3D Printing of PCL/HA Composite Scaffolds for Bone Tissue Regeneration: A Brief Review

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Tissue engineering aims to develop devices that assist in cell growth and tissue formation, making the use of biocompatible, biodegradable, and non-toxic scaffolds fundamental to promoting, for example, tissue regeneration. This review aimed to investigate the production of composites of poly(ε-caprolactone) (PCL) and hydroxyapatite (HA) applied to bone regeneration using 3D printing with the fused deposition modeling (FDM) technique. It is known that composites obtained from PCL, which is biocompatible and resorbable, combined with HA, which is also biocompatible and bioactive, exhibit osteoconductive properties and cell adhesion, making them effective for manufacturing scaffolds aimed at bone regeneration. The research shows that PCL/HA composite scaffolds obtained through 3D printing have promising results, which could serve as an alternative for use in bone regeneration.
Keywords: Tissue Engineering. Bone Regeneration. Composites. Scaffolds.

Intending to create biological materials that promote the restoration, maintenance, or enhancement of tissue regeneration, tissue engineering has been the subject of numerous studies over the past few decades. This has intensified especially after technological advances related to bone fractures and bone tissue regeneration, which enabled improvements in patient treatments and, consequently, in outcomes [1].

Thus, scaffolds for bone tissue engineering require the use of bioactive materials, in addition to needing specific organization at both macroscopic and microscopic levels [3]. To meet these needs, one of the technological innovations that has shown positive results in this field was 3D printing, with fused deposition modeling (FDM) being the most popular technique. This process uses a heated nozzle that, when fed with a polymeric material, deposits material layer by layer onto a heated platform to create a three-dimensional object previously modeled by computer-aided design (CAD) software [2].

For scaffolds, they must provide support to the defective tissue, requiring specific mechanical strength. It is also essential that they present an adequate porous structure, allowing a favorable external environment for the proliferation and differentiation of the compromised tissue cells, thereby facilitating tissue repair. Therefore, this technology enables the creation of polymeric scaffolds with improved control over pore morphology, pore size, and porosity, aspects that are challenging to achieve with conventional methods [1,3].

Traditional techniques for obtaining scaffolds present several limitations, primarily because they are inadequate for producing pores with precise sizes, specific shapes, high levels of interconnectivity, and significant mechanical strength. In contrast, 3D printing has emerged as an innovative technology to overcome the limitations of traditional methods, thereby enhancing the efficiency and cost-effectiveness of final products, such as scaffolds with complex geometric designs [4,5].

Tissue engineering typically begins with a scaffold, which must be biocompatible, as well as its degradation products. This implies that the materials used in the scaffold must be non-toxic to cells, easily removable from the body, and elicit a minimal immune response due to their presence [6]. Thus, in tissue engineering, it is

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crucial to comprehend the biological processes underlying cell proliferation and differentiation [4]. In general, the ideal scaffold should be made of a material that is both biocompatible and biodegradable, exhibiting mechanical characteristics similar to those of the tissue in which it will be inserted [6]. However, there is currently no biomaterial, whether inorganic or organic, that can meet all the requirements of an appropriate scaffold for bone tissue engineering. Therefore, composites emerge as a promising class of biomaterials aimed at regenerating this type of tissue [6].

Poly(ε-caprolactone) (PCL) is frequently used in scaffold manufacturing, standing out as an important polymeric matrix due to its notable characteristics, including biocompatibility, gradual resorption after implantation, and good shape retention properties [3,5]. Due to its melting point below 100 °C, PCL becomes an excellent choice for scaffold applications. This occurs because most polymeric biomaterials do not degrade at the temperature at which PCL melts, which is an advantage in polymeric operations that use thermal fusion [5,7].

This characteristic enables the combination of PCL with new types of composites, thereby enhancing the matrix properties. However, when used in bone tissue engineering, the new bone tissue does not adhere effectively to the polymer surface due to its low bioactivity. Hydroxyapatite (HA), which exhibits high bioactivity, has been utilized as a bone substitute since it constitutes approximately 70% of the composition of natural bone. Thus, it is believed that PCL/HA composites, combined with the biocompatibility of both materials, are viable for scaffold applications in bone tissue engineering [3,8].

Therefore, this research will present, clearly and concisely, a review of a composite biomaterial formed by PCL, a thermoplastic, and hydroxyapatite (HA), a bioceramic, for the production of scaffolds in bone regeneration applications.

Materials and Methods

The method approach adopted for this work was qualitative, combining an analysis of a set of keywords in a database with the reading of works generated as a result of this search, to increase understanding of the topic and comprehend the various methodologies and material applications.

