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Composite Materials Based on Calcium Polyphosphate, PVA and Mg^{2+} for Bone Applications †

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Abstract: Polyphosphate (PP) is an inorganic polymer formed by the condensation of orthophosphate groups and represented by the formula $[PO^{3-}]_n$. Due to its properties, such as biocompatibility and low toxicity, polyphosphate presents itself as a biomimetic compound of hydroxyapatite, the main constituent of bone tissue. PP can be applied for bone tissue applications as a ceramic material in the form of calcium polyphosphate (CPP), due to its chemical similarity with hydroxyapatite. Thus, CPP has been used to develop scaffolds for bone tissue repair. However, CPP does not have adequate mechanical properties for application in bone, requiring the use of substances that add other properties to the material, such as resistance to compression and tension. For this, polymers, ions, and nanoparticles have been used as additives. In this context, this work presents the development of composite materials based on CPP, PVA, and Mg^{2+} as candidates for bone applications. The production of materials was based on the precipitation of CPP in an aqueous medium containing a pre-solubilized polymer, followed by the addition of Mg^{2+}. The materials were characterized by TGA, SEM, EDS, and Raman. The results confirmed the formation of the composites, presenting a porous structure and containing a Ca/P ratio of 0.90. Thus, these composites have the potential to be applied in bone regeneration applications.

Keywords: hydroxyapatite; polymer; biomaterials; tissue repair

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1. Introduction

Polyphosphate (PP) is an inorganic polymer formed by a linear or cyclic chain of orthophosphates which can present a degree of polymerization (n) between 2 and 10^6. This compound can be synthetically obtained through condensation reactions at a high temperature and varying experimental conditions, such as pH and concentration of reagents. As for its application, the presence of PP has been observed in industry, agriculture, and science. In the industrial sector, the application of PP depends on its properties, such as the ability to form complexes with metal cations and a high potential to retain considerable amounts of water. Furthermore, it is non-toxic and biodegradable, in addition to being a low-cost product [1,2]. In agriculture, PP is used in the form of ammonium polyphosphate, serving as a phosphoric fertilizer [3,4].

In science, PP has been highlighted in health sciences and tissue engineering in the form of calcium polyphosphate (CPP), being used in the development of biomaterials aimed at bone tissue repair and substitution [5]. Overall, CPP acts as a calcified matrix serving as an alternative to hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$), the main component of human bone tissue [6]. In addition, studies showed that CPP is biocompatible, non-toxic, osteoinductive, osteoconductive, and has osseointegration potential, participating in bone formation and recovery [7,8]. In addition to these characteristics, CPP presents the possibility of producing a porous material with interconnectivity between the pores. Porosity and interconnectivity

between pores are essential parameters in bone substitutes. The pores are needed for cell migration in the interstices of the material, influencing the processes of vascularization, cell growth, and the rate of bone growth [9,10].

As in several areas of science, the search for improvements and optimizations in the properties of biomaterials is something relevant that enables the emergence of new medical devices. In this way, research involving CPP for bone applications also aims to produce materials with properties that are increasingly cohesive and similar to bone tissue. Therefore, cations [11], polymers [12], and metallic nanoparticles [13] have been added to calcium polyphosphate. The addition of these components results in changes in the bioresorbability, bioactivity, solubility, and physical and biological properties of these materials.

The Mg^{2+} ion, for example, has been applied to the development of bone biomaterials since it is a species that occurs naturally in the body at low concentrations, and it is associated with mineralization and bone growth processes, influencing the proliferation of osteoblasts in the osteogenesis stage [14]. Another strategy used to improve or add properties to CPP is the addition of synthetic and/or natural polymers. Commonly, polymers are used to add mechanical and structural properties to CPP, since it does not have mechanical properties to be used [15–17]. The association of polymers with ceramic materials, such as CPP, is carried out through co-precipitation techniques, mixing of the ceramics with the polymeric matrix, and biomimetic mineralization, by the immersing of polymeric matrices [17].

