Research Article

The pH Effect on the Growth of Hexagonal and Monoclinic Hydroxyapatite Synthesized by the Hydrothermal Method

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Summary. In the present work, a study of H⁺ effects on the microstructure and morphology of hydroxyapatite synthesized by the hydrothermal method is reported. The synthesis was realized with pH values of 10, 9.6, 9, 8, and 7. To know the particle size distribution, growth habit, chemical composition, and crystalline phases present, SEM-EDS, XRD, AFM, and FTIR spectroscopy techniques were used and completed with Rietveld analysis. The obtained results showed an important effect of H⁺ on the morphological and crystallographic characteristics of the hydroxyapatite, demonstrating that the shape and nanoparticle size, as well as the number of crystalline phases, can change depending on the pH during the synthesis. It was observed that there is an increase in the formation of the monoclinic phase and a decrease of the hexagonal phase when the pH value diminishes from 9.6 to 7. The crystallite size also decreases from 46.69 to 19.56 nm. An explanation of the role of pH on the final characteristics of the hydroxyapatite was related to the amount of H⁺ and OH⁻ ions, and it was included in this work.

1. Introduction

Hydroxyapatite (Ca₁₀(PO₄)₆(OH)₂) is a major inorganic component in teeth and bones, which forms approximately 70% of the skeleton and 90% of tooth enamel [1–3]. Hydroxyapatite (HAp) is the most thermodynamically stable phosphate phase in the human organism [1]. This mineral has many properties, for instance, bioactivity, biocompatibility, osteoinduction, nontoxicity, thermal stability, and high potential osteogenic, which makes it an excellent biomaterial [4–7].

For this reason, different chemical-processing methods to synthesized HAp have been developed, such as solid-state, mechanochemical, chemical precipitation, hydrolysis, sol-gel, hydrothermal, and emulsion. Also, there are high-temperature methods such as pyrolysis and combustion by the synthesis of biological sources [8, 9]. The use of different precursors based on sources of calcium and phosphate has also generated a world of possibilities for obtaining HAp.

In past decades, works about the synthesis of HAp by hydrothermal [10] and chemical precipitation method have been reported [11], in which the dissolution stages, crystal growth, and aging time are carried out at high temperature (above the boiling point) and pressure inside of a reactor/autoclave [12]. Nowadays, the hydrothermal method synthesis presents a greater dissolution of the precursors and more homogeneous mixtures; in addition, the pressure exerted by the equipment generates structures of smaller size and
minimal porosity. Also, this method has an advantage because when temperature (>350°C) and pressure (>1 atm) inside the container increases, the water behaves like an amphoteric substance. This facilitates the formation of more stable acid or base solutions.

On the other hand, the synthesis conditions must also be considered, such as the precursor’s concentration, reaction temperature, reaction time, and pH, since these variables strongly influence the shape and size of the HAp (mainly in the nanometric scale). These last characteristics may dramatically increase the HAp applications, for example, as cancer cells inhibitor as well as in different biomedical and industrial applications, such as a catalyst for Michael type addition, lasers host materials, fluorescence materials, ionic conductors, and gas sensors [13–17].

For this reason, recent studies have focused on the synthesis of hydroxyapatite with specific size and shape, in which synthesis parameters such as the kind of precursors, concentration, reaction time, reaction temperature, and pH are closely monitored. Specifically, the initial pH (ipH) is a determinant in the final morphology of structures; if the ipH increases or decreases, it is possible to appreciate a morphology change; then, sphere, rollers, needle, wire, leaves, spherulites, belts, etc. can be formed [2, 18–25]. Besides, the size of the formed structures can also change drastically. This is because the pH is a supersaturation indicator since it influences the ions balance; by varying it, different OH− concentrations are generated, and as a consequence, the Ca2+, PO43−, (HPO4)2− ion concentrations are also modified. It should be mentioned that a high concentration of OH− can facilitate the precipitation during the synthesis of HAp [26, 27].

