Novel **Polymer-Ceramic Nano Composite Graft with BMP** for Critical-Sized Bone Defects: Towards Personalised Rehabilitation of Maxillofacial Trauma Patients

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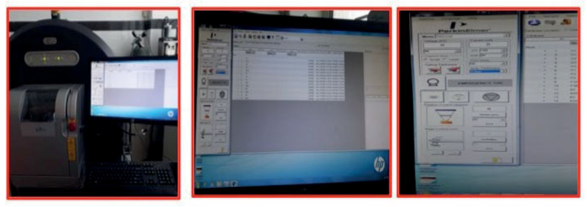
Introduction

The limitations associated with reconstruction of critical-sized bony defects arising from maxillofacial trauma has averted researchers towards bone tissue engineering employing scaffolds prepared from biomaterials having osteogenic potential.[1-3] In the present study, we have developed a novel composite material comprising chitosan-gelatin-Nanohydroxyapatite (nHaP) with polycaprolactone (PCL), a biocompatible, slow degrading polymer. nHaP, a natural component of bone, was added to enhance mechanical strength of the fiber and to impart osteoinductivity. The final composite scaffold was made osteo-inductive by the incorporation of BMP-2 (Bone Morphogenic Protein).

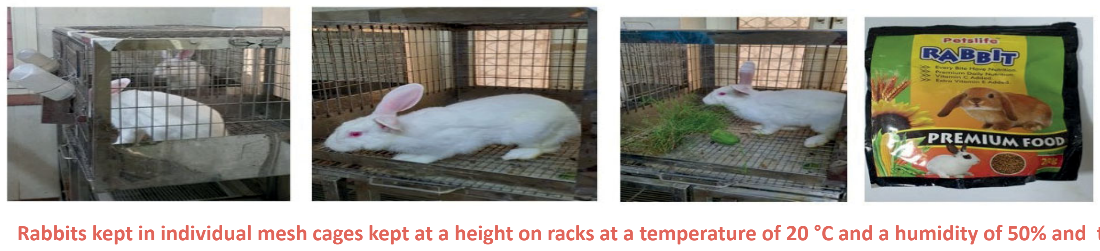
Material and method

Novel Chitosan-gelatin nanohydroxy Apatite (nHaP) scaffold reinforced with PCL-nHaP Nanofibres was developed. Physical characteristics were evaluated through SEM analysis. Sterilized scaffolds- Novel Graft + BMP2 (G), Polycaprolactone /HA (P) and βTCP (B) were placed in surgically created critical-defects in rabbit bone and analysed at an interval of 2, 4, and 6 weeks post implantation. Bone formation was evaluated through micro CT and histomorphometry.

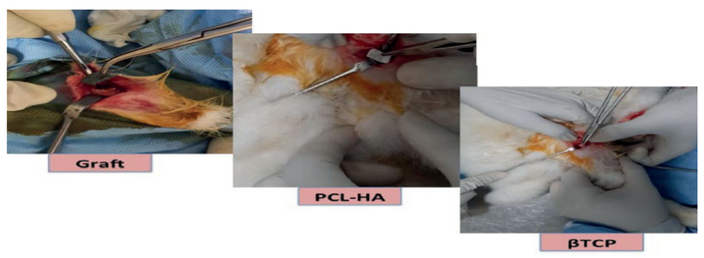
PCL-nHaP nanofiber reinforced Chitosan-gelatin-nHaP composite scaffolds compared with PCL/HA scaffolds and βTCP granules



Micro-computed tomography (micro-CT) scanner (SkyScan 1076, Bruker, Kontich, Belgium) energy level 55 kV and 18 µm pixel resolution.



Rabbits kept in individual mesh cages kept at a height on racks at a temperature of 20 °C and a humidity of 50% and their diet consisting of food concentrates, fresh hay, fresh vegetable and water along with preprocessed food pellet

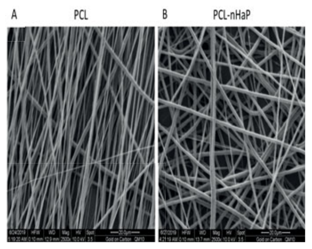


Animal surgery followed by graft placement- Novel composite (G); PCL-HA (P); BTCP (B)

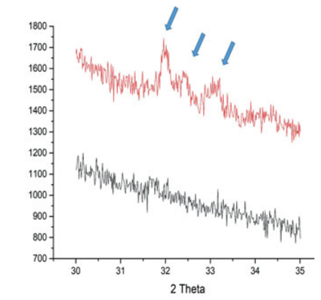
In vitro Analysis

Results

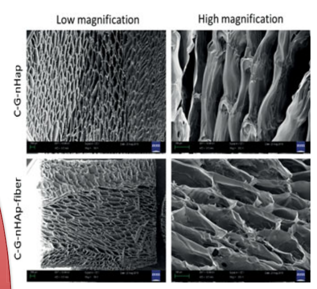
Scanning electron microscopic analysis revealed smooth, bead-free continuous PCL fibers with unique hydroxyapatite-specific peaks in the PCL-nHaP fiber meshes. It is highly porous with Smooth pores in the transverse section and long partially interconnected polygonal pores in the longitudinal section.



