

Gelatin Methacryloyl Bioscaffolds: A Viable Option for Alveolar Bone Tissue Engineering?

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Introduction

The concept of tissue engineering involves the deposition of cells on bioscaffolds in a particular location that ultimately leads to regeneration of tissues. The combinatorial effect of cells, bioscaffolds and molecular signaling factors, works conjunctly to provide exact microenvironment mimicking the native in vivo system. Alveolar bone regeneration due to its location, poses certain challenges where appropriate mechanical loading and microbial flora need addressing during construction of the scaffold [1]. Three dimensional (3D) bioprinting has unfolded vast possibilities for bone regeneration through fabrication of 3D constructs that support adhesion and proliferation of pluripotent stem cells in desired location. 3D printing allows individual-specific construction of scaffolds of a certain shape and size that allow regeneration of bone through cellular proliferation, differentiation, and molecular-signalling pathways in a guided fashion.

The biomaterials used in alveolar bone regeneration requires component that supports mechanical and biocompatibility properties, and osteo-conductive properties. Certain biomaterials that have been utilized in the past and current times for bone regeneration are polylactic acid, polyglycolic acid, poly (lactate- hydroxyacetic acid), titanium alloy, biological ceramics, bioactive glasses and calcium phosphate [2]. Gelatin methacryloyl (GelMA) is one such biomaterial which is known for its excellent biocompatibility, low antigenicity, and tuneable physical properties, which could be used alongside bone-marrow derived

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mesenchymal stem cells (BMSCs) for osteogenesis. Our group has been successfully able to synthesise GelMA and bioprint them into 1 cm² scaffolds. Figure 1(a) shows the FTIR graph of GelMA and in 1(b) 3D printed GelMA structures are represented.

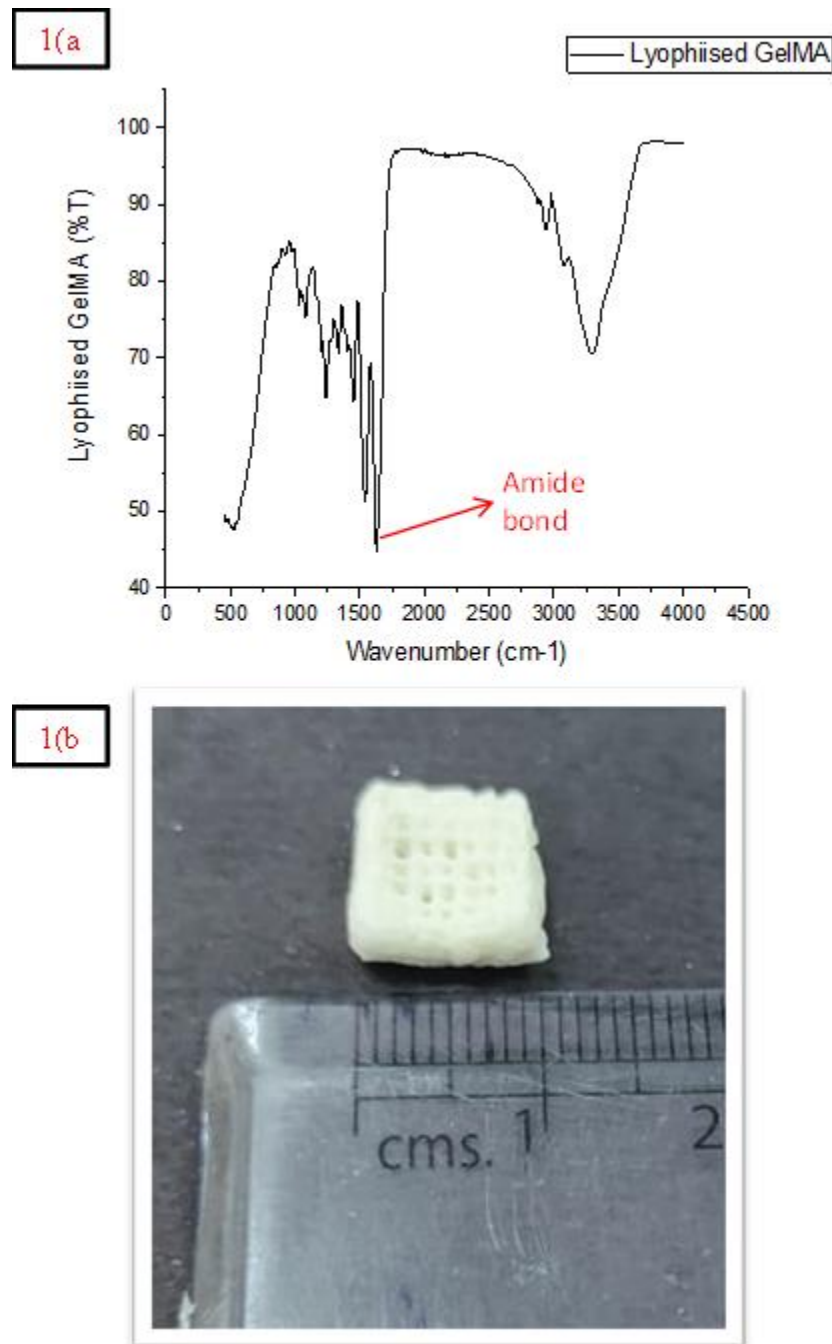


Figure 1: (a) FTIR spectra of GelMA confirming the presence of amide bond; (b) 3D printed structures of GelMA.