In this sense, the majority of scientific papers report the presence of hexagonal HAp at low temperatures, without reporting the presence of monoclinic phase. The explanation provided indicates that the monoclinic HAp is mainly obtained at higher temperatures than 1000°C [28]; however, there are few papers in which it has been shown that monoclinic HAp can be obtained at lower temperatures [25]. Moreover, there are minimal morphological and crystallographic differences among them, then, the identification of monoclinic HAp is very difficult. G.Ma and X. Y. Liu [29] had to use electron microscopy and electron diffraction techniques to show the presence of monoclinic HAp. Regardless of the applications of the synthesized HAp, it is believed necessary to use several tools to be sure of the presence of hexagonal, monoclinic, or both crystalline phases in the final product of the HAp synthesis. The aim of this work was to study the H+ effects on the microstructure and morphology of hydroxyapatite synthesized by the hydrothermal method; emphasis was placed on determining the possible presence of hexagonal, monoclinic, or both crystalline phases. To carry out this study, SEM-EDS, XRD, AFM, and FTIR spectroscopy techniques were used. As it will be shown, it was identified the presence of monoclinic HAp; that is very interesting because the synthesis was made at low temperature. For this reason, a reasonable explanation based on the pH effects on the final hydroxyapatite characteristics by hydrothermal method was included [26–29].

2. Materials and Methods

In our experiments, all the reagents were analytical grade and used without further purification: calcium hydroxide (Ca(OH)2) was purchased from Sigma Aldrich (98% purity) and dibasic ammonium phosphate (NH4)2HPO4 supplied by Meyer brand (98.5% purity). Nitric acid (HNO3, 2 M concentration) and ammonium hydroxide (NH4OH, 30%) were purchased from Meyer Chemical Reactive, and they were used for pH control.

2.1. Synthesis of Hydroxyapatite. The hydroxyapatite was synthesized varying the pH (7, 8, 9, 9.6, and 10), taking into account that at lower pH it has a higher amount of H+ ions, while at higher pH it has higher OH− ions [30]; the corresponding labeled samples were HAp-7, HAp-8, HAp-9, and HAp-10, respectively, keeping the synthesis temperature and the stoichiometric concentrations according to the chemical reaction presented in the following equation.

\[
10\text{Ca(OH)}_2 + 6(\text{NH}_4)_2\text{HPO}_4 \rightarrow \text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 + 12\text{NH}_3 + 18\text{H}_2\text{O}.
\]

Firstly, 40 ml of NH4)2HPO4 (0.09 M) and 40 ml of Ca(OH)2 (0.15 M) solutions were prepared independently (Figure 1(a)). Subsequently, they were mixed, adding the ammonium phosphate solution onto the calcium hydroxide solution dropwise with constant stirring for 10 minutes (Figure 1(b)); the pH was 9.6 (ipH). The final solution was added to a stainless-steel autoclave reactor and kept at 200°C for 24 hours (Figure 1(c)). Then, the obtained product was allowed to slowly cool at room temperature, the solids contained within the autoclave were removed, washed three times with deionized water, and filtered by vacuum filtration (Figure 1(d)). After that, the solid was dried in a drying oven at 80°C for 12 hours (Figure 1(e)). Finally, the powders were subjected in a calcination treatment at 500°C for 3 hours to remove other impurities (Figure 1(f)). The same methodology was followed for samples obtained at different pH. The pH10 has been achieved by adding (dropwise) 25 ml of ammonium hydroxide while the mixture of ammonium phosphate and calcium hydroxide was maintaining constant stirring (Figure 1(b)). For the pH of 9, 8, and 7, nitric acid was added in volumes of 15 ml, 30 ml, and 45 ml, respectively.