With the possibility of developing bone medical devices based on CPP, this work aimed to prepare a composite biomaterial constructed from CPP, $Mg^{2+,}$ and polyvinyl alcohol (PVA), in order to add chemical and mechanical properties to the material. The composites were prepared by precipitating calcium polyphosphate in an aqueous medium containing PVA, followed by the addition of Mg^{2+}. The materials were characterized by thermogravimetric analysis (TGA), scanning electron microscopy (SEM), energy dispersive X-ray spectroscopy (EDS), and Raman spectroscopy.

2. Materials and Methods

Two materials were prepared from the following precursors: polyvinyl alcohol (PVA, Aldrich, Mw = 89,000–98,000, 99%), anhydrous calcium chloride (Aldrich, 99%), magnesium chloride (Sigma, 98%), and sodium hexametaphosphate (NaPP, Aldrich, 96%).

Initially, the synthesis was initiated with the dissolution of PVA in water at 75 °C. After homogenization of the polymer, NaPP was added, and the system was kept under homogenization for 20 min. Then, an aliquot of $MgCl_2$ 1.0 mol L^{-1} was added and the mixture was stirred for 10 min. At the end of the homogenization process, an aliquot of $CaCl_2$ 1.0 mol L^{-1} was added to the system, which was again stirred for 10 min. The solid material formed was filtered, washed with distilled water at 25 °C, and oven dried at 60 °C. Finally, a solid white material was obtained. Table 1 details the quantities used for the preparation of CaP-P-1 and CaP-P-0.5 materials.

Table 1. Amounts used in the preparation of materials based on CPP, PVA and Mg^{2+}.

Sample	NaPP (mmol)	$CaCl_2$ (mol)	$MgCl_2$ (mmol)	PVA (g)
CaP-P-1	1.07	1.22	2.7	1.0036
CaP-P-0.5	1.07	1.22	2.7	0.5109

3. Results

In this study, two composites were prepared by varying the amount of PVA during the synthesis. At the end, the materials were characterized to identify mainly the morphology, the Ca/P ratio, thermal decomposition with increasing temperature, and their Raman vibrational bands.

3.1. Thermogravimetric Analysis

The thermogravimetric curves of the materials are shown in Figure 1 and in Table 2. This technique was used to determine the volatile material content of the reagents and samples. As revealed by TGA, samples CaP-P-1 and CaP-P-0.5 showed a mass loss between 17 and 29% up to 100 °C, respectively. Furthermore, there was a loss of mass up to approximately 450 °C, leaving mostly inorganic matter at this temperature. The TGA revealed that the CaP-P-1 sample lost 38% and the CaP-P-0.5 sample lost 45%.

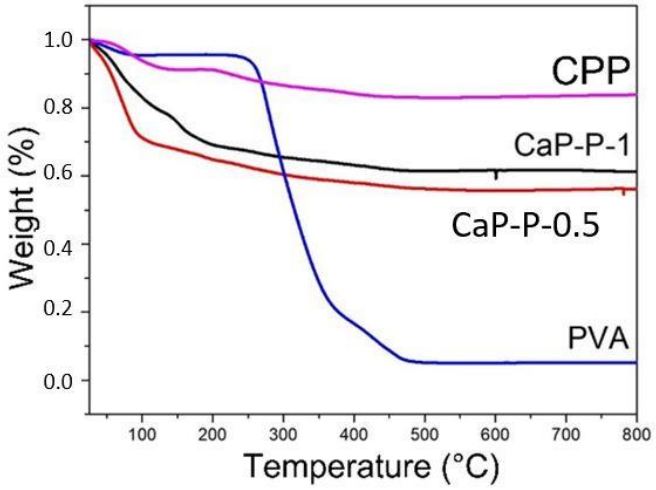

Figure 1. Thermogravimetric curves of CPP, PVA and materials CaP-P-1 and CaP-P-0.5.

