is associated with life-long morbidity for affected patients, and both the incidence and prevalence are increasing globally. Current treatment strategies focus on providing symptomatic relief to the patients by systemic delivery of drugs, however, these drugs frequently fail or are inadequate to prevent or reverse the damage and often cause off-target systemic side-effects and malignancies. The purpose of this study is to develop a colonoscope-based treatment option that specifically target the diseased area of the colon and locally deliver drugs through sprayable application of a thermoresponsive polymer formulation during diagnostic procedures.Thermoresponsive polymers can facilitate controlled delivery and retention of drugs and other therapeutic agents on intestinal tissue through rapid gelation.This could lead to increased intestinal function, reduce symptoms and deep remission, and thus provide a higher quality of life for patients.Towards this end, poly(*N*-isopropylacrylamide) (PNIPAM) and hyaluronic acid-based polymer formulation was synthesized to obtain a sprayable, thermoresponsive polymer system having optimum biocompatibility, immunomodulatory as well as mucoadhesive properties for targeted delivery of drugs and therapeutic agents onto diseased tissues.This polymer formulation was synthesized by two a step procedure. Firstly, amine-terminated poly(*N*-isopropylacrylamide) was synthesized and in next step, this amine terminated PNIPAM was conjugated with the carboxylic group of hyaluronic acid to obtain hyaluronic acid grafted poly(*N*-isopropylacrylamide) polymers. After successful synthesis and characterization of the polymer, its biocompatibility was investigated in Caco-2 cell lines. Results from current studies suggest that this polymer system could be used as a drug-delivery platform for targeted and localized delivery of drugs in colon tissue and is also applicable for intestinal tissue engineering applications.

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Exosome-functionalized, antibacterial bone substitute along with antioxidant herbal membrane for bone and periosteum regeneration in osteomyelitis

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Osteomyelities is a progressive microbial infection of bone, bone marrow and adjacent osseus structure, resulting in severe inflammation, necrosis and oxidative stress. The prime source of this infection is *S. Aureus* which outstretches to bone by hematogenous and direct inoculation during surgical procedures. The treatment includes debridement at the infected site followed by antibiotic therapy. Debridement creates a dead space that compromises with bone mechanical strength and disruption in blood supply owing tosurgical resection of periosteum (the outer vascular layer of the bone), ultimately leads to fracture. We have already established a treatment regime of S. Aureus infected osteomyelities rat model using local delivery of Rifampicin in a biodegradable bone cement. However, prevention of infection, along with regenerating periosteum at the defect site is a formidable orthopaedic challenge. Herein, we are integrating the antibiotic therapy with rat bone marrow derived exosomes, for enhancing the bone regeneration at bone nidus. Also to regenerate periosteum besides preventing the spread of infection, an antioxidant herbal scaffold has been developed, which will combat the oxidative stress related secondary complications and recapitulate the natural bone healing process. The fabricated scaffolds were successfully characterized and evaluated for osteogenic, antimicrobial and antioxidant activity in- vitro and its potential is further being explored in an in-vivo rat tibial osteomyelitis model.

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Synthesis, Characterization and Remedial action of p-Ag nanoparticles

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The development of non-toxic metallic nanoparticles (NPs) offers an imperative key for their broader use in the biomedical field. The toxicity of NPs generally arises from their origin of synthesis. Among different synthesis procedures, the green method is being considered as a promising approach in nanobiotechnology that bestows environmental as well as the economic benefits. Therefore, in the present study, the silver (Ag) NPs were fabricated using *pakhoi* (*p*), a traditional alcoholic beverage that is popularly used in the Garhwal region of Uttarakhand which has been known to possess significant antimicrobial properties. These *p*-Ag NPs were physicochemically characterized by different techniques. UV-Visible spectroscopy confirmed the formation of *p*-Ag NPs as indicated by a maximum absorption peak between 240 and 260 nm. Transmission electron microscopy showed almost spherical shape of *p*-Ag NPs with a particle size in a range of 50 – 100 nm. FTIR spectra exhibited reduced *p*-Ag NPs. The net charge on *p*-Ag NPs was calculated to be + 23.8 mV. Next, *p*-Ag NPs displayed strong antibacterial activity against *Escherichia coli* (MTCC 42) compared to Ag NPs and *pakhoi*. In conclusion, the p-Ag NPs possess potent antibacterial activity in environmental remediation and can be used in biomedical applications.

Keywords: *pakhoi*; Ag Nanoparticles; *E. coli*, antibacterial

Laser mediated surface modification of Poly (methyl methacrylate) for dental applications

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Longer life expectancy has led to an increase in the aging population worldwide with a proportional increase in the number of people requiring removable partial/complete dentures. Poly (methyl methacrylate) has been the material of choice for the fabrication of removable and complete denture prostheses. However, it allows micro-organisms to adhere and colonize readily on its surface, facilitating biofilm formation. It has been widely reported that denture biofilm acts as a reservoir for opportunistic microorganisms that can cause local infections or even systemic diseases. Candida albicans, the predominant oral yeast isolated from dentures, is one of the common causative factors for the development of denture stomatitis/oral candidiasis, which affects approximately 72% of denture wearers. Other microorganisms such as Streptococci spp., Actinomyces spp., and Lactobacilli have been reported to be associated with the onset of caries, periodontal diseases, or even respiratory tract infections.

Efforts have been made to reduce the microbial adhesion on the denture base by adding antimicrobial agents or by modifying the polymer present in the denture base material. Both these attempts would either result in the alteration of the polymeric network structure or the structure of the polymer itself possibly leading to detrimental effects on the properties of the resultant denture base material.

The present study aims to investigate the suitability of laser-assisted surface modification of biomaterials for dental applications with a particular interest in materials used for the fabrications of dental prostheses. Focused application of Lasers with sufficient energy on a material would lead to localized ablation thus imparting unique surfaces features and may produce “self-cleaning surfaces” with textures composing of micro/nanopillars and low surface energies that will minimize microbial adhesion/colonization. This will hinder the formation of biofilm and prevent the onset of associated oral and systemic diseases.

Designing silk fibroin-based biopolymeric nano drug delivery system for cancer therapy

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Nanoparticle-based drug delivery systems have offered a vast improvement in drug loading, targeting, and efficacy in cancer treatments. The aim of this study is to determine the efficacy of ligand-modified silk fibroin nanoparticles as a controlled release delivery system. Silk fibroin offers remarkable biocompatibility and can be chemically modified to alter surface properties or to immobilize growth factors.

Silk fibroin nanoparticles (SFNPs) were synthesized by the method described by Rahmani et al. (Rahmani et al., 2019). Poly-L-lysine, containing amine groups, can be efficiently conjugated to the hydrophobic substances with carboxyl moieties. SFNPs were surface coated with poly-L-lysine. The best method to maximize the efficacy of a drug is to deliver a proven therapeutic agent with a targeting ligand that exhibits little affinity for healthy cells but relatively higher affinity for diseased cells. Nanoparticles were further decorated with hyaluronic acid (HA) as a targeting ligand, a polysaccharide known to interact with hyaluronan receptor (CD44), overexpressed in several tumor types. Epidermal growth factor receptor (EGFR) has been found to be overexpressed in majority of cancer cell types. Hyaluronic acid-decorated SFNPs were further covalently linked with EGFR antibody and loaded with DNA intercalating drug, doxorubicin (DOX) (Vangara et al., 2013). The nanoparticles and nanoparticle-targeting ligand conjugates were characterized by scanning electron microscopy (SEM), dynamic light scattering (DLS), fourier transform infrared spectroscopy (FTIR), and X-ray diffraction (XRD) studies. Further, loading and pH-responsive drug release profiles were determined, and cell viability study (MTT assay) using U-87 MG cell line was carried out.

The study showed ligand-modified SFNPs to be an efficient drug delivery system for dual-targeted cancer therapy.

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In silico Pathway Analysis of target for Osteoporosis

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Osteoporosis is a metabolic bone disease leads to porosity and mild fracture of bone irrespective of trauma or injury. There are several therapies were undergone by clinicians to overcome osteoporosis like medications, hormonal therapeutics and biomaterial based therapies. However, these shows certain risk factors like stroke, osteonecrosis and other heart related disorders. These may be due to inappropriate targets which may involve in several other signaling mechanisms. These can be overcome by analyzing an appropriate targets of bone remodeling to reduce bone resorption. Insilico approach towards pathway analysis of target molecule using bioinformatics tools like cytoscape will help to reduce such risk factors.In further evaluating the osteoclast mechanism and analyzing molecules involved in bone resorption and their molecular pathways using cytoscape will be useful to find specific target and their pathways with reduced risk factors towards other organs.

KEYWORDS: Osteoporosis, Therapeutic molecules, Bone resorption, Pathway analysis, Cytoscape

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Chitosan- TPP/ Keratin Based Bioink for Cartilage Tissue Engineering

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Cartilage tissue engineering plays a pivotal role in repairing damaged cartilage as cartilage has limited self-repairing ability. Three dimensional bioprinting (3DBP) is a technique in the field of tissue engineering which enables the formation of bioprinted structures that can resemble the native tissue or organs using a bioink which is a combination of biomaterial and cells. The biomaterial can be of natural or synthetic origin. One such natural polymer known to be effectively used in cartilage tissue engineering is chitosan. Chitosan is biocompatible in nature and supports cell attachment and proliferation. Despite being a good biomaterial, chitosan has a disadvantage of making mechanically unstable hydrogels. Polymeric fibers can be added to hydrogel to increase the strength of the hydrogel. Keratin is one such material which is also recognized as a biomaterial and supports the growth and attachment of multiple cell lines. Keratin fibers from hair are extracted by oxidation method and are added to chitosan solution. The chitosan which has engrained keratin fibers is then crosslinked by tripolyphosphate (TPP), an anionic crosslinker that binds to cationic polymers and forms hydrogels. The present study was limited to viscoelastic and gelation analysis. For the study, the concentration of chitosan solution was 2.1% (w/v). The concentration of chitosan to TPP was in the ratio of 7:3 (w/w). The keratin fibers dispersed were in the concentration of 1:2 (w/w) to chitosan. The fiber embedded hydrogel was analysed to have increased mechanical strength with high porosity. The gelation was spontaneous resulting in stable gels which had high swelling property. The chitosan- TPP/ keratin based bioink can be further analysed by biological assays and in vitro analysis to determine its biocompatibility and biodegradation so that this bioink can be developed as a potential bioink for cartilage tissue engineering and regenerative medicine.