2.2. Characterization. The structural and elemental characterization was performed using a scanning electron microscope (SEM) JEOL, model JSM5900-LV, equipped with an X-ray energy dispersive spectrometer (EDS). For XRD analysis, a Bruker D8 Discover diffractometer was used (with a CuKα = 1.5406 Å radiation source) operating at 40 kV and 40 mA. Diffraction patterns were collected in a 2θ range from 10° to 70° with an incremental step size of 0.03°. The X-ray diffraction patterns were subjected to a Rietveld analysis using a Topas® software; Rwp and chare were parameters used to indicate the accuracy of the refinement of XRD patterns. FT-IR analysis was performed in a Bruker Vertex 70 brand device with an attenuated total reflection (ATR); the analysis was in a spectral range of 4000-400 cm−1. The
topology analysis was carried out in an atomic force microscope (AFM) and Asylum Research model Cypher. The particle size distribution was determined using the ImageJ software in a total of 300 particles per sample.

3. Results

3.1. X-Ray Diffraction (XRD). The X-ray diffractograms of hydroxyapatite samples obtained at different pH values (7, 8, 9, 9.6, and 10) are presented in Figure 2. All the samples revealed the presence of both hexagonal (H) and monoclinic (M) crystalline phases with different quantities. The hexagonal phase with chemical formula Ca₅(PO₄)₃OH is consistent with the phases listed in the JCPDS card No. 74-0565, while the monoclinic phases with chemical formula Ca₁₀₀₈(PO₄)₅₉₄(OH)₃₉ are consistent with the card No. 76-0694. The main (h k l) Miller indices for monoclinic HAp are (020), (002), (211), (122), (300), and (042) (Figure 2(a)). While Figure 2(b) shows the corresponding (h k l) for hexagonal HAp are (002), (211), (112), (030), and (022). To determine the quantity of the crystalline phase and crystallite size present in all samples, a Rietveld method was applied using the data obtained from X-ray diffractogram, for each sample. Table 1 presents the crystalline parameters calculated for each sample. It can be observed that for HAp synthesized at pH 9.6, the quantity of monoclinic and hexagonal phases is 82.64 and 17.36 weight percent (wt%), respectively. If the pH decreases, the presence of hexagonal phase has been drastically reduced and the monoclinic phase increased, as it can be observed in Table 1; an important reduction of the crystallite size is also observed.

3.2. Scanning Electron Microscopy (SEM). Figure 4 shows SEM images of HAp samples synthesized at different pH and the corresponding particle size distribution. For the sample at pH 10, agglomerates between 0.15 and 2 μm in size are observed; these agglomerates are made up of nanoparticles. At pH 9.6 (ipH), agglomerates of anhedral form with dimensions between 0.13 and 1.38 μm are appreciated. For the sample at pH 9, agglomerates with a rough surface and "spongy" shape and sizes between 0.18 and 4.44 μm are observed. At pH 8, the micrograph shows agglomerates with a "spongy" surface and sizes between 0.18 and 3.83 μm. Finally, the micrograph associated with the sample obtained at pH 7 shows the presence of agglomerates with a rough surface and sizes between 0.14 and 2.80 μm. These SEM results clearly show the effect of the pH of the synthesis on the morphological characteristics of the hydroxyapatite. In order to know the Ca/P ratio, an EDS analysis was performed in 3 different areas per sample, obtaining the average weight percent. According to the results, in the HAp-7 sample, the Ca/P ratio was 1.88, while in all other samples the Ca/P ratio was 1.67.

3.3. Atomic Force Microscopy (AFM). Figure 5 corresponds to AFM micrographs of synthetized HAp samples showing greater detail of the nanoparticles constituting the agglomerates observed by the SEM technique. The particle size distribution was graphed in order to classify them by dimensions and identify the most representative class for each sample. For samples synthesized at pH 10, classes of different sizes of particles with rod shape are identified; the majority of...
these particles present diameters in a range between 34 and 39 nm and lengths between 58 and 74 nm; however, nano-particles with semispherical shape were also observed. In the sample with pH 9.6 (ipH), structure in rods form with lengths from 22 to 37 nm and diameters from 22 to 134 nm are observed.
Sample synthesized at pH 9 showed structures in rod form with lengths between 29 and 38 nm and diameters between 54 and 72 nm. In samples with pH 8, rod structures with lengths from 29 to 34 nm and diameters from 49 to 63 nm are distinguished. In comparison to the above, the corresponding micrograph of the Hap-7 sample, a decrease in particle size can be seen, which consists of particles with length from 17 to 21 nm and diameter from 28 to 38 nm. These results indicated that if the pH is lowering (by adding more nitric acid), the particle size decreased both diameter and length. In the discussion section, a model of growth in particle formation according to the variation in pH is graphically described.