Discussion

Bone tissues have a complex spatial arrangement composed of cortical bone, spongy woven bone, and marrow spaces with blood vessels supplying nutrition to the regenerating bone. This architect is challenging to mimic, especially when functional properties of load bearing need to be preserved. GelMA is a photo crosslinkable derivative of denatured collagen that exhibit modifiable mechanical properties under diverse conditions. The controlled photopolymerization reaction in varying conditions of temperature, pH, and aqueous environment, and with variation in GelMA and/or photo initiator concentrations could be utilized to create unique cellular patterns and structures. The presence of arginine-glycine-aspartic acid (RGD) sequences promotes cellular adhesion, and the target sequences of matrix metalloproteinases allow cellular proliferation and remodeling [3]. Although there is little literature available to support the application of GelMA in alveolar bone regeneration, previous attempts have established favorable results which could serve as a foundation for undertaking future studies.

In a study involving Sprague-Dawley rats, GelMA hydrogels were used with encapsulated human periodontal ligament stem cells for alveolar bone regeneration. A substantial amount of bone regeneration was found at 4 and 8 weeks after surgery, suggesting significant alveolar regenerative potential of GelMA to treat alveolar bone defects. Moreover, study of physical properties of GelMA revealed a highly porous and interconnected network of hydrogels, with compressive stress values reaching up to 13.67 ± 0.03 kPa, strain values to 55%, and swelling ratio to $700 \pm 47\%$ at the fifth hour [4].

Further studies have combined GelMA with other materials such as β -tricalcium phosphate (β -TCP) [5] and, zeoliticimidazolate framework-8 (ZIF-8) [6] to enhance the properties of the scaffold in alveolar bone regeneration. Luo D et al constructed a 3D printed GelMA/ β -TCP hybrid scaffold with an aim to fuse β -TCP with BMSCs, thus improving the osteogenic potential of the scaffold. It was found that the scaffold exhibited good biocompatibility and mechanical properties along with better stem cell proliferation, differentiation, survival rate, and osteogenic induction [5].

Similarly, in another study, ZIF-8 was incorporated in GelMA, forming a composite hydrogel (GelMA-Z) to treat the bone loss and reduce the bacterial load in periodontitis. This resulted in a continuous release of Zinc ions producing antibacterial effect against periodontogenic flora, upregulation of expression of osteogenesis related genes, and increased alkaline phosphatase activity with enhanced extracellular mineralization in vitro. The results were duplicated on placing the hydrogel in the periodontal pockets in vivo. The hydrogel showed good biocompatibility both in-vitro and in-vivo [6].

Therefore, from the above discussion, we could conclude that GelMA offer a great potential to be used as a biomimetic scaffold to engineer alveolar bone. Moreover, the osteogenic bioactivity of GelMA could be improved by supplementing it with other inorganic materials such as calcium phosphate, or nanomaterials such as silica or nano hydroxyapatite. GelMA hydrogels provide an optimum niche for stem-cell migration, proliferation and osteogenic differentiation, which coupled with its simple, rapid, and inexpensive nature, makes it a popular biomaterial for the delivery of stem cells.

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References

1. Yu N, Nguyen T, Cho YD, Kavanagh NM, Ghassib I, Giannobile WV. Personalized scaffolding technologies for alveolar bone regenerative medicine. *Orthod Craniofac Res.* 2019;22:69-75. [PubMed](#) | [CrossRef](#)
2. Dong Z, Yuan Q, Huang K, Xu W, Liu G, Gu Z. Gelatin methacryloyl (GelMA)-based biomaterials for bone regeneration. *RSC Adv.* 2019;9(31):17737-44. [PubMed](#) | [CrossRef](#)
3. Nichol JW, Koshy ST, Bae H, Hwang CM, Yamanlar S, Khademhosseini A. Cell-laden microengineered gelatin methacrylate hydrogels. *Biomaterials.* 2010;31(21):5536-44. [PubMed](#) | [CrossRef](#)
4. Pan J, Deng J, Yu L, Wang Y, Zhang W, Han X, et al. Investigating the repair of alveolar bone defects by gelatin methacrylate hydrogels-encapsulated human periodontal ligament stem cells. *J Mater Sci Mater Med.* 2019; 31(1):3. [PubMed](#) | [CrossRef](#)
5. Luo D, Chen B, Chen Y. Stem Cells-Loaded 3D-Printed Scaffolds for the Reconstruction of Alveolar Cleft. *Front Bioeng Biotechnol.* 2022;10:939199. [PubMed](#) | [CrossRef](#)
6. Liu Y, Li T, Sun M, Cheng Z, Jia W, Jiao K, et al. ZIF-8 modified multifunctional injectable photopolymerizable GelMA hydrogel for the treatment of periodontitis. *Acta Biomater.* 2022; 146:37-48. [PubMed](#) | [CrossRef](#)