Table 2. Mass losses referring to PVA, CPP, CaP-P-0.5, and CaP-P-1 in the temperature ranges 25–100 °C and 25–800 °C.

Sample	Mass Loss up to 25–100 °C	Mass Loss up to 25–800 °C
CPP	7%	27%
PVA	5%	95%
CaP-P-0.5	29%	45%
CaP-P-1	17%	38%

3.2. Scanning Electron Microscopy and Energy Dispersive X-ray Spectroscopy

The morphology evaluation was performed by SEM (Figure 2). The sample of CaP-P-1 material showed roughness and cavities in the surface region (Figure 2A,B). On the other hand, the micrographs of the CaP-P-0.5 sample revealed a surface consisting of cavities with some plates projecting out of the material (Figure 2C,D).

The energy dispersive spectroscopy of composite materials showed the Ca/P ratio of the materials. The CaP-P-1 composite sample showed Ca/P = 0.90, while the CaP-P-0.5 composite showed Ca/P = 0.82.

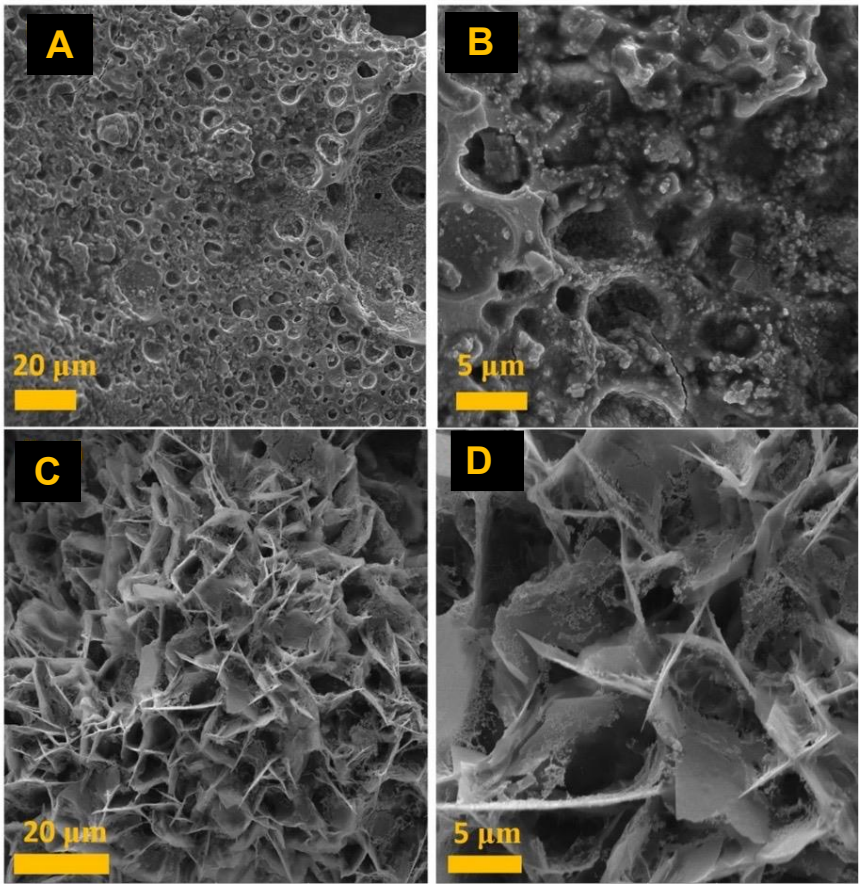

Figure 2. SEM images of materials CaP-P-1 (**A**,**B**) and CaP-P-0.5 (**C**,**D**).

3.3. Raman Spectroscopy

Raman spectroscopy was used to identify the presence of bands referring to the precursors. As shown in Figure 3, vibrational modes were identified at 120, 350, 510, 745, 908, and 1035 cm^{-1}.

