Porosity and compressive strength of PLA-based scaffold coated with hydroxyapatite-gelatin to reconstruct mandibula: a literature review

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Abstract. Ameloblastoma is one of odontogenic tumours that is classified as benign, aggressive, and destructive. Mandibular tumours potentially cause bone disruption or damage, so it is necessary to do a resection to remove the infected part. Treatment done by resection may cause defects starting from the gap in the alveolar bone to the discontinuity of the mandible. Thus, it is necessary to reconstruct the mandible using a scaffold. Scaffold is made by using the PLA 3D-printing with the Fused Deposition Modelling (FDM) method. PLA is non-bioactive and hydrophobic, so the surface needs to be modified by coating PLA with hydroxyapatite (HA) and gelatine. This article aims to examine the effect of PLA surface modification using HA-Gelatine through a review article. The searching strategy for articles is by using databases of internationally reputable journals with certain keywords. From the search, journals were obtained (with status Q3, Q2 and Q1) as reference journals in this review. Literature review shows that the addition of hydroxyapatite can improve the bioactive properties of PLA, while the addition of gelatine can increase its hydrophilicity properties. Therefore, HA-Gelatin coating on 3D PLA has the potential to be used as a scaffold for mandibular reconstruction.

1. Introduction

Many cases of bone damage are caused by diseases, especially tumors in the mandible. Ameloblastoma is a benign odontogenic tumor originating from epithelial remnants during tooth formation. There were 31 cases of ameloblastoma of various subtypes reported. Of these cases, 90.32% occurred in the mandible, while 9.67% occurred in the maxilla [1]. Mandibular tumors have the potential to cause bone destruction and require resection to remove the infected part. This results in defects ranging from gaps in the alveolar bone to mandibular bone discontinuity [2]. As a result of this resection it is necessary to reconstruct the mandible.

One of the replacement materials for mandibular reconstruction that is being developed is the scaffold. The scaffold is biodegradable, so that it is replaced by osteoblast cells that attach to the scaffold [3]. Scaffold manufacture must be precise and consistent with regard to porosity, pore size, pore distribution and interconnectivity between pores [4]. The way to make scaffold is by using conventional techniques or depending on the process and design. Conventional techniques have limitations in controlling pore size, pore geometry, interconnection between pores, pore distribution
and construction of internal scaffold channels [5]. Making scaffold in accordance with these criteria can be done by using 3D-printing technology.

3D-printing is one of the latest innovations that offers solutions for creating three-dimensional objects with various desired shapes. In medical applications, 3D-printing helps to make replicas of human body parts, as is being developed, namely the manufacture of scaffold. Sophisticated techniques that are alternative in controlling the scaffold design include Fused Deposition Modeling (FDM), which is a method of melting thermoplastic material using an extruder mechanism. The FDM method has the feasibility of making scaffold directly and is a high-precision technique [6].

Materials that are often used in 3D-printing with the FDM method generally come from a thermoplastic polymer material, the type of Polylactic Acid (PLA). PLA is biodegradable and biocompatible so that this material has many applications in the medical world such as tissue regeneration, healing of fractures and surgical threads. However, PLA has non-bioactive and hydrophobic properties so that a coating is needed to support the scaffold properties in the body [7]. Material which hydroxyapatite and gelatin can be used to improve the properties of PLA.

Hydroxypatite (HA) with the chemical formula \(\text{Ca}_{10}(\text{PO}_4)_{6}(\text{OH})_2\) is one of the compounds that make up hard tissue in the human body such as bones, teeth, and etc [8]. HA has bioactive, bioactive, and osteoconductive properties. However, the weakness is that it is brittle and less elastic so it is necessary to add gelatin \((\text{C}_{102}\text{H}_{151}\text{N}_{31})\). Gelatin has hydrophilic properties (contact angle 47.3°) so that it can improve PLA properties [9]. Gelatin plays a role in migration, mineralization, and can increase cell adhesion [10]. Gelatin is often composited with hydroxyapatite because it can improve mechanical properties and is able to stick and fill the pores of hydroxyapatite so that the resulting matrix becomes stronger [11].