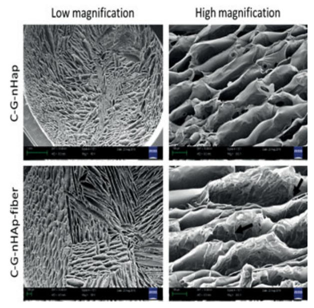
Morphological evaluation of nanofiber (A) Scanning electron micrograph of PCL nanofiber and (B) PCL-nHaP fibers respectively. Scale bar 20 µm.



Characterization of PCL and PCL-nHaP fibers for the presence of hydroxyapatite. X-ray diffraction (XRD) spectra for PCL (black line) and PCL-nHaP (red line), Blue arrow indicates presence of hydroxyapatite specific peaks.



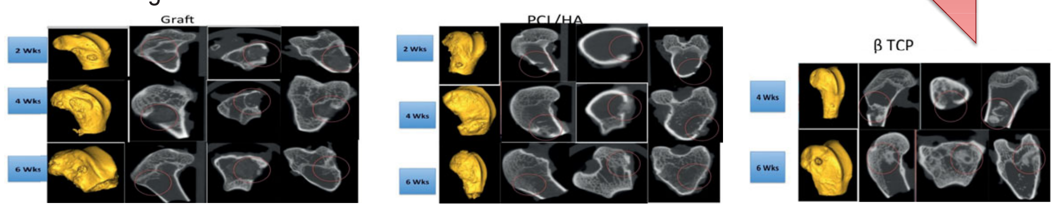
Scanning electron micrographs showing longitudinal section of chitosan-gelatin-nhydroxyapatite (CG-nHaP) and chitosan-gelatin-nhydroxyapatite reinforced with PCL-nHAP (C-G-nHaP- fiber) scaffolds



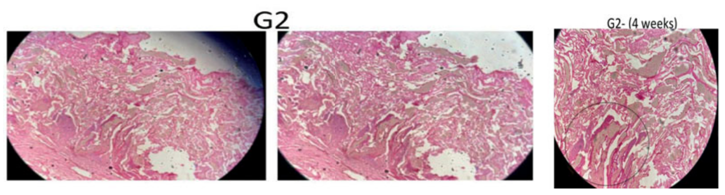
Scanning electron micrographs showing transverse section of chitosan-gelatin-nhydroxyapatite (CG-nHaP) and chitosan gelatin nhydroxyapatite reinforced with PCL-nHAP (C-G-nHaP-fiber) scaffolds

In Vivo Analysis

Micro-CT with Materialise 3D imprint technique revealed wound healing and neo-bone formation that was histologically confirmed by HE staining, revealing appreciable bone formation at the vicinity of the graft



Micro CT analysis comparison of Graft, PCL-HA and βTCP at 2, 4, 6 weeks post-operatively



The Haematoxylin –Eosin stained sections of the bone with graft in Group 2 revealed appreciablen Bone formation at the vicinity of the graft.

Publications

Dwivedi R, Kumar S, Pandey R, Mahajan A, Nandana D, Katti DS, Mehrotra D. Polycaprolactone as Biomaterial for bone scaffolds: Review of Literature- *J Oral Biol Craniofac Res.* 2020;10(1):361-88. **(Citations-265)**

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Dwivedi R, Mehrotra D. 3D bioprinting and craniofacial regeneration. J Oral Biol Craniofac Res. 2020;10(4):650-59. **(Citations=12)**

Mehrotra D, **Dwivedi R**, Nandana D, Singh RK. From injectable to 3D Printed hydrogels in maxillofacial tissue engineering: A review. J Oral Biol Craniofac Res. 2020; 10(4): 680-89 **(Citations=17)**

Patent

Novel bone graft material for the regeneration of critical-sized bone defects
(Application number- 202211055922)

Discussion & Conclusion

PCL was our material of choice for the scaffold owing to the qualities of PCL like being biocompatible and biodegradable, easy availability, cost efficacy and suitability for modification, biological properties and mechanical strength to withstand physical, chemical and mechanical insults without significant loss of its properties.[2, 4] Chitosan has a structural resemblance to glycos-amino-glycans, but it is deficient in mechanical properties if used alone and therefore requires blending with other biomaterials. The basic role of gelatin in the composite scaffold was to facilitate cell adhesion and attachment along with cellular spreading.[5, 6] The novel Chitosan-gelatin nHaP graft reinforced with PCL-nHaP nanofibres is a tested bone substitute for critical-sized bone defects. Its superior physical properties as compared to other commercial bone substitutes, adequate cell attachment and growth, and better neo-osteogenesis and bone healing may contribute to personalised rehabilitation of maxillofacial trauma patients in the near future.

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Funding

Research grant *IRIS No. 2015-0331* -by Indian Council of Medical Research, New Delhi, India.

Acknowledgements

- Indian Council of Medical Research, New Delhi
- Department of Health Research- Multi disciplinary Research Unit, KGMU
- Animal Facility at Central Drug Research Institute, Lucknow
- Institutional Animal House, KGMU.

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