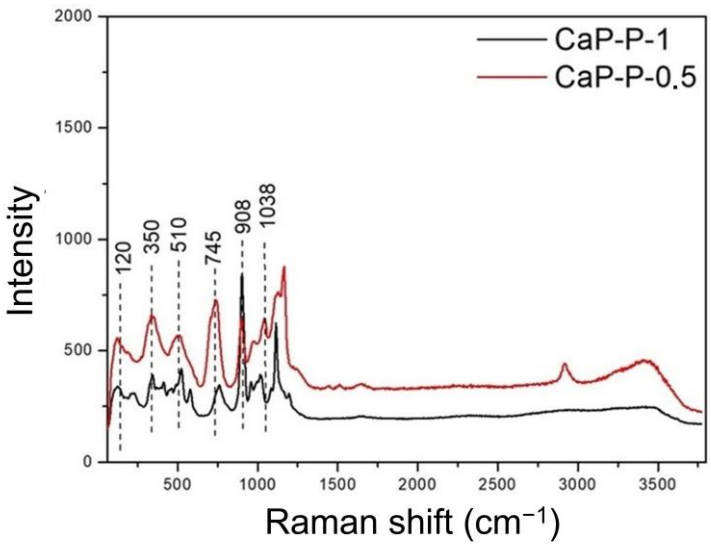

Figure 3. Raman spectrum of CaP-P-1 and CaP-P-0.5 materials.

4. Discussion

According to the results, the CaP-P-1 and CaP-P-0.5 are mostly composed of inorganic matter, since the decomposition of the samples revealed a loss of mass between 38% and 45%, which was associated with water evaporation and PVA decomposition.

The CaP-P-1 sample presented a morphology with cavities, in accordance with results presented in the literature involving the fabrication of materials based on CPP. [5] On the other hand, the morphology of the CaP-P-0.5 material showed the formation of plates off the surface. This type of morphology is observed by Ginebra (2012) when evaluating SEM micrographs of apatite cement formed by the hydrolysis of alpha calcium phosphate (α-TCP). [18] According to the literature, porosity and interconnectivity between pores are parameters that can help cell migration in the interstices of the material, influencing the processes of vascularization, growth cell, and bone growth rate. [9]

HAp is the main component in the bone and presents a ratio of Ca/P = 1.67. Our composites presented a Ca/P ratio of around 0.90, which was lower than HAp. The decrease in the Ca/P ratio can be observed in calcium phosphates that have the ability to form polymeric chains of orthophosphate groups, as is the case with PP. [19] The Ca/P ratio predicts the behavior of the in vivo degradation of materials, in which low values of Ca/P indicate higher degradation rates and greater bioavailability for the composite. Thus, these biomaterials could have higher solubility and a higher rate of degradation in comparison with HAp.

Raman spectra of calcium polyphosphate are generally defined by the presence of four main absorption bands, with maxima located in the wave number ranges at 1050–1200 cm^{-1}, 800–1050 cm^{-1}, 550–700 cm^{-1}, and 300–500 cm^{-1}, which may present some deviations due to the presence of alkaline earth dopants [20]. In the Raman spectra of the materials, CPP bands were identified at 350, 510, 745, 908, and 1035 $cm^{-1,}$ and associated with the stretching. In addition, a band was observed around 120 cm^{-1}, which may be associated with the PP and Mg^{2+} interaction. According to Sano (2002) and Capwell (1972), magnesium chloride has two characteristic bands at 243 cm^{-1} (strong) and 157 cm^{-1} (weak), associated with the A_{1g} and E_g modes, respectively [21].

5. Conclusions

In this study, we obtained two composites. In both systems, the presence of Ca, P, and O in the matrix were confirmed, confirming that they were materials based on a calcium phosphate derivative. The materials produced with PVA-presented water content between 17–29% and two types of morphologies, one formed by cavities and the other formed by plates. The distinction between the morphologies may be associated with the different concentrations that were used during the production of the materials. In addition, Ca/P values were estimated to be 0.90 and 0.82. The results obtained showed the potential of these materials to be used in the development of bone scaffolds.

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