Keywords: Bioink, Chitosan, Keratin, Tripolyphosphate, Cartilage Tissue Engineering

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Development of 3D Bioprinted Biomimetic Mini Liver Organoids as a Drug Screening Platform

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Tissue and organ regeneration is a regulated process to maintain the health and functioning under both normal conditions as well as during the sub-critical tissue defects. Nonetheless, problem arises in case of critical defects where conventional medical intervention renders inadequate outcome. Thus, there is utmost need to develop alternative strategies that can augment the regeneration process. One of the most challenging yet unrecognized organ that is in desperate need of such solutions is the liver, that lacks proper treatment strategies on its injury. According to latest data published by WHO in 2018, liver disease deaths in India reached 264,193 or 3% of total deaths. Till date the proven treatment for end stage liver disease is liver transplantation or new developments in liver-support devices, however, the limited availability, expenses, and related-complicationsis not always a solution for the immediate risk the disease may pose. Purpose of this study is to utilize cutting edge technique of multiple extruder 3D bioprinting (3DP)to fabricate and develop functionalized biomimetic mini liver constructs as drug screening platform and personalized medicinal approach. We explored caprine decellularized ECM (D-ECM) as an active component of the bioink that could mimic niche characteristics of native liver tissue as well as support the growth of liver cells. The work focused on development of GelMA/PEGDA-D-ECM based bioink and perform extensive physico-chemical and biological characterization of the fabricated constructs. Cytocompatibility analysis with HepG2 (hepatocellular carcinoma) showed that the constructs allowedcell proliferation and differentiation for a period of 18 days. Further, by utilising dual extruder 3D Bioprinting technique, native like lobular architecture was developed. Results from current studies suggest that with the addition of D-ECM as a bioink component, provided shear-thinning property to the bioink enabling the bioprinting of anatomically and spatiotemporally similar structures to the native liver tissue.

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Nano Thickness Film-forming Bioactive Composition For Tissue Regeneration

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The present study aims to develop cotton fibers reinforced nanoporous tissue regenerative scaffold to intensify tissue regeneration or wound healing. The scaffold is composed of randomly arranged cotton fibers as dispersed phase (Dp) and nano thickness film-forming tissue regenerative composition as continuous phase (Cp) which was composed of a mixture of chitosan (0.5%) and PVA (0.5%). The Dp was mixed with Cp and cryodesiccated for 48 h to obtain the fibers reinforced scaffold. The composition can surface coat the dispersed phase and interconnect the fibers which resulted in the formation of the nanoporous scaffold. The obtained scaffold was assessed for pore size, moisture uptake ability by dynamic vapor sorption, intactness of surface coat, compatibility with erythrocytes, the thickness of the film, and antimicrobial property. Further,the thickness of the surface coat, polymer deposition, the morphology of RBC, and hemolysis of RBC due to scaffold were studied by FESEM. The pharmacodynamic activity of the developed product was studied in the excisionwound model (12 mm wound size) by using wistar rats and histopathology of the wound tissues.The results obtained from various in vitro studies showed, pore size <5 nm, film thickness ranges from 400 to 1000 nm, the scaffold is hygroscopic in nature, no hemolysis was observed in presence of scaffold, <25 % polymer loss was observed when exposed to sonic waves. The developed scaffold was able to intensify the wound healing process and resulted in quick wound healing within 12 days of wound induction. The histopathology of skin samples showed thick epidermis, granulation tissue, angiogenesis, fibroblast proliferation, and collagen disposition in the treated group. We conclude that the developed cotton fibers reinforced nanoporous tissue regenerative scaffold can be used to intensify tissue regeneration and can be used as a wound dressingmaterial for open wounds or foot ulcers.

Figure. 1 Represents the digital image of thecotton fibers reinforced nanoporous tissue regenerative scaffold.

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3D Bioprinting of Photo-crosslinkable Kappa-Carrageenan Hydrogels to Fabricate Bio constructs

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3D bioprinting is a promising approach and has made remarkable advances in developing artificial organs for tissue regeneration and in-vitro drug testing models.[1] In 3D bioprinting of biological constructs, biomaterial-based-hydrogel systems have the advantage of good swelling features, availability, biocompatibility, biodegradability, good interaction with the host tissues, and have cell-binding sites that promote cell attachment, growth, differentiation, and proliferation within scaffold matrix.[2] Here, photocurable methacrylate-κ-carrageenan (MA-κ-CA) was synthesized as an appropriate biomaterial for light-based digital light processing (DLP) printing technology to fabricate complex three-dimensional (3D) cell-laden structures for tissue engineering applications**,** Figure 1. 3D printed hydrogels with different concentrations of 1, 2, 3, 4, and 5 % (w/v) of MA-κ-CA were fabricated and were entirely investigated for properties of rheological, mechanical, swelling, degradation, and suitability for bioprinting with living cells. Viscosity and shear thinning behavior of MA-κ-CA were found optimal for the bioprinting of cells. Through the DLP printing, we have successfully demonstrated the processing of MA-κ-CA hydrogels into complex 3D hydrogel structures with high resolution and accuracy, high fidelity, and good biocompatibility.

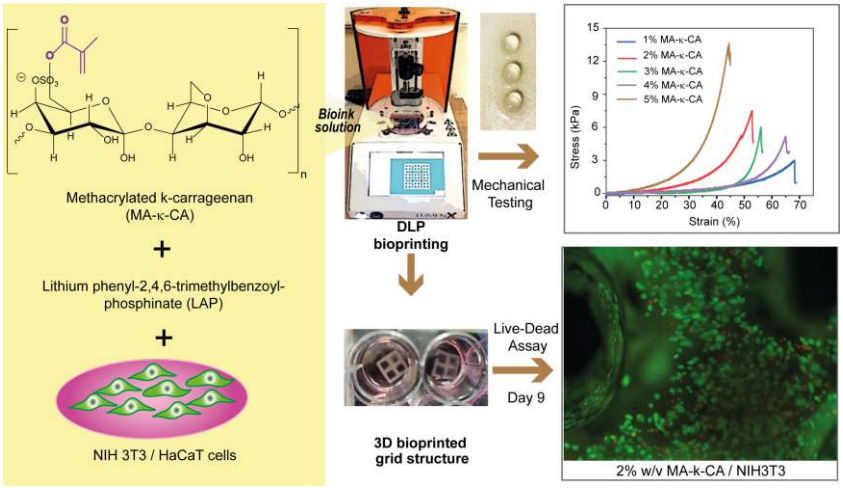

Figure 1. Schematic representation shows the photocuring process of MA-κ-CA hydrogels and mechanical properties of 1, 2, 3, 4 and 5 % (w/v) MA-κ-CA hydrogels.

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Graphene Oxide incorporated polymeric hydrogels for Drug delivery applications

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Natural bones are made up of organic and inorganic components such as collagen, chitosan and nano crystalline materials like hydroxyapatite and beta tricalcium phosphates respectively. Recently, naturally derived polymers along with graphene materials based hydrogels are gaining importance in the field of biomaterials especially in the biomedical applications such as drug release, wound healing and bone tissue engineering. These hydrogels possess several properties which majorly include non-toxicity, swelling and deswelling property, porous network structure and excellent biocompatibility. Along with these advantages, there are certain disadvantages like low tensile strength, initial burst release and rapid disintegration. These can be eradicated by the incorporation of graphene-based materials such as carbon nanotubes, graphene oxide, reduced graphene oxide etc. Graphene oxide is a single layered structure consisting of number of functional groups such as epoxy, carboxyl and hydroxyl groups present all along the surface and edges. Polymeric hydrogels along with the tailored graphene oxide increases the mechanical strength, suppresses the initial burst which makes it a favourable candidate for the biomedical applications. This present work focuses on the preparation of multicomponent chitosan incorporated graphene oxide-based hydrogel for drug delivery applications. The hydrogels have been characterized by using various characterization techniques such as FTIR, FESEM, XRD etc. The drug delivery applications have been performed for the antibiotic drug cefotaxime at the pH 7.4 using Phosphate Buffered Saline (PBS) and evaluated at various time intervals. The *Invitro* bio-resorption studies has been carried out by using the Simulated Body Fluid (SBF) for a period of 21 days.

Pharmacological efficacy on silver Nanoparticles caped with piper betle Flower Extracts

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In recent years, most of the researchers reported the potential, non-toxic and biocompatible silver nanoparticles routed through eco-friendly biosynthesis using various plant parts as caping agent. Silver nanoparticles have been synthesized using aqueous extract of *Piper betle* flower caping agent.These silver nanoparticles would be incorporated as a dopant with nano hydroxyapaptite and graphene composites biomaterials. The obtained silver nanoparticles were characterized by Ultraviolet-visible spectroscopy (UV-Vis), Fourier transform-infrared spectroscopy (FT-IR), X-ray diffraction (XRD), Scanning Electron Micrograph (SEM) and Energy dispersive X-ray (EDX) techniques. The triangle shaped nanoparticles observed from SEM technique and the presence of silver and its atomic state proved by EDX have strengthened the impact of this investigation. The pharmacological data proved the potential function of silver nanoparticles against microbes.The anti microbial and biocompatibility studies underway show promising data supporting its use as biomaterials.

Keywords: Silver nanoparticles, *Piper betle* flower and antimicrobial activity.