Based on this background, in this article the authors conducted a literature review from various reputable international journals to determine the effect of surface modification of PLA scaffold using hydroxyapatite-gelatin material. Literature review is carried out by comparing various properties such as porosity and mechanical properties from internationally reputed journals. The results of this narrative review are expected to add insight and can become a theoretical reference for further research in the development of scaffold as a material for mandibular reconstruction.

2. Method

This research was conducted through a literature review. The literature review provides a framework related to new findings and previous finding to identify indications of progress of the results of a study through comprehensive research and interpretation of literature related to particular topic. The articles that used in literature review are focused on original empirical research articles or research articles that contain results from actual observations or experiments where there are abstracts, introductions, methods, results, and discussions. The literature review stage begins with a search for articles relevant to the topic being discussed. The article search strategy using a database of articles in journals of international repute such as ScienceDirect and Google Search with keywords that mandibular reconstruction, PLA 3D scaffold, modifications scaffold PLA and fused deposition modeling. The journal criteria used are journals published in the last 5 years, full text articles in English indexed by Scopus. The search results were then carried out by scanning the journal based on the type of material, namely polyactic acid (PLA) which is composited with hydroxyapatite and gelatin and is biocompatible if used as a scaffold for bone tissue engineering. After doing the screening, journals with the status of Q3, Q2, and Q1 will be used as reference journals in this review. Furthermore, research journals that match the criteria are collected and journal summaries are made. The journal summary is then analyzed for the content contained in the research objectives and research result. The journal is analyzed by compiling, determining the strengths and weaknesses of each literature, looking at the relationship between one literature and another, and comparing each literature obtained from various properties such as porosity and mechanical properties.
3. Result and Discussion

3.1. Advantages of 3D-Printing Scaffold with Fused Deposition Modelling (FDM) Method

The use of 3D printing allows the design of scaffold with an adapted structure and produces synthetic bone grafts with a multifunctional effect suitable for bone repair [12]. One of the ideal requirements scaffold should be biomimetic i.e., it mimics the extracellular matrix and provides a suitable environment for cell growth. The characteristics that a scaffold must have are biocompatibility, osteoconductivity, osteoinductivity, biodegradability, porosity, and appropriate pore size, as well as mechanical strength [13]. 3D printing technology with the FDM method has several advantages, including raw materials and equipment that are cost effective, easy to use, and the ability to blend polymers. In addition, this technology supports the creation of thermoplastic products that are mechanically and environmentally stable. Complex geometric shapes and cavities can be generated easily using FDM technology [14]. The FDM technique is feasible for modeling the mandible used for reconstructive surgery. This technique has been used in the surgical planning and design of maxillofacial and mandibular prostheses [15].

Several studies have reported the process of making scaffold PLA 3D using FDM. Research has reported the process of making scaffolds using PLA filaments with a diameter of 1.75 mm (Figure 1) [16]. PLA is used as a raw material in 3D FDM printing for porous scaffolding applications because of its biodegradability, good mechanical properties and low toxicity. The temperature used in the printing process on the nozzle is 200°C, the hotbed is 60°C, the nozzle diameter is 0.4 mm and the speed of the 3D printer motor is 30 mm/s. The results of this study indicate that it has succeeded in making scaffold porous with 3D printing.

![Figure 1. Scaffold fabrication scheme [16].](image1)

One of the study report the process of making scaffolds using PLA/HA filaments with a diameter of 1.6 ± 0.2 mm [17]. The scaffold design is made using SolidWorks as shown in Figure 2A, then converted into stereolithography (.stl) format so that it can be applied to 3D object printing software.

![Figure 2. Computer model (A), cut model (B), and PLA/HA 3D-printed result (C) [17].](image2)
such as (Figure 2B). Furthermore, the PLA filament was extruded at 210°C with a nozzle diameter of 200 µm and a 3D printer motor speed of 30 mm/s.