For the search, Scopus was used, a widely known and disseminated database in academia for its reliability in selecting published works. Applied to the titles, abstracts, and keywords of the articles, the searched strings were: (“FDM”) OR ("Fused Deposition Modeling") AND (“PCL”) OR (“Polycaprolactone”) AND (“Hydroxyapatite”) AND (“scaffolds”), limited to English-language articles only. All resulting works were considered, covering the period from 2015 to 2025.

As a result of the search, 58 articles were generated, and the titles were screened to identify those containing the words “PCL” or “Polycaprolactone,” “Hydroxyapatite,” and “Scaffolds.” After that, the abstracts were read to identify the works that best fit the purpose of this review, resulting in 6 articles.

Theoretical Background

Fused Filament Fabrication (FFF), known as Fused Deposition Modeling (FDM), is an additive manufacturing (AM) technique that enables the creation of customized objects using a three-dimensional (3D) model developed through computer-aided design (CAD) software [2].

This process works by extruding a polymer through a heated nozzle and depositing it onto a platform (base). Upon contact with the base, which is also heated but at a lower temperature than the nozzle, the material solidifies. After the deposition of one layer, the cycle restarts until the structure designed in CAD is completed [4].

FDM stands out as one of the most popular and accessible methods within AM, also including techniques that provide a promising perspective for the production of 3D implants with variations in pore size and spatial distribution, enabling the adaptation of device geometry to patient needs [9].

This type of technology offers several advantages over conventional manufacturing, including the ability to create more complex parts and reduce production time and costs for unique items. With this, it becomes feasible to develop new products and significantly accelerate market launch, demonstrating that the applications of additive manufacturing technologies are broad, ranging from pre-production models and temporary parts to final components for aircraft, medical implants, and in tissue engineering, such as bone reconstruction [2].

Among the polymers most commonly used in 3D printing for bone reconstruction, PCL stands out as a semicrystalline polymeric material that is hydrophobic and soluble in organic solvents at room temperature. Its reduced melting temperature and ease of blending favor its processing. Combined with its biocompatibility and high permeability, this makes it ideal for several biomedical applications, such as scaffolds for bone regeneration and long-term implantable drug delivery systems [8,10].

However, its application in bone tissue engineering highlights its qualities in a particularly favorable way, enabling load support. In contrast, the original tissue gradually transforms into bone, due to its high mechanical strength and slow degradation rate [6].

Scaffolds made from a PCL matrix do not naturally exhibit osteoinductive properties; however, research indicates that they have high solubility and integrate well with other biomaterials, such as hydroxyapatite and tricalcium phosphates, which possess high bioactivity. This characteristic paved the way for an effective strategy to overcome these limitations, enabling the development of composites with various materials, including ceramics. There are studies aimed at promoting cell proliferation, migration, and nutrient transport by creating PCL/HA scaffolds [3,11].

HA, being an inorganic element of natural bone, stands out as a biomimetic material that presents excellent biocompatibility and bioactivity in bone tissue engineering applications [12].For this reason, HA is frequently used in bone implant and bone cement applications, thanks to its similarities in both composition and biological characteristics with natural tissues [13].

HA is a crucial component in scaffold formation, as it constitutes approximately 70% of the natural bone composition. However, its fragility restricts its application; therefore, PCL is often combined with HA to provide the mechanical strength a scaffold requires [8,14].

In tissue engineering, a bone scaffold can be created by combining PCL and HA. This structure promotes bone cell migration, an essential process for vascularization and bone development. Additionally, it provides temporary mechanical support in fractured or injured areas [8].

Scaffolds are not designed to be permanent implants; their goal is to promote the deposition of extracellular matrix by host cells, thus replacing the scaffold structure over time. For this reason, an ideal scaffold must be made of a material that is biocompatible and biodegradable. Furthermore, its mechanical properties must be similar to those of the tissue in which it will be inserted, where the three-dimensional structure must be highly porous and interconnected, allowing for cell migration and nutrient passage [6].

Conclusion

This work provides an overview of the application of PCL and HA in the production of composite biomaterials for tissue engineering, with a focus on bone regeneration. The qualitative research is based on the review of scientific articles and academic works, highlighting the relevance of continuous advancement in this area for improving practices and methodologies that aid in building bone structures to accelerate and ensure good regeneration of fractured bone tissue, emphasizing patient individuality and the particularity of each clinical case.

In the selected studies, it is evident that FDM makes a significant contribution to tissue engineering. This technology enables the manufacture of scaffolds with complex porous geometries, making it particularly useful in bone tissue engineering. It provides superior control and optimization of pore structure at the microscale, favoring bone healing and vascular infiltration.

Furthermore, it enables exact customization of scaffold geometry at the macroscale to meet the specific needs of each patient.

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