Novel alternative surgical technique for the assessment and reconstruction of spinal tuberculosis with bioactive implants

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The presence of tuberculosis (TB) is evident from the way that it was seen in mummies from Egypt and Peru (9000 BC) and has additionally been depicted as "Yakshama" in the most established Indian clinical compositions of Charaka Samhita and Sushruta Samhita, tracing all the way back to 1000 and 600 BC, respectively. Tuberculosis is caused due to a bacterial colony named *Mycobacterium tuberculosis* complex. MTBC has a low DNA sequence diversity. TB is known for causing HIV in an average of nearly 374,000 patients, which leads to death despite a successful history of seven decades of chemotherapy. Spinal TB is an exceptionally high-risk kind of skeletal TB. As a result of the strain placed on contiguous neural structures and the severe distortion of the spine, spinal tuberculosis is an unusually high-risk variety of skeletal tuberculosis. It is possible that it is linked to a neurologic deficiency. It is also referred as *Pott's disease.* Spinal tuberculosis (TB) must be detected and treated early in order to minimise the risk of catastrophic sequelae in this situation. Tuberculosis can be detected via MRI scans, CT scans, and needle biopsy, among other methods (TB). To diagnose the illness, laboratory tests and imaging techniques can be performed; however, tissue results using histology and polymerase chain reaction provide the highest level of accuracy. It is impossible to exaggerate the significance of biopsies in determining the existence of tuberculosis in the spine. The use of DNA amplification technologies expedites and improves the accuracy of infection detection. Steel includes ferrite, a magnetic substance that renders it unsuitable for MRI imaging due to its high magnetic field. There are significant electrochemical differences between the two alloys, and it is determined that titanium alloys have a high potential for Hank's solution and a low corrosion current when compared to other metals.

Key words: Tuberculosis, Spinal TB, Biomaterials, Novel reconstruction, Biomedical imaging

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Synthesis, Characterization of NanoHydroxy Apatite Doped Fe_3O_4/ZnO Binary Metal Oxide Composites from Oyster Shells

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Hydroxyapatite is a bio compatible material naturally occurring in our bones and teeth as a mineral form of calcium apatite. In the form of nHAP is highly used as a bio active material in various bio applications as well as in the field of waste water treatment. In this present study, waste Oyster shells was used as a biogenic source to prepare nHAP. To enhance its tensile and mechanical strength nHAP was doped with Fe_3O_4/ZnO metal oxides. nHAP doped metal oxides are prepared by wet precipitation method. The synthesized composites were characterized by using FTIR, XRD and SEM techniques, where UV-visible study were applied to characterize the adsorbents.

The synthesized nHAP/ Fe_3O_4/ZnO metal oxide composites are screened for their biomedical applications for the development of scaffolds. *Invitro* and Antibacterial activity studies carried out to evaluate the biocompatibility and toxic nature of the composites indicates their suitability as biomaterials.

Keywords: Nano Hydroxyapatite, Composites, Biomaterial, Antibacterial.

Decreased osteopontin release form MSC-seeded 3D-micro fibrous matrix improves the expansion of hematopoietic stem cells

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Ex vivo expansion of umbilical cord-blood derived hematopoietic stem/progenitor cells (HSCs) for bone marrow transplantation is a significant challenge. Mimicking the native environment of HSCs *ex vivo* is one of the potential approaches to circumvent this challenge. Culturing of mesenchymal stem/progenitor cells (MSCs) as a base-layer in the cell-culture plastic and growing HSCs in the presence of MSCs is the widely used approach to recapitulate the native environment of HSCs[1]. However, recent findings demonstrating the influence of matrix stiffness on the fate of MSCs highlight the need for developing improved culturing systems for MSCs for recreating their natural environment. Therefore, this study investigated the potential of a bioengineered 3D matrix, developed using collagen surface functionalised poly-caprolactone (PCL) microfibers as an improved 3D environment to expand HSCs. The newly developed micro-fibrous matrix favoured the attachment and proliferation of MSCs and provided a highly interconnectedly porous environment for MSCs growth. The developed 3D system significantly reduced osteopontin (OPN) release, one of the critical regulators of HSC quiescence in the bone marrow. HSCs isolated from umbilical cord blood showed a nearly 40-fold increase corroborating with the decrease in the osteopontin levels in the culture media in the developed 3D matrix. These results indicate the potential for using the developed microfibrous matrix as an improved HSC expansion system.

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Rationally designed scaffolding matrix and dot-printing of cells minimize thermal damage to cells during hybrid bioprinting of living constructs

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3D bioprinting is a promising strategy to engineer living 3D tissue constructs with precisely defined structures and geometries using living cells and biomaterials. Hybrid bioprinting allows printing of thermoplastic biocompatible polymers at defined patterns from the high-temperature print-head and cell-loaded bioinks from the low-temperature printhead in a sequential manner[1]. The thermoplastic polymeric scaffolding part provides structural and mechanical stability along with shape fidelity in the printed living construct. However, the thermoplastic polymers extruded with high temperature getting in contact with the printed bioink results in thermal damages to the cells encapsulated within the bioink. This remains as a major limitation for developing living constructs through hybrid bioprinting. Therefore, in this study, we have designed of a novel architecture for the thermoplastic scaffolding matrix and a strategy which can minimize direct contact between the high-temperature strands and thecells encapsulated bioink during hybrid bioprinting. The newly developed architecture showed large pores with high porosity and pore interconnectivity without compromising the mechanical properties of scaffolding matrix. Dot printing of the cells encapsulated within bioink at defined locations within the scaffolding matrixin a layer-by-layer fashion was identified as the optimal strategy to avoid direct contact between the high temperature polymeric strands with the bioink. Dot printing of human mesenchymal stem cells (MSCs) encapsulatedalginate-bioinkfrom low-temperature printhead with thermoplastic polymer polycaprolactone (PCL) printed from the high temperature printhead in the newly developed architecture showed significantly higher viability and functionality in cells in comparison to hybrid bioprinting of MSCs encapsulated bioink on PCL printed with conventional architectures. Thus, this particular study provides a scalable novel method for reducing thermal damage to cells during hybrid bioprinting of living constructs.

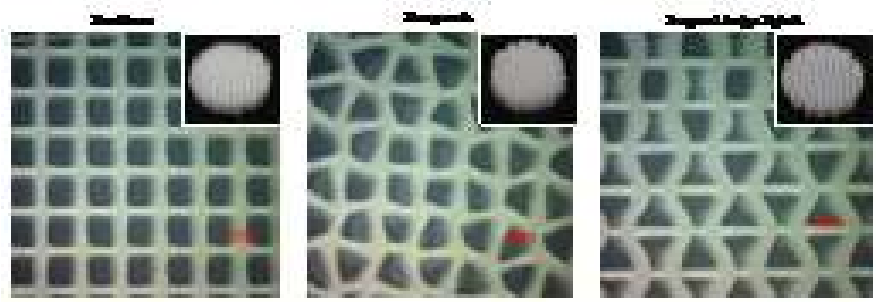

Figure 1: Stereo-microscopic images of 3D-printed PCL scaffolding matrix with different architectures. Insets shows the photographs of printed matrices.

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Controlling macrophage polarisation using immunomodulatory scaffolds for tissue regeneration

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The immune response against tissue-forming scaffolding matrices (SMs)can be influenced by itsarchitecture, structural dimensions and surface characteristics (1). Inflammation is known as the first step in the immune response and modulating the immune response can improve the tissue regeneration at the defect site. Polarization of macrophages is a key step in the initiation and prolongation of the inflammatory response. Several studies in the past independently investigated the influence of size, shape, alignment and surface characteristics of SMsand implants on macrophage polarization (2). However, the combinatorial effect of the structural, functional and topographical features of the SMsin modulating the immune response still remains obscure. Therefore, this study investigated the effect of structural, functional and topographical properties of SMs on macrophage polarization, separately and in combination. We developed SMs having fibersin different structural dimensions (100nm to 350 µm diameter) in isotropic and anisotropic organizations using the synthetic polymer polycaprolactone. Thereafter, the developed SMs were surface functionalized withstem cell derived extracellular matrix (ECM). Polarization of macrophages in response to the developed SMs was investigated by seeding human primary macrophages on to the scaffolds *in vitro*. The experimental results indicate that, nanoscale structural dimensions influenced the polarization of macrophage towards the M2 polarization. This resulted in the suppression of inflammatory cytokines production from the macrophages in response the SMs with nanoscale structural features. In addition, surface functionalization of the SMs with ECM enhanced the overall anti-inflammatory cytokine levels, regardless of the changes associated with the structural and topographical changes. These findings suggest that, the fundamental understanding on the influence of the scaffolding matrix-driven inflammatory signals may help in developing immunomodulatory scaffolds for improved tissue regeneration.

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Evaluation of Time Dependent Corrosion Inhibition Rate for the Graphenated Calcium Deficient Apatite Coatings on 316L Stainless Steel in Simulated Body Fluid

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This successful development of graphenated β-calcium phosphate (β-TCP) by typical physical method and its coatings on medical grade 316L SS (316L Stainless Steel) substrate for orthopedic and dental applications. The synthesized material was confirmed by physical and analytical techniques. The improved adhesion property was clearly shown in the field emission scanning electron microscopy (FESEM) cross-sectional view. The apatite formation ability tested in the simulated body fluid (SBF) with fixed interval (4, 7 and 14 days) and its results revealed that the corrosion inhibition level on time dependent of SBF immersion. The potentiodynamic polarization and electronic impedance studies resulted that the developed materials are potential enough to use it as a biomaterial to correct and repair the hard tissue defects.

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Evaluation of Anti Oxidant Property of Nanocurcumin Derived from Curcumin Longa Rhizome

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Curcumin is a highly non-toxic, bioactive agent found in natural turmeric herb (Curcuma longa) and has been known for centuries as a household remedy to many ailments. However, it shows low solubility nature. The study aimed to develop a method to prepare curcumin nanoparticles to improve their aqueous-phase solubility and examine the effect of its anti-oxidant properties. Nano-curcumin was prepared by a process based on a wet-ball milling technique and was found to have a narrow particle size distribution in the range of below 150nm. Unlike curcumin, nano-curcumin was found to be readily dispersible in water in the absence of any surfactants. The chemical structure of nano-curcumin was obtained as same as that of natural curcumin, and there was no modification during nanoparticle preparation. The prepared yellow-colored nano-curcumin was analyzed by using various physio-chemical techniques. A low inhibitory concentration of nanocurcumin was determined for anti-oxidant strain which was compared with curcumin. It was decided that the aqueous dispersion of nanocurcumin was much more effective than curcumin is radical scavenging assays. The results demonstrated that the anti-oxidant activity and water solubility of curcumin markedly improved by particle size reduction up to the nano range. These results conclude that the ball-milled nano-curcumin is efficient for anti-oxidant application.