3.2. Porosity of PLA-Based Scaffold
Porosity is an important factor in characterization scaffold because it serves to facilitate cell migration, blood circulation and the vascular process [13]. The porosity of the developed scaffold was determined by the liquid displacement method [13]. Sufficient porosity and pore size are needed in the process of cell distribution and nutrition throughout the structure [17]. In one of study, the porosity produced from the scaffold 3D PLA/Gelatin fibrous by immersing for 90 minutes ranged from 77.52% to 86.18% [19]. These results are in accordance with the criteria for bone porosity values, namely at least 40% to 80% [20]. The value of the porosity of the scaffold in accordance with the value of the bone porosity criteria was also reported which ranges from 76% to 83.3% [21]. In making PLA/HA scaffold using the 3D-printing method, the results are as shown in Table 1 [22]. Based on these results, the addition of HA to the scaffold will increase density and decrease porosity [22]. Even so, the 3D-printing PLA/HA scaffold porosity value is in accordance with the bone porosity value reported previously [20].

| Material properties | Poisson ratio | Elastic modulus (GPa) | Density (g/cm³) | Compressive strength (MPa) | Porosity (%) |
|---------------------|---------------|-----------------------|-----------------|----------------------------|--------------|
| PLA                 | -             | -                     | -               | 35                         | 85           |
| PLA - 5 HA          | 0.30          | 3.6                   | 1.1             | 42                         | 75           |
| PLA - 10 HA         | 0.33          | 4.2                   | 1.5             | 48                         | 79           |
| PLA - 15 HA         | 0.34          | 5.6                   | 2.0             | 56                         | 73           |
| PLA - 25 HA         | 0.35          | 6.9                   | 3.0             | 58                         | 64           |

3.3. Mechanical Properties of PLA-Based Scaffold
In Esmaeili research, it shows that the higher the HA concentration, the more the compressive strength and modulus of elasticity of the scaffold [22]. These results have met the criteria for the compressive strength value of the trabecular bone, which is at least 0.5-50 MPa to receive stresses such as chewing loads [23]. The increase in compressive strength and modulus of elasticity are proportional to the increase in scaffold density, which is about 1.1-3.0 g/cm³[22]. The mean trabecular and cortical bone densities of the mandible were 1.18 g/cm³ and 1.85-2.0 g/cm³. In the research of Zhang, compressive strength increased with the addition of HA in PLA, from 39.96 MPa (pure PLA) to 45.00 MPa (PLA/HA 5: 5) [21]. However, as the HA concentration decreased and the PLA concentration increased, the compressive strength also decreased, from 43.29 MPa (8: 2) to 19.00 MPa (9: 1). These results also prove that the presence of HA will increase the compressive strength of the scaffold [21]. In the research of Deng which examined the characteristics and physical properties of the gelatin-nano hydroxyapatite (nHAP) nanofiber film electrospiration was carried out by a tensile test and the results were listed in Table 2 [24]. Based on Table 2, it is known that an increase in nHAP levels by 10% reduces tensile strength, an increase in nHAP levels by 25% resulted in severe agglomeration and exposure to nanoparticles as defects in the fibers. This results in a significant reduction in tensile strength and makes the scaffold brittle. The modulus young value is in accordance with the criteria for the modulus young value of the trabecular bone, namely 24.9-240 MPa [25].
Table 2. Young’s modulus, tensile strength and elongation at break of the electrospun nanofibrous films. Different letters indicate significant difference (P<0.05) [24].

| Film sample | Young’s modulus (MPa) | Tensile strength (MPa) | Elongation at break (%) |
|-------------|-----------------------|------------------------|-------------------------|
| HAP0        | 68.6 ± 6.98<sup>a</sup> | 1.75 ± 0.17<sup>a</sup> | 4.73 ± 0.03<sup>a</sup> |
| HAP10       | 67.1 ± 10.4<sup>a</sup> | 1.66 ± 0.24<sup>a</sup> | 5.08 ± 2.04<sup>a</sup> |
| HAP25       | 47.2 ± 4.61<sup>b</sup> | 1.13 ± 0.07<sup>b</sup> | 4.19 ± 0.27<sup>a</sup> |
| HAP50       | 60.2 ± 6.27<sup>ab</sup> | 1.12 ± 0.16<sup>b</sup> | 3.04 ± 0.77<sup>a</sup> |

4. Conclusion

Based on the literature review, it can be concluded that the addition of hydroxyapatite to the PLA 3D-printing scaffold can improve the bioactive properties of the PLA scaffold. Modification of the PLA scaffold surface with hydroxyapatite can support cell proliferation and differentiation which leads to increased mineralization of the PLA-HA scaffold and increases osteoinductive properties. The addition of gelatin to the PLA scaffold can increase the hydrophilicity properties so that it can improve the hydrophobic properties of PLA and gelatin is biocompatibility and supports cell proliferation.

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