

Developments in bone tissue bioceramics: Effects of preparation on properties

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Abstract

Bone tissue is the second most transplanted tissue each year. A demand for synthesized bone substitutes has led the development of materials that are biocompatible, bioactive, and bioabsorbable while also mechanically similar to bone tissue. Hydroxyapatite and calcium phosphate-based bioceramics have been the gold standard for substitute bone tissue development. Techniques have been developed such as formulation manipulation, freeze-drying, and 3D-printing gels that show promise in changing particle size and porosity. Higher porosity has been found to increase bioactivity, but also reduces compressive strength. Simple statistical methods and novel 3D-printing techniques have been shown to improve ultimate compressive strength and optimize scaffold formulas.

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1. Introduction

Millions of patients require bone substitutes or repair of diseased or damaged bone tissue each year, making bone the second most transplanted tissue [1, 2]. Environmental, economic, and technical needs have led to four million annual operations utilizing different bone alternatives globally [3, 4, 5]. As the need for new structures increases, preparation techniques have been developed to produce bone tissue alternatives of varying mechanical, structural, and biological properties.

Calcium phosphate and hydroxyapatite (HA) are commonly synthesized for bone tissue scaffolds in bone tissue transplants due to their similar composition and properties with natural bone [3, 6, 7]. However, mechanical and structural properties of calcium phosphate and HA rely heavily on the method of preparation [2, 6]. In this review, novel preparation methods and additive manufacturing techniques of HA and calcium phosphate-based bioceramics were investigated and assessed on their effects on structural, biological, and mechanical properties of the bone tissue scaffold.

2. Effects of porosity and particle size

HA and calcium phosphate-based bioceramics are common biocompatible materials due to their similarities with natural bone [6]. These materials are relatively simple to synthesize in a lab setting and have been used in varying preparation methods to impart different properties for scaffold use. Particle size and porosity characteristics of the material used for bone tissue scaffolds will primarily dictate its mechanical and biological properties.

Particle size should normally not have an effect on the porosity of a material, but due to random sorting, increased porosity is often found with smaller particle and grain sizes [8]. A common technique to reduce particle size is freeze-drying. Freeze-drying HA and calcium phosphate bioceramics have been shown to reduce particle size due to the prevention of agglomeration [9]. Zeta potential analysis found that reduced particle size lead to increased protein absorption, SEM and TEM scans that morphology did not change, and XRD scans showed no change in composition [9].

Zhang et. al concluded that by altering the ratio between Ca/P in the calcium phosphate bioceramic, the particle size of the material can be changed and the material can also be prepared for 3D-printing [7]. Particle size of the ceramic powder was also about 37 μm , suitable for degradation. The

compressive strength of the material was also evaluated at 1.03 MPa, suitable for cancellous bone repair, but far from natural iliac bone at 10-27 MPa [10]. Creating a more porous material increased water absorption, but also decreased shrinkage and the compressive strength [7]. The authors suggest that the decrease in shrinkage and compressive strength may have been due to the different composition produced by altering the Ca/P ratios after sintering [7]. Chen et. al. also 3D-printed HA scaffolds and found that through decreased porosity, highly structured 70 wt% HA, freeze-drying, and sintering, ultimate compressive strength can be improved up to 14.3 MPa [10]. Porosity effects and bioactivity were not considered in the study, but Chen et. al. suggest that porosity can still be controlled through refined 3D-printing techniques while maintaining the structural improvements. Similar observations have concluded promise in the use of 3D-printing for tissue scaffolds [11, 12].

When observing the effects of porosity on the HA scaffolds, similar results were found compared to the calcium phosphate [2]. Cao et. al concluded that by altering different HA formulations and reducing the porosity of the material, compressive strength of the material was increased [13]. Experiments with both HA and calcium phosphate-based scaffolds suggest a general trend between the porosity of the scaffold and its compressive strength due to the highly random structure of the scaffold [14, 15, 16]. The composition of the scaffolds would affect the assortment, and Chen et. al. found that scaffolds made of similar materials had improved compressive strength through a highly-ordered arrangement through 3D-printing compared to random arrangements [10]. Jodati et. al compiled and derived statistical models from several studies using HA and calcium phosphate-based bioceramics, showing the relationship between porosity and compressive strength of varying compositions [2]. While highly porous scaffolds are beneficial for cell growth and stimulation, it poses an ongoing challenge between optimized bioactivity and structural integrity.

It has been established that the different compositions of HA and calcium phosphate-based materials will affect the mechanical and biological properties of the material. This data can then be analyzed through statistical models to develop advanced simulations. Paknahad et. al examined the bending and tensile failure of different calcium phosphate formulations and sizes to develop a method of simulating mechanical tests [17]. While the study concluded that current calcium phosphate formulations have unsuitable fracture toughness for trabecular and cortical bone, gradient profiles can be accurately made using stress profiles (**Figures 1&2**) [17]. The study also did not take into account for structural differences of scaffolds that could be introduced through additive manufacturing or other processes. However, the statistical model proposed serves as a foundation for more complex solutions.

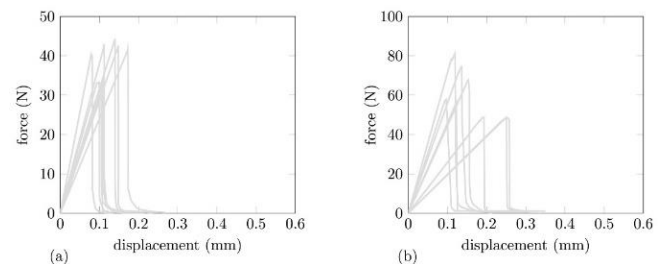


Figure 1. Force-displacement curves for the three-point bending test (a) and the tensile test (b) tests of rectangular CPC specimens (40 x 10 x 10 mm) [17].

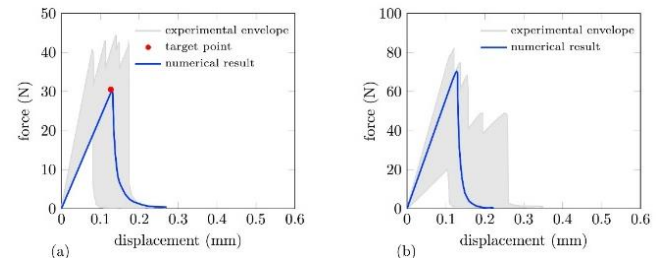


Figure 2. Numerical prediction for three-point bending test (a) and tensile test (b) of rectangular CPC specimens (40 x 10 x 10 mm) [17].

3. Conclusion

Bone tissue repair and regeneration alternatives are highly sought after in tissue engineering. Millions of transplants are performed every year, but supply of natural bone is limited or may evoke immune responses and rejection. Highly porous HA and calcium-phosphate based materials have shown promise in structure, biocompatibility, bioactivity, and bioadsorbability, but lack in mechanical strength necessary for bone tissue repair and engineering. Through the incorporation of 3D-printing it is possible to overcome some of the mechanical limitations of highly porous materials. Statistical models have also shown some efficacy in determining optimal scaffold recipes for improved mechanical strength. However, even with these advances, HA and calcium-phosphate based scaffold still struggle to completely replace natural bone. In order to improve the mechanical strength of bioceramic scaffolds, more sophisticated 3D-printing and statistical modeling techniques are needed. Fortunately, novel 3D-printing techniques have emerged that show vast improvements from the first 3D-printed bioceramic scaffolds from the 1980s.

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Conflict of Interest

The author has no conflict of interest.

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