Keywords: Curcumin, Nanocurcumin, Ball milling, Antioxidant

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The hidden mystery behind total artificial heart - a woman's heart beats in backpack

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Heart, one of the most imperative organs of the human body, not only humans, even for almost all living organisms. Due to innumerable reasons heart problems are flattering a major health issue day by day. The probable reasons for heart failure are lifestyle, food habits and rarely by genetic inheritance. As the heart pumps the blood throughout the body, a severe failure leads to death. As the time passed, a major complication of the requirement of heart for transplant became very high, which led to an increase in waiting of patients with severe cardiac failure. In this scenario the Total Artificial Heart (TAH) came into screen, which gave hope to the patient's misery from severe cardiac failure. This was a watershed moment for patients waiting for a new heart, paving the path for mechanical devices to be utilized as a bridge to transplantation. In the advancement of technology, the TAH is further upgraded and finally the Food and Drug Administration (FDA) has approved SynCardia Systems, LLC's 50cc temporary Total Artificial Heart System (50cc TAH-t) as a bridge to heart transplantation for patients. Future perspective is that the TAH therapy is on the edge of being long-drawn-out to include patients who are not candidates for heart transplantation. Including the Total Artificial Heart transplantation this article depicts the overview and comparison of both natural and artificial hearts transplantation and their complications.

Key words: Total Artificial Heart, Cardiac failure, Heart transplantation, Mechanical circulatory assist device.

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Biomineralization and Nano-hydroxyapatite synthesis by Bacteria

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Biomineralization is the process through which living organisms produce minerals and this method has great potential in various technical applications. Hydroxyapatite (HA) is calcium phosphate ($Ca_{10}(PO_4)_6(OH)_2$), a naturally occurring mineral of biological and agricultural importance. HA has been used as a bone substitute and implant coatings due to its high similarity to inorganic components in bone and tooth structures, ability to improve biocompatibility, and integration to the native bone tissue. Nanostructured hydroxyapatite (nHA) has significant advantages over HA due to its nanostructure, crystallinity, and chemical similarity to human bone and dentine. It has large surface area and has multiple uses like drug, protein, and gene carriers.

Microorganisms are ubiquitous in nature and possess surprising methods to synthesize various minerals by biomineralization. Certain bacteria can produce nano-hydroxyapatite (nHA) due to the presence of phosphatase enzyme. This enzyme liberates phosphate ions, which react with calcium and forms nHA. Phosphatase enzyme activity of the Enterobacteriaceae family was tested. *Serratia marcescens* and *Klebsiella pneumoniae* produced high-level phosphatase enzyme. Culture conditions for bacterial synthesis of nHA were established and synthesized nHA was characterized by XRD and FTIR. Experiments are ongoing to improve yield.

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Nano-Silica/Silk Fibroin-based Bilayered Foam for Rapid Haemostasis

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Uncontrolled bleeding caused due to traumatic injuries is a major cause of preventable deaths. Haemorrhage accounts for 40% of trauma mortality, 56% of which occur in the pre-hospital setting.1 In this scenario, researchers worldwide are trying to develop local haemostats that could induce rapid blood coagulation for emergency assistance. This study reports a novel strategy by fabricating a bilayered hemostatic foam. Herein, the foam consists of a top bioactive layer (silica nanoparticles (SNPs)/silk fibroin nanocomposite); and a passive chitosan layer (fig. 1). SNPs and chitosan are strong procoagulants; however, they possess mucoadhesive that causes rebleeding during post-application removal.[2,3] Therefore, SNPs were loaded into a non-adhesive matrix (fibroin) to aid in easy removal while leaving its clotting behaviour unaltered. The second layer in the foam is a thick, porous chitosan foam that adds to the absorption capacity of the developed haemostat. Herein, a facile fabrication process was established to enable commercialization. The foam composition was optimized based on the clotting behaviour of the individual components. The haemostatic efficacy of the developed foam was compared with the recently FDA-approved product, Axiostat. The *in vivo* study demonstrates that the foam could achieve rapid haemostasis (30 s) with significantly lower blood loss ($p < 0.05$). Additionally, the limitations of adhesiveness and rebleeding were addressed. Considering the ease of fabrication and haemostatic ability, the developed bilayered foam could be a promising haemostat to be used in various emergency scenarios.

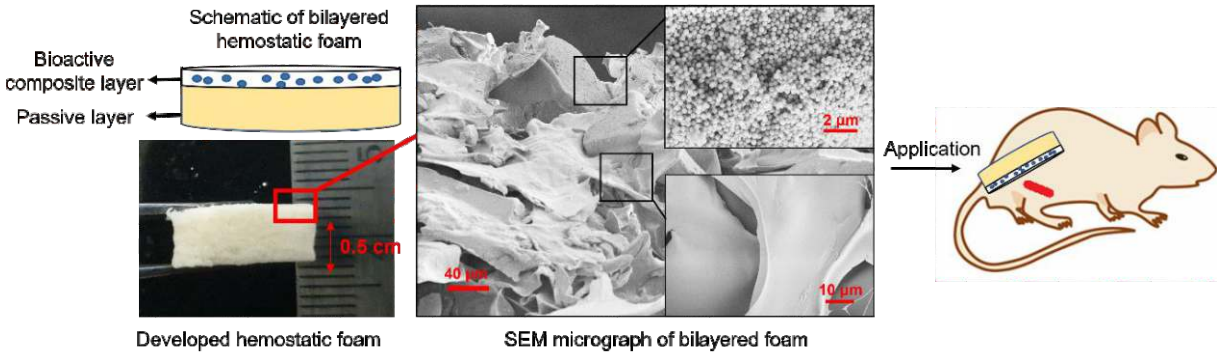

Fig 1: Schematic abstract of bilayered composite hemostatic foam

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Fabrication and characterization Poly- (Lactic Acid) based radial gradient porous scaffold for bone augmentation using fused filament fabrication

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This research work is focused on design and development of scaffolds of controlled porosity with interconnected pores to facilitate sufficient supply of oxygen, blood and nutrients for healthy growth of bone cells. Firstly, scaffolds with square, rhombus45°, rhombus60°, hexagon and triangular pore geometry was designed in solid works 2016 with overall dimensions of Ø15 × 5.12 mm and 600 µm air gap. Fused filament fabrication (FFF) process was used for three dimensional (3D) printing of these scaffolds. Based on the porosity, surface area and compression test results of these single phased scaffolds, the radial gradient porous (RGP) scaffolds was designed mimicking the cortical and cancellous regions of a natural bone having the dimensions of Ø25 × 5.12 mm with 500 µm and 800 µm air gap respectively. RGP Structure with outer pore geometry of square and inner pore geometry of hexagon was designed and fabricated considering the enhanced compressive strength of square pore geometry and enhanced surface area of hexagonal pore structure. The lack of sufficient hydrophilicity of the printed scaffold hinders an efficient cell seeding and subsequent cell-materials interaction leading to failure of tissue regeneration. These printed scaffolds were hybridized with bioactive natural polymers chitosan (2 wt. %) via physical surface modification using vacuum impregnation methods and cross-linked with 20 % of Glutaraldehyde (GA). All these scaffold had porosity in the range of 50-60% well within the recommended value for proper vascularization. The maximum compressive strength obtained was 39 MPa for square pore scaffolds. SEM result provided the evidence of controlled and interconnected pores, a key feature for cell proliferation and differentiation.

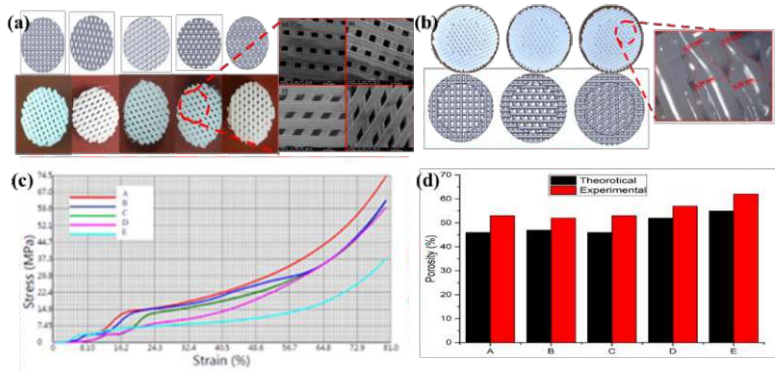

Figure1(a) Single phasic scaffolds with square, rhombus45, rhombus60, hexagon and triangular pore geometry and respective SEM images **(b)** CAD model and respective 3D printed RGP scaffolds with microscopic zoomed view at boundary of two regions. **(c)** stress- strain curve of all scaffolds **(d)** graph showing deviation in porosity from theoretical to experimental value

Novel synergistic antimicrobial agents using pendant group modifications on chitosan

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Antimicrobial resistance of pathogens to antimicrobial pharmaceuticals is of a growing concern to humanity. Alternative methods of microbial inhibition are being explored, and in particular, the use of biopolymers is of significant interest. Biopolymers are nontoxic, bio-degradable, efficient and renewable. Chitosan is one such biopolymer with intriguing biological and physicochemical properties.[1] Chitosan is an antimicrobial agent which is biocompatible and can also act as a delivery vehicle. Chitosan has been known to inhibit biofilm formation and also causes significant permeability alteration of the pathogen's cellular membranes. Chitosan, however, is not equally effective against gram-positive or gram-negative nature based microbes.[2] In the present work, we have focused on improving the antimicrobial effect of chitosan by including bioactive scaffolds such as heterocyclic rings and chromophoric linkers which may assist in biofilm inhibition.[3] The antimicrobial effect of the novel modified chitosan was explored against clinically relevant microbial pathogens and showed an improved response as compared to plain chitosan. The novel modified chitosan showed synergistic effect with respect to the degree of modification done to the polysaccharide backbone. The modifications of the current biopolymer resulted in a novel biopolymer that is vastly superior in its antimicrobial activity when compared to its starting materials. Novel chitosan films displayed improved thermal stability as well.

