DEVELOPMENT AND EVALUATION OF SCAFFOLDS FOR BONE TISSUE ENGINEERING

THESIS SUBMITTED IN PARTIAL FULFILMENT FOR THE AWARD OF DEGREE

DOCTOR OF PHILOSOPHY

By

Shikha Kumari

School Of Biochemical Engineering
Indian Institute Of Technology (Banaras Hindu University)
Varanasi-221005
India

Roll No. 17011505 **2022**

भारतीय प्रौद्योगिकी संस्थान
काशी हिन्दू विश्वविद्यालय

IIT INDIAN INSTITUTE OF TECHNOLOGY
BANARAS HINDU UNIVERSITY

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Supervisor
Prof. Pradeep Srivastava
(Professor) (On Deputation)
School of Biochemical Engineering
Engineering
Indian Institute Of Technology (BHU)
(BHU)
Varanasi -221005

Abha Mishra
16.12.2
Co-Supervisor
Dr. Abha Mishra
(Associate Professor)
School of Biochemical
Indian Institute Of Technology
Varanasi -221005

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Date: 16/12/22
Place: Varanasi, India

Shikha
Shikha Kumari
Signature of the Student

CERTIFICATE BY THE SUPERVISORS

It is certified that the above statement made by the student is correct to the best of my knowledge.

Supervisor
Prof. Pradeep Srivastava
(On Deputation)

Abha Mishra
Co-Supervisor
Dr. Abha Mishra
(Associate Prof.)

Dr. ABHA MISHRA
ASSOCIATE PROFESSOR
SCHOOL BIO CHEMICAL ENGG.
I.I.T., (B.H.U.)

Forwarded
Signature of Coordinator of School

समन्वयक
Coordinator
जैव रासायनिक अभियांत्रिकी स्कूल
School of Biochemical Engg
भारतीय प्रौद्योगिकी संस्थान
Indian Institute of Technology
(का०हि०वि०वि०) वाराणसी-221005
(B.H.U.) Varanasi-221005

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काशी हिन्दू विश्वविद्यालय
INDIAN INSTITUTE OF TECHNOLOGY
BANARAS HINDU UNIVERSITY

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Shikha

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Date: 16.12.2022 **Shikha**

Kumari

Place: Varanasi

PREFACE

Tissue engineering has emerged as a solid approach to bone tissue regeneration. It has helped in developing artificial bone substitutes that can overcome the limitations of existing bone disease therapies. Bone tissue-engineered constructs can completely reproduce the characteristics of a graft, hence ending the patient's discomfort. Tissue engineering of biological bone focuses on regenerating new functional tissue that successfully merges with the host without generating any adverse effects. In recent years, research in tissue regeneration has focused on developing biomaterials for replacing, regrowing, or restoring damaged cells or tissues. These biomaterials serve optimum support and act as a framework for cellular attachment, replacement and ingrowth of tissues. The literature review suggests that several materials are utilized for bone tissue restoration or regeneration, like natural and synthetic materials. Biomaterials with proteins have found primary utilization in various industries and areas like biosensors, food and agricultural industry, drug delivery mechanisms, pharmaceutical drugs, contact lenses, bone plates, etc. These biomaterials include natural materials like chitosan, gelatin, collagen, alginate, chondroitin sulfate, etc. which exhibit good biocompatibility and biodegradation properties. Similarly, synthetic materials are also there like polylactic acid, polyvinyl chloride, polyglycolic acid, etc. The synthetic materials possess good mechanical strength but there exist some limitations like poor cell cytocompatibility, poor degradation rate, etc. Therefore, both these biomaterials are used in composite forms to attain the desired properties in achieving good cell proliferation and physiochemical properties.

Chapter- 1 focuses on the introduction of tissue engineering and its significance, key challenges in bone tissue engineering and different strategies for bone tissue regeneration. It discusses porous scaffold fabrication and its need in current bone repair technology.

Chapter- 2 consists of a literature survey of bone, its types and the cells involved in its formation. It discussed the various scaffold fabrication techniques and the scaffold's properties. It also covers the requirement of bone tissue engineering in the current scenario.

Chapter- 3 represents the detailed experimental methods and materials involved in this research study. It also gives a detailed description of the instruments involved in this research.

Chapter- 4 discusses the development and evaluation of different scaffolds developed for Bone tissue regeneration. Their efficacy and properties are elaborated via various examinations and tests performed. It includes the chitosan and gelatin-based scaffold with the incorporation of different bioactive nanoparticles. Among all the developed scaffolds, it was observed that the best-optimized scaffold was graphene oxide and nanobioglass-based scaffold (Ch-G-NBG-60%GO) with the highest mechanical strength and enhanced biocompatibility among all the other scaffolds and also CN based Ch/G/nHAP/0.02%CN scaffold with good mechanical strength as well as cytocompatibility.

Chapter- 5 gives the conclusion and future perspective for the conducted research work in the area of Bone tissue engineering

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LIST OF ABBREVIATIONS

TE	**Tissue engineering**
BTE	**Bone Tissue engineering**
MSCs	**Mesenchymal stem cells**
ECM	**Extracellular matrix**
HAP	**Hydroxyapatite**
TCP	**Tricalcium phosphate**
3D	**Three dimensional**
PVA	**Polyvinyl alcohol**
HP	**Hyperbranched polymer**
ICP-OES	**Inductively coupled plasma-optical emission spectrometry**
PCL	**Poly ε-caprolactone**
PEG	**Polyethylene glycol**
GFs	**Growth factors**
PLGA	**Poly (lactic-co-glycolic acid)**
CL	**Cellulose**
NHS	**N-hydroxysuccinimide**
EDC	**1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide**
rhBMP-2	**Recombinant human bone morphogenetic protein**
SBF	**Simulated bodily fluids**
Alg	**Alginate**
CS	**Chondroitin sulfate**
AA	**Amino acid**
SF	**Silk fibroin**
PD-RGO	**Polydopamine-reduced graphene oxide**
HA	**Hyaluronic acid**
Ch	**Chitosan**
Gel	**Gelatin**
Col	**Collagen**
VEGF	**Vascular endothelial growth factor**
BMPs	**Bone morphogenetic proteins**
TNF-alpha	**Tumor necrosis factor-alpha**
SLRPs	**Small leucine-rich proteoglycans**
MGO	**Magnetic graphene oxide**
PVA/SA/HAP	**Polyvinyl alcohol/sodium alginate/hydroxyapatite**
AM	**Additive manufacturing**
PMPV	**Polyacrylamide/poly (vinyl alcohol)**
HNTs	**Halloysite nanotubes**
BG	**Bioactive glass**
PADH	**Polymer of acrylamide -Urethacrylate dextran**
PLLA	**Poly(L-lactic acid)**

Dex-U	**Urethacrylate dextran**
PMMA	**Polymer of acrylamide**
PGA	**Polyglycolic acid**
PU	**Polyurethane**
PPF	**Poly(propylene fumarate)**
QDs	**Quantum dots**
rBMSC	**Recombinant Bone marrow stromal cells**
SMAD	**Mothers against decapentaplegic**
hASC	**Human adult stromal cells**
SBMs	**Smart biomaterials**
PVDF	**Polyvinylidene fluoride**
SAMs	**Self-assembled monolayers**
CNTs	**Carbon nanotubes**
f-MWCNT	**Multiwalled Carbon Nanotubes**
ERMs	**Enzyme-responsive materials**