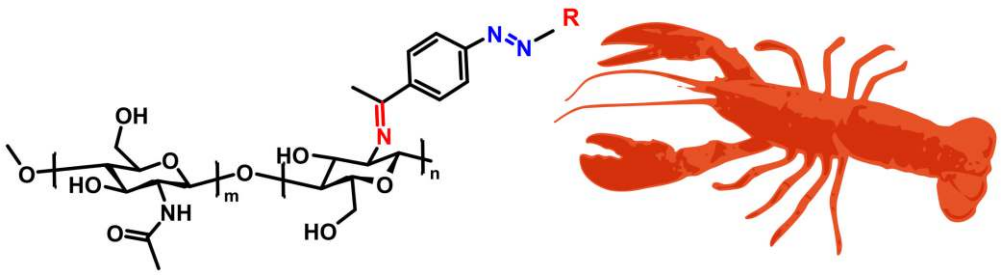

Figure 1: Novel modified anti-microbial chitosan

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Sacrificial Template-assisted Synthesis of Inorganic (Silica) Nanotubes and Evaluation of its Properties for Biomedical Applications

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Mesoporous silica network nanotubes were fabricated using both organic and inorganic templates such as citric acid (CA), cetyltrimethylammonium bromide (CTAB), and sodium bicarbonate (SBC). The phase analysis of synthesized silica network was confirmed by X-ray diffractometer (XRD) analysis, and the present functional groups were revealed by Fourier Transform Infrared Spectroscopy (FTIR) and the formation of tubular morphology was analyzed by transmission electron microscopy (TEM). The mesoporous nature of each template sample was studied using Brunauer–Emmett–Teller (BET) instrument. The surface area and porous size were calculated successfully for fabricated silica network nanotubes.

Keywords: Silica Nanotubes, Mesoporous, Surfactant, Surface area

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A Novel Biopolymer-Calcium Deficient Apatite Composite Small Diameter Blood Vessels for Cardiovascular Applications

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The substitution of biologically relevant ions into the calcium-deficient apatite matrix enabled the composite materials suitable for the formulation of hemocompatible devices. In the present work, CS-apatite composite substituted with Ni^{2+} ions was prepared to fabricate small-diameter blood vessels through the extrusion process. The extruded small-diameter blood vessels are tested for their physical and chemical properties by using analytical tools such as FTIR, XRD, TGA, and FESEM. The obtained analytical and hemocompatible study results revile that the fabricated blood vessels are the potential to be used for cardiovascular applications.

Keywords: Bioceramic, Extrusion, CDCP, Hemocompatible, and Small-diameter Blood Vessel

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Computational analysis of degradation inporous scaffolds under simulated *in vivo* conditions

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Scaffolds are widely used in tissue engineering. Scaffolds serve as a porous, degradable yet temporary supporting structure that assists in tissue regeneration process. A porous scaffold is known to provide the substitution of an extra cellular matrix (ECM) to support cell-material interaction for a new tissue formation. Cell-material interaction involves cell proliferation, differentiation and migration. During tissue regeneration process, a scaffold degrades with time and the new tissue replaces the degraded structure with its own ECM. The rate of degradation of these materials should match with the rate of new tissue regeneration, while the scaffold material provides the necessary structural stability and degrades in the due time. To predict this aforementioned behavior of scaffolds, computational methods are adapted to design and develop scaffolds with appropriate degradation time. In this work, the degradation behaviour of a synthetic polymer scaffolds was studied in simulated *in vivo* condition. The material used in this study is PLA. The model proposed in this work was designed using computer-aided design software SOLIDWORKS 2019 and was simulated in finite element analysis software, ANSYS 2020. The solid model was discretized into small voxel elements using tetrahedron mesh and the required material properties of each domain were provided. This process was repeated till adequate erosion rate is determined. In order to validate the model, the simulations results were compared with the empirical degradation experiments of scaffold in a bone tissue available in literature. The result obtained has substantially affirmed the homogeneous degradation of proposed model.

	Input		Output	Erosion Rates (kg/m²s)
	Inlet velocity (m/s)	Interaction velocity (m/s)	Outlet velocity (m/s)	PLA
Case 1	1.7	1.7	5.42	3.34e-03
Case 2	2.0	2.0	5.455	3.34e-03
Case 3	2.5	2.5	5.72	3.34e-03

Table 1. Input parameters along with output and erosion rate

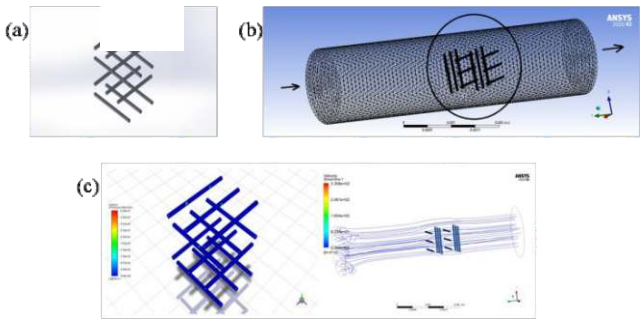

Figure 1. Computational flow domains and flow analysis results

Stress Evolution in Coronary Stent using Finite Element Method

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Coronary stents are meshed liked tubular structures that are implanted inside the blood vessels to cure the narrowed arterial segment. These stents are deployed using inflatable balloon mechanism mounted on a catheter. As the balloon inflates, it generates radial load on the inner walls of the stent resulting in expansion in radial direction. This expanded stent holds the arteries wide open for ensuring continuous blood flow in blood vessels even after deflation of the balloon. The performance of the coronary stent can be determined by various factors such as materials used and mechanical strength of those materials. However, geometric design is the most influencing factor that affects the functionality and self-life of a stent. An ideal stent possesses high radial strength to withstand the pressure inside the blood vessels. It also has high flexibility for deployment, causing minimum injury to the artery during expansion. Stent expands in a non-uniform arrangement, in which the ends expand more than the middle section. This non-uniform deformation is termed as dogboning. Similarly, the reduction in the length of the stent after expansion is known as foreshortening. These non-uniform deformation defects can cause severe damage to arteries and also positioning difficulties, while in operation.

In this study, we analyzed the stress induced during deformation of a coronary stent. The stent deformation is analyzed during the expansion due to applied radial load by inflated balloon, through finite element method. In this work, we also examined different deformation defects such as dogboning, foreshortening and recoil of expanded stent made from Stainless steel and WE43 magnesium alloy. The simulation was performed using COMSOL Multiphysics numerical simulation tool. The stresses induced in the stent is compared for stainless steel and WE43 magnesium alloy. Palmaz-Schatz and Lozenge stent model is used and expanded up to 2 mm diameter. In accordance to the finite element analysis performed, it was found that magnesium alloy stent has developed nominal Von-mises stress equals to 44 MPa and 0.57 effective plastic strain as compared to stainless steel stent 400 MPa and 0.33 respectively (Table 1). Hence from the study conducted, it could be concluded that WE43 magnesium alloy is suitable for the therapy of coronary diseases.

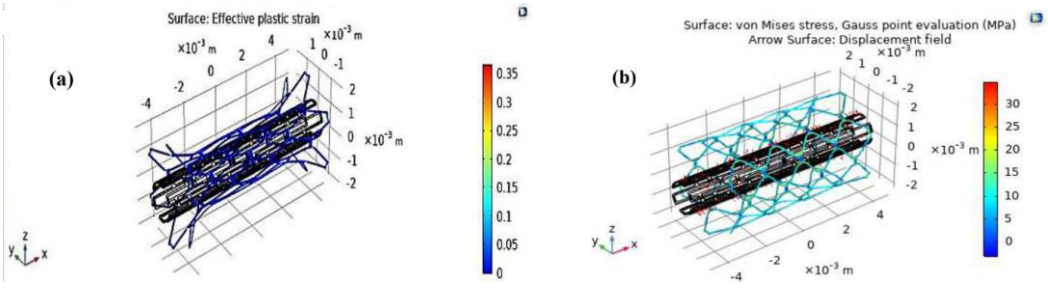

Figure 1. Deformed stent after deflation of balloon, (a) Effective Plastic Strain after stent deformation for Mg alloy, (b) Von-Mises stress (MPa) for Mg alloy.

Table 1. Finite element simulation result comparison of Mg alloy (WE43) and stainless steel (SS-316L).

Material	Von-mises stress [MPa]	Effective Plastic Strain	Non-Uniform Deformation		Recoil Evolution
			Dogboning	Foreshortening	Radial Recoil
WE43 Mg alloy	**44**	0.57	0.5	-0.18	0.67
Stainless steel (SS316L)	**400**	0.33	0.59	-0.001	0.674

Development of Olive Oil-based Degradable Polyurethanes with tunable properties for Bone Tissue Regeneration

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Designing the biomaterial for bone tissue regeneration with an intermediate degradation rate between slow degrading polyesters and fast degrading surface eroding polymers is challenging. Polyurethanes are known for their noteworthy physico-mechanical properties along with good biocompatibility and thus used extensively in the biomedical field. In this study, two different polyurethanes were synthesized from olive oil and optionally including polyethylene glycol (PEG). The use of a plant-based oil monomer imparts degradability to synthesized polyurethane. The hydrophilicity and thus degradability of polyurethanes were improved by addingPEG into the polymer system. Both the synthesized polymers were analyzed through physical, chemical, mechanical, and thermal characterization. The result showed that the degradation rate increases and mechanical properties decrease with the incorporation of PEG. The synthesized polymers can be fabricated in various 2D and 3D structure using compression molding and salt leaching technique. The prepared polyurethanes showed good cytocompatibility *in vitro*.The differentiation study revealed that polymers exhibited osteogenic differentiation of pre-osteoblast cells. Thus, these polyurethanes can serve as effective biomaterials for developing scaffolds for bone tissue regeneration with tunable intermediate degradation and mechanical properties.

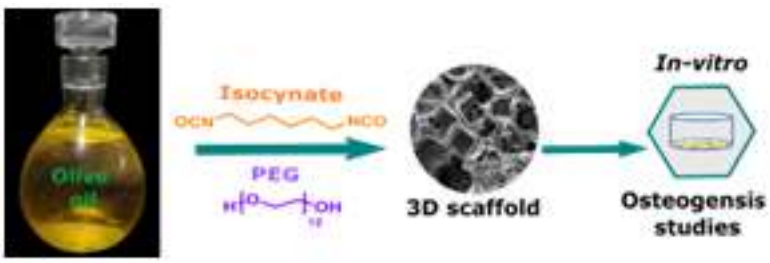

Fig.1: Schematic of olive oil based polyurethane system for bone regeneration

Capecitabine loaded novel functionalized PLGA nanoparticles targeting colon cancer using a ph-sensitive polymer approach

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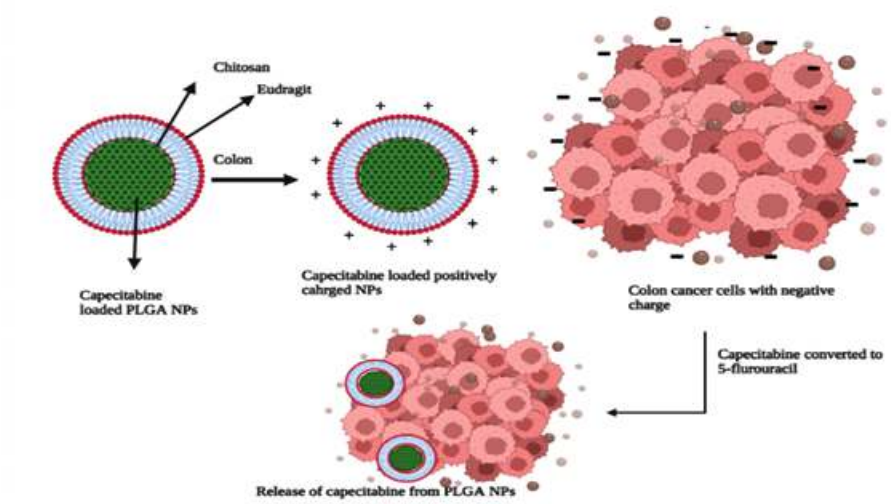
Patients with colon cancer have a high incidence of tumor recurrence and metastasis. The majority of standard drug delivery techniques for treatment fail because the drugs do not reach the site of action in a sufficient concentration, necessitating colon-specific medication delivery. Recently, it was discovered that poly (lactic co-glycolic acid) (PLGA) has the potential to be used as a wide therapeutic drug delivery polymer. Biodegradable polymeric nanoparticles have the potential to encapsulate hydrophobic drugs, preserve therapeutic molecules, and offer a number of other benefits over their bulk counterparts. Surface modification (Galactosylation) also improves the efficiency of in vivo navigation and prolongs the release of anticancer medicines. For colon targeting, galactosylated PLGA nanoparticles of Capecitabine (CAP) were synthesized by double emulsion solvent evaporation and coated with a pH-sensitive polymer (eudragit S-100). The formulations' particle size, polydispersity index (PDI), drug loading efficiency, and drug release were all assessed. The activities of developed nanoformulation in Caco-2 cells were investigated using flow cytometry. According to the data, Eudragit coated galactosylated PLGA NPs of CAP (Eud-gal-CAP-PLGA-NPs) had an average size of 178 nm and a drug loading efficiency of 8.49 percent, according to the data. In addition, in vitro release was pH-dependent. In colon cancer cells, targeted NPs had greater cellular uptake than non-targeted NPs. Eud-gal- CAP-PLGA-NPs decreased cell viability and triggered apoptosis in CACO-2 cells more effectively than non-targeted NPs. According to the findings of this study, a biocompatible nanodrug delivery system based on functionalized nanoparticles might provide a unique technique for the targeted delivery of chemotherapeutic drugs to tumors in the colon.



Corona poled gelatin - magnesium hydroxyapatite – multiwalled carbon nanotube composite scaffold exhibits antibacterial action with osteogenicity

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Bone filler materials possessing excellent biocompatibility and osteoconductivity clinically are used to promote the repair of bone defects. These materials have attracted the attention of many researchers to investigate their effect on bone growth with electrically active properties. In the present study, $Ca_8Mg_2(PO_4)_6(OH)_2$ – Gelatin (MgHA-GEL) bone scaffold embedded with multi walled carbon nanotube was fabricated by freeze-drying method. Multi walled carbon nanotube-based scaffold can be used in bone defects and bone repair that would promote the strength of the scaffold. The primary objective of this study was to evaluate the osteogenic properties of scaffold after negatively poling its surface and the corresponding scaffold was cultured with MG63 osteoblast like cells. The *in vitro* results showed that the cell viability was increased after 7 and 14 days of culture along with increase in the relative expression of RUNX2, COL 1 and OCN osteogenic markers by 27%, 21% and 33%. Alkaline phosphatase activities showed increased mineralization. Elevated compressive strength (196 ± 6 kPa) with 45% porosity was observed for MWCNT–MgHA-Gelatin scaffold. These results envisaged that the prepared negatively polarized scaffolds can be used as promising materials in bone tissue engineering.

[1] T. R. Rautray, R. Narayanan, K. H. Kim:Progress in Materials Science. 56 (2011) 1137-1177. DOI: 10.1016/j.pmatsci.2011.03.002

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Arjunic acid incorporated Strontium hydroxyapatite scaffolds: A future perspective for bone tissue engineering

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The potential of Arjunic acid, an extraction product of *Terminalia arjuna* to be used as medicines for treatment of cardiovascular diseases, muscular tissue damage and in various other fields is quite satisfactory. However, there is a scarcity of data describing use of arjunic acid as nanobiomaterials for bone tissue engineering. Arjunic acid shows excellent gel forming ability with many of the organic solvents which is because of nano fiber formation implying to obstruction of solvent molecules within the fiber. The present work demonstrates the extraction of arjunic acid by ethanol treatment and incorptaion of it in strontium hydroxyapatite scaffold by polymer sponge method. The fabricated scaffolds were characterized and bioactivity was studied. Results obtained from the current research indicate *Terminalia arjuna* incorporated strontium hydroxyapatite scaffold may act as low cost bone graft substitutes and also as bone filler materials.

Polarised multiwalled carbon nanotube - Cu substituted hydroxyapatite – chitosan composite scaffold exhibits enhanced osteogenicity and antibacterial efficacy *in vitro*

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To meet the requirement of clinical applications, composite scaffolds meant for filling bone voids can be used. The objective of this study was to fabricate polarised multiwalled carbon nanotube - Cu substituted hydroxyapatite – chitosan (MWCNT-CuHA-CS) composite scaffolds by freeze drying method for bone tissue engineering applications and they were characterized by X-ray diffraction, thermally stimulated depolarisation current etc.. Further, their ability to promote proliferation of the MG63 human osteoblast like cells for bone regeneration and antibacterial activity against *S. aureus* bacterial cells were studied. It was inferred from the study that polarized MWCNT-CuHA-CS composite scaffold enhanced the spreading of the osteoblasts and helped with the antibacterial activities on the surface of the scaffold with enhanced RUNX2, Osteocalcin, type-I collagen production on these scaffolds compared to unpolarised ones. MTT assays with the MG 63 cells demonstrated better cell proliferation on polarised MWCNT–CuHA-CS scaffold as compared to unpolarised ones. Enhanced mineralization over time was observed in the alkaline phosphatase (ALP) activity. A higher compressive strength (198 ± 7 kPa) was observed for the polarised MWCNT–CuHA-CS scaffold with 52% porosity. These results ascertained that the prepared scaffolds can be used as promising materials in bone tissue engineering.

[1] T. R. Rautray, R. Narayanan, K. H. Kim:Progress in Materials Science. 56 (2011) 1137-1177. DOI: 10.1016/j.pmatsci.2011.03.002

[2] S. Swain, T. R. Rautray, In: B. P. Swain (Eds), Nanostructured Materials and their Applications, Springer, Singapore (2021) 55-80. DOI: 10.1007/978-981-15-8307-0

Fabrication of Polyhexamethylene biguanide /18β-Glycyrrhetinic acid-modified titanium implants with nanorods arrayed enhanced antibacterial and osseointegration activities

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Controlling bacterial infections and promoting osseointegration are two significant issues for titanium implants in biomedical research. Surface activation is needed to endow titanium-based orthopedic implants with antibacterial efficacy and thus enhanced osteogenic activities. In the current investigation, titanium dioxide nanorod arrays (TNRs) were fabricated on the polished Ti substrates using anodization and sintering methods. Then co-modified titanium dioxide nanorod substrates with antimicrobial and anti-inflammatory agents such as Polyhexamethylene biguanide (PHMB) and 18β-Glycyrrhetinic acid (GA) via dip-coating method. *In vitro* culture of MG-63 osteoblasts, *E. coli,* and *S. aureus* bacterial cells were performed on common TNRs, PHMB/TNRs, and PHMB/GA/TNRs substrates to find the effects of polymer conjugate nanorods on adhesion of cells, osteogenic differentiation, and bacterial efficacy. The current in vitro results indicated that the surface modification of implants with PHMB/GA/TNRs inhibits bacterial growth while promoting osteogenic activity concurrently and has excellent potential for future clinical applications.

Dual action of polarised Zinc Hydroxyapatite - Guar gum – multiwalled carbon nanotube composite scaffold as bone filler materials

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In this study, multi walled carbon nanotubes (MWCNTs) and zinc substituted hydroxyapatite (ZnHA) powder were reinforced with Guar gum (GG) and the composite scaffold was fabricated by freeze drying method. The resulted scaffold was then electrically polarised to induce surface negative charge on the scaffold to act as bone substitute material. MWCNT promotes stem cell differentiation, adsorption into osteoblasts and neuronal cells providing extra affinity to bone regeneration. MWCNT embedded with ZnHA-GG scaffolds provides great strength, durability and elasticity to bone implantation, furthermore making it work effectively in load transfer. The purpose of this experiment was to study the assessment of biocompatibility and antibacterial activity of the composite scaffold. *In vitro* culture of MG63 osteoblast cells and *S. aureus* bacterial cells were then carried out on polarized composite scaffolds in conjunction with non-polarized scaffolds to find the effects of polarization on adhesion of cells, osteogenic differentiation as well as antibacterial efficacy. It was inferred that the composite scaffold increased the osteoblasts spreading, boosts antibacterial activity on the scaffold surface, and amplifies RUNX2, osteocalcin, type I collagen formulation by osteoblasts.

Herbal Xanthan Gum based Hydrogel Sheet for Wound dressing

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Hydrogels sheets are considered to be the most distinct material for wound dressing. They play a key role in absorbing and retaining wound exudates and maintaining hydration in dried wounds. A wound dressing has to be safe and biocompatible for its long exposure accelerating the healing properties in the wounded area. Several natural hydrogel materials like agarose, gelatin, elastin have been used for synthesis of hydrogels. Xanthan gum is one of such anionic, high molecular weight exopolysaccharides a versatile biopolymer used for biomedical and technological application. Moreover, several traditional medicine like plant and weed extracts have displayed marked wound healing potential due to its analgesic, antimicrobial, anti-inflammatory properties. In this work we report use of aqueous and solvent based extract of an ignored weed *Chromolaena Odorata* and a pantropical plant *Cassia Occidentalis* adsorbed to xanthan gum-based hydrogel sheets. The physical and morphological characterization of the fabricated hydrogels sheets were carried out by SEM, XRD, FTIR along with its swelling studies. Further biomedical properties of the herbal Xanthan gum sheet were carried out by checking blood compatibility, antimicrobial activity, microbial penetration and mucoadhesive properties. Based on these results, the fabricated plant extract adsorbed hydrogel sheets were considered to an effective way of wound dressing.

Fabrication of Titanium dioxide Nanotube layer by Rapid and Homogenous anodization in Perchloric acid medium

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In biomedical application, implants having titanium dioxide nanotubes (TNTs) on their surface show good fixation to bone. In this investigation, fabrication of TNTs in perchloric acid and strontium chloride solution has been reported. It was also demonstrated that the length and diameter of the nanotubes could be varied by changing the anodization conditions such as electrolyte and anodic potential. The dimensions of TNTs were analysed by using Field emission scanning electron microscopy. The phase composition and crystallinity of TNT layer was investigated by X-ray diffractometry. The cytotoxicity of TNT sample was studied by Lymphocyte cell culture method.

Synthesis of polarized strontium hydroxyapatite - xantham gum – Multiwalled carbon nanotube scaffold exhibits osteogenicity *in vitro*

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Clinical applications of bone tissue engineering demand that bone filler materials should be extremely biocompatible, osteoinductive and osteoconductive so as to accelerate the repair or replacement of bone defects. In this respect the development of scaffolds, aligned with multiwalled carbon nanotubes(MWCNT) is gaining relevance owing to its highly biomimetic and osteoconductive nature. This study was directed to explore the effect of growth of surface charges on scaffolds consisting of strontium substituted nano hydroxyapatite embedded with xanthan gum and multiwalled carbon nanotubes with respect to osteoblast activity in a bone-mimicking environment. Multiwalled carbon nanotubes being a nanomaterial alter the surface characteristics of scaffolds by amplifying the neural cells and biomaterial interaction, provide superior electrical conductivity and also enhances mechanical strength of the scaffold structure. The porosity of the scaffold was increased by 53% in the presence of xantham gum. Polarization of composites were carried out to induce negative charge on the scaffold surface and the specimen was then seeded with MG-63 cells. After 7and14 days of culture, cell viability of polarized scaffolds increased as compared to non-polarized scaffolds. On day 14 of culture, the relative expression of RUNX2, COL1, and OCN on polarized scaffold were elevated by 23%, 41%, and 39% respectively as compared to non-polarized ones. Impressively, in all media used for finding out the contact angle, the negatively polarized scaffold resulted in contact angles lower than unpolarized scaffold, which suggest greater osteoconductivity of polarized scaffold. The present *in vitro* results suggest that negatively polarized scaffolds can be favoured over non-polarized ones (as implant materials) as they enhance osteogenesis and therefore present optimistic applications for bone tissue engineering applications.

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S. Swain, T. R. Rautray, In: B. P. Swain (Eds), Nanostructured Materials and their Applications, Springer, Singapore (2021) 55-80. DOI: 10.1007/978-981-15-8307-0

Skin injury: Dealing burn and keloid with bioactive electrospun fiber

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Skin being the first line of defense is the most important barrier. Any damage to the skin follows various events including recruitment of many cytokines and other inflammatory factors to heal the wound. Burn, a common type of skin injury leads to the traumatization of tissues in epidermis and dermis. Depending on the severity and stage of burn, the migration of keratinocytes and collagen formation often changes with time. Along the cell migration and proliferation in the injured area to fasten healing process, keloid formation is reasonably a major challenge. Restraining physical movement and psychological hindrance due to keloid affect day-to-day activities. The focus is now directing towards preventing scars rather than reducing their visibility with different treatment regimes available,. However, despite of the efforts made to avoid scars, designing a clinically effective anti-scarring treatment has been abstinent. With an emerging use of electrospun fibers, we have tried to address the problem of healing the burn damaged area further avoiding keloid development. The fibers offer mechanical support and structure required for cell invasion to the injured site. Different components incoported in fiber assists in reinforcing cell adhesion and proliferation while retaining moisture in the uppermost layer of the skin for its proper formation. We intend to facilitate the tissue construct of designed biologically active polymeric biomaterial with futuristic goal of developing device for medical use.

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Fabrication of multifunctional luminomagnetic nanoparticles for image guided magnetic hyperthermia

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Multifunctional nanostructured materials offer desirable properties in a single entity and development of such system is gaining attention among the researchers in the recent past. Grafting the nanoparticle with both luminescent and magnetic entities makes it a suitable agent for a wide range of applications such as multimodal imaging, drug delivery, diagnostics and therapeutics. Magnetite nanoparticle is a widely studied agent for magnetic hyperthermia due to its biocompatibility and superparamagnetic property. Likewise, rare earth ions doped apatite nanoparticles have been studied for near infrared optical imaging. Coating of rare earth doped apatite over the Fe_3O_4 can prevent leach out of magnetic ions into the *in vitro* or *in vivo* medium and further ensures the biocombatibility in addition imparts luminescent property. Here, we will discuss the fabrication and characterization of multifunctional Nd^{3+} doped FAP coated Fe_3O_4 nanoparticle.

Decellularized goat tendon derived extracellular matrix (tdECM) hydrogel for stem cell culture in a microfluidic device: Towards tissue specific ECM on chip

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The decellularized extra cellular matrix (dECM) is used as a bioink for 3D bioprinting or as a hydrogel for studying the physiology of tissues. In this study, we obtained dECM from goat digital flexor tendon using physical and chemical methods. The dECM was subjected to enzymatic digestion and the final hydrogel was termed as tendon-decellularized ECM (tdECM). The tdECM was characterized for its physicochemical properties using Fourier Transform Infrared Spectroscopy (FTIR) and Scanning Electron Microscopy (SEM). Collagen, dsDNA, GAGs, and protein contents were quantified using spectrophotometric assays. The cell viability and proliferation of human umbilical cord derived mesenchymal stem cells (*UMSCs*) encapsulated in the tdECM hydrogel inside the microfluidic device was checked using Calcein-AM/PI. The FTIR data showed prominent peaks of amide group indicating the presence of collagen. The SEM data showed intact fiber morphology after the decellularization process. There was 94% reduction in double-stranded DNA (dsDNA) content, hence, proving the effectiveness of decellularization technique. There was no significant difference in the collagen content of tdECM as compared to the native tissue. The GAGs and protein contents were reduced due to the decellularization process but were in the acceptable range. Over 90% cell viability in UMSCs was observed both qualitatively and quantitatively. In conclusion, we demonstrated the effectiveness of decellularization process using a combination of physical and chemical methods followed by tdECM biocompatibility in a microfluidic device for understanding the stem cell behavior in a 3D condition.

Keywords: Tendon-derived extra cellular matrix (tdECM), decellularization, microfluidic model, umbilical cord-derived mesenchymal stem cells (UMSCs)

Current status of self- healing, antimicrobial and remineralization capabilities of dental composites- A literature review

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Dental composites have become the most widely used restorative materials and consist of a resin matrix with inorganic filler particles for reinforcement. Despite their many outstanding properties, composite restorations are challenged by two main problems: bulk fracture and secondary caries due to gap formation and microleakage. Replacing failed, restorations accounts for a large percentage of all restorations performed pose a significant financial burden on the patient.

Self-healing ability of dental composite is due to the release of encapsulated polymerizable monomer into the crack which undergo polymerization within the crack and seal it. Besides the fracture issue, secondary caries is another reason for restoration failures. A novel dental composite was developed with triple benefits of self-healing, antibacterial and remineralization capabilities due to presence of Triethylene Glycol Dimethacrylate (TEGDMA) with N,N-dihydroxyethyl-p-toluidine (DHEPT), Quaternary Ammonium Methacrylates and Calcium Phosphate (CaP) filler particles, respectively. Self-healing was achieved with 65–81% recovery in the virgin fracture toughness, thereby recovering the load-bearing capability of a cracked dental composite.

This review poster provides the reader with an overview with the achievements to date about such materials.

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Role of the ionic species from a divalent salt during the development of alginate hydrogel

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Alginate hydrogels are prepared by using sodium alginate in the presence of divalent ionic salt. The physicochemical property of the hydrogel varies with respect to the type of salt used.

The viscoelastic property of the hydrogels depends on both the cationic part as well as the anionic part of the divalent salt. In this study different cations like Ca^{2+}, $Zn^{2+}$and Cu^{2+}, and their salt with acetate, sulphate, and chloride are analysed. Rheological analysis of all the hydrogel shows acetate salt has high gel strength, whereas among all the cation Cu^{2+} produce gels with a high viscoelastic property. So, it is evidence that the viscoelastic property of the hydrogels depends on both the ionic species. All the concentration was optimized by the image analysis method and stable planar gel surfaces are settled by the paper casting method. Image are analysed by the help of Image J softwere where the opacity of the gel varies along with time. Intensity plot shows at 0.2 M concentration of all the salt form Ca and Zn is optimal for saturation of aqueous sodium alginate where as 0.1 M concentration for Cu ion salts. Storage modulus (G) of all the materials is obtained by soft solid modulus testing which stands with a piece of evidence that mechanical behavior of all hydrogel is the resultant influence of both the cationic as well as anionic part of the used salt.

Key words: Divalent salt, Rheology, Papercasting, Image j

Finite Element Analysis And Multiple Regression Analysis Of Femur Bone Implant For Various Day-To-Day Walking Activities

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Osteoarthritis is a common problem in a patient with hip prostheses. This work aims to discover the stresses in the femur bone implant in the human body so that the implant should not fail during various day-to-day activities. Fatigue testing of the hip implant is used to determine stress-strain properties by simulating the dynamic loading of the implant during the gait cycle in ANSYS and its multiple regression analysis. The preload on the femur bone is extremely important for successfully calculating stresses on the implant. Due to existencence of preload, axial load, and bending load, the implant behaviors are non-linear and cannot be evaluated by simple mathematical formulation. 3-Dimensional finite element analysis approach is only the techniquethatshows some satisfactory results.

Keywords: femur implant, gait cycle, force, finite element analysis, multiple regression analysis

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Utilizationof Biomaterialsin designing cranial implantand its related clinical challenges.

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Cranioplasty is the surgical technique to repair the cranial defect from the cosmetic and the functional point of view and further alleviate the physiological drawbacks. For many years cranial bone repair has been a challenging task for neurosurgeons as it involves significant complications and morbidity in patients. Several factors like Traumatic Brain Injury, Meningioma, Osteoma, Cerebral infarction, etc., are the primary cause of cranial defects. To counter this situation, continuous efforts are taken to improve, and in response, the researchers have come up with varied techniques. Cranioplasty is performed after decompressive craniectomy to restore the integrity of the skull and improve neurological functions. Traditional methods like Autografting and Allografting are effective methods that are looked upon but have drawbacks like bone resorption and graft rejection in the receiving patient. Thus, demand is for looking up for their substitutes. Recently, various biomaterials are suitable for cranial reconstruction like Poly (methyl methacrylate), Titanium, Hydroxyapatite, Calcium phosphate-based bone grafts, which possess higher tear resistance stiffness, strength, and thermal conductivity, inertness, biocompatibility. Cranial defects and their clinical outcomes are tough to deal with, and hence an effective strategy is to be planned to carry out craniectomy and cranioplasty. Multiple factors like patient age, comorbidity, time of surgery, duration between the surgeries, surgeon's biomaterial preference, implant site-specific infections, physiological, functional, and aesthetic issues of the implant biomaterials are crucial factors for success and favorable clinical outcomes of cranioplasty.

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Comparative antibacterial action of polarised HA-UHMWPE and CSA13 loaded HA-UHMWPE omposites as orthopedic implant biomaterial

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Ultra-high molecular weight polyethylene (UHMWPE) being bioinert and having favorable properties like high wear resistance and low coefficient of friction is often used as a bone substitute material. To make it bioactive, hydroxyapatite is added to make a composite of the same. This composite has proved to be a better candidate for orthopedic implants owing to the additional biocompatibility, bioactivity as well as non-toxicity. Nevertheless, the unintended bacterial infection poses serious threat to the success of the implant material. The aforementioned issue is addressed in the current study in which an antibacterial agent CSA13 is added to the composite. Both *S. aureus* bacterial cells and osteoblast cells are seeded on HA+UHMWPE composite surface. In order to assess the antibacterial effect, the bacterial viability test is performed after the culture. In our previous study, polarized HA+UHMWPE composite has shown significant antibacterial property. Comparing both the results, it is revealed that both the methods arrive at similar outcome. However, the introduction of anti bacterial agents like CSA13 inhibits new bone formation. Hence we conclude that, polarized HA+UHMWPE composite is superior in performance as it provides additional benefit of enhanced osteogenicity apart from antibacterial property.

3D Printed Poly (lactic acid) Scaffold integrated with hydrogel for Bone Tissue Engineering

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There is currently high demand for synthetic biodegradable scaffolds with enhanced osteogenic and angiogenic performance for regeneration of large-size bone defects. Alginate hydrogel is widely used as cell-laden bio-ink. In this study, hybrid scaffolds were prepared by integrating either alginate or alginate-bioglass composite hydrogels with three-dimensional (3D) printedpoly(lactic acid) (PLA) porous structure for bone regeneration. The as-deposited PLA scaffolds were surface treated with polyacrylic acid (PAA), which significantly enhanced the wettability of the PLA scaffold. The surface-modified porous PLA scaffolds integrated well with hydrogels and provided shape and mechanical rigidity for the alginate or alginate-bioglass hydrogel. The degradation behavior of the scaffolds during 21-day immersion inphosphate buffered saline was studied. The lowest weight loss was measured forthe PLA scaffold, while a significant weight loss (~1.9%) was observed for alginate-bioglass scaffolds during the first seven days of immersion. In vitro cytocompatibility tests carried out with human fetal osteoblast cells (hFOB) indicated good cell viability and proliferation of cells on the scaffolds. Alizarin red assay showed that the bioglass-containing hybrid scaffold promoted osteogenic differentiation and calcium mineralization. In actual application, the hydrogel could be cell-laden and integrated with PLA scaffold. Thus, the excellent biocompatibility, good mechanical stability, and shape retention of hydrogel due to the PLA skeleton suggest that these hybrid scaffolds can be applicable for large bone regeneration.

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A pilot study on the effect of disinfectants on the solubility and colour stability of two denture base materials

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Background:

Infection control is critical, especially during an outbreak of a pandemic disease. Disinfection of removable dentures is mandatory to avoid microbial growth in the dentures, possible cross-contamination and associated problems. During disinfection procedures, there is a chance for alteration of the physical properties of the denture base materials. Solubility evaluation is a simple technique to understand the dissolution of components in processed dentures. Discolouration after chemical immersion is an indicator of the surface irregularities and flaws present in the processed denture. Therefore the present study aimed to evaluate the effect of disinfectant immersion on the solubility and shade of two differently cured denture base materials.

Materials & Methods:

A total of 36 samples were prepared (n=36) from heat and light-cured polymeric materials. Ozonized water (control group), Chlorhexidine and Vinegar (test groups) as disinfection liquids. Shade measured before and after immersion for both control and test samples using Spectroshade digital colorimeter. Solubility was measured by weighing the sample before and after immersion. H^0 & H^1 set and the results obtained were analyzed statistically using One Way Anova followed by Tukey- Kramer multiple comparison test.

Results:

No dissolution and colour change was observed for both control and test samples after 12 hours of disinfectant immersion ($p > 0.05$).

Conclusion:

H_0 is accepted as there is no significant variation in the weight and shade of the studied samples. However, the study is performed for 12hours of immersion once. Therefore the effect of repeated immersion needs to be further studied.

Keywords: Denture base, colour stability, solubility

ANTIBACTERIAL EVALUATION OF NANO SILVER DOPED BASED BONE SCAFFOLD

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Bone tissue engineering is the challenging research for the growing researchers. All senior age groups commonly undergo bone surgery for various complications such as osteoporosis, osteochondrosis, and bone infection due to trauma. These surgeries highlight the need for scaffold substitutes for the bone. Biomaterials when used as nano composites in tissue engineering application shows excellent biological properties that suits to replace the natural bone. These nano composite biomaterials are also prone to microbial infections which could lead to the implant failure inpost-surgery. These kinds of infections are normally due to the bacterial colonies formed on the biomaterial surface. These colonies disturbs the biomaterial bone interface and leads to poor adhesion. Hence, the development of biomaterial based scaffolds with antibacterial strategies are found to be more important along with other characterization studies. The present studies focuses on the preparation of bone scaffold with composites made of nHAP/nβTCP/PEG. To impart antibacterial properties the composite doped with Ag metal ion. Thus, nAg-nHAP/nβTCP/PEG was synthesised with proper proportion and the characterization studies were carried out using XRD (X-ray Diffraction) and SEM (Scanning Electron Microscope) to prove its crystalline structure and surface morphology. Antibacterial studies were carried out using the Disk diffusion method to confirm its property. The cell adhesion can be verified using alkaline phosphatase studies and the cytotoxicity assay was performed using MTT (Methyl Tetrazolium thiozolyl compound) done with osteoblast cell line MG63 helps to evaluate the biocompatibility. A brief discussion on evaluation techniques associated with antibacterial response with common bone affecting gram positive bacteria *Staphylococcus* aureus helps to assess the performance of tissue engineered silver based nano compositen-HAP/n-β-TCP/PEG for bone replacement surgery.

Key words. Nano silver, nano composites, antibacterial, MTT assay.

QSAR study of Hydroxyquinoline and its Choloro and Amino derivatives as Antimicrobialand Antioxidantagents.

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Quinoline is one of the most popular N-hetero aromatic compounds combined into the structures of many pharmaceuticals. Numerousquinoline-containing compounds exhibit a wide spectrum of pharmacological activities such as antiplasmodial, cytotoxic, antibacterial, antimalarial, anticancer, and antitumor activities.The antimicrobial and antioxidant activity of 8HQ, as well as its derivatives, had been examined. A monochloro (5-Chloro 8HQ) and Dichloro (5,7 - dichloro 8HQ) revealed unsurpassed anti-bacterial activity while an amino-derivative (5-NH2 8HQ) has the most readily useful activity that is antioxidant. The QSAR study can help in designing new compounds which can be 8HQ-based anti-microbial activity.

Keywords: 8-hydroxyquinoline, chloro8HQ, Amino8HQ, antimicrobial activity, antioxidant activity, QSAR.

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