Figure 4: SEM micrographs and agglomerate size distribution for prepared samples.
3.4. Fourier Transform Infrared Spectroscopy (FTIR). Figure 6 shows the FTIR spectra of HAp samples, and Table 2 shows the compilation of the results obtained by this technique. In the figure, it is possible to observe the characteristic absorption bands of the hydroxyl (OH⁻) group and the radical $\text{PO}_4^{3-}$ of phosphate apatite, confirming the successful
OH- band at 637 cm⁻¹ is observed; the same happens for ing with the pH 9.6 spectra (natural), an increase in the adding ammonium hydroxide to reach pH 10 and compar-
It can be observed that when attributable to the absorbed water, and it happens for HAp-9, HAp-8, and HAp-7 samples, corresponds to (NO₃)²⁻ stretch bands, which it was incorporated during the pH control in the synthesis. The broad bands at 3432 and 1642 cm⁻¹ were attributable to the absorbed water, and it happens for HAp-9, HAp-8, and HAp-7 samples. It can be observed that when adding ammonium hydroxide to reach pH 10 and comparing with the pH 9.6 spectra (natural), an increase in the OH⁻ band at 637 cm⁻¹ is observed; the same happens for the OH⁻ group (3570 cm⁻¹). In the (PO₄)³⁻ group, a slight increase in the bandwidth of the hydroxyl group corresponds to 566 cm⁻¹, it can be observed that pH was reduced by adding nitric acid to the natural pH, and compared to pH 9, 8, and 7 spectra, an increase in the bandwidth of the OH group (3573 cm⁻¹) was observed, as well as a decrease in the bandwidth of the hydroxyl group (634 cm⁻¹), for the (PO₄)³⁻ group, an increase in the bandwidth corresponding to 565 cm⁻¹ is observed.

### 4. Discussion

SEM analysis shows the formation of agglomerates of nanoparticles; the size of these particles decreases as the pH value also decreases. The AFM characterization led to the following asseveration: by decreasing the pH value from 9.6 to 7, a decre-
Table 3 shows a summary of the most important results of some recent scientific papers that used the hydrothermal method to synthesize hydroxyapatite. They all report the presence of the hexagonal crystalline phase with rod structure; none of them reported the presence of the monoclinic phase.

As it was mentioned above, in samples at pH 10 (OH⁻ ions are predominant), rod structures with lengths from 58 to 74 nm and diameter from 34 to 39 nm were observed; in lower proportion, semispherical nanoparticles were also identified. At pH 9.6, rod structures of lengths from 22 to 134 nm and diameters from 22 to 37 nm were observed. When the pH values decreased from 9 to 7 (the concentration of OH⁻ diminishes), the nanoparticle size also decreased. This behavior could happen because of the decrease in saturation of the solution as a result of the decrease in the concentra-

| Group                  | pH 7 | pH 8 | pH 9 | pH 9.6 | pH 10 |
|------------------------|------|------|------|--------|-------|
| OH⁻, δ bending (cm⁻¹)  | 1088 | 1088 | 1088 | 1088   | 1088  |
| OH⁻ unattached (cm⁻¹)  | 1033 | 1033 | 1033 | 1033   | 1033  |
| ν₁(PO₄)³⁻ (cm⁻¹)       | 963  | 963  | 963  | 963    | 963   |
| ν₂(PO₄)³⁻ (cm⁻¹)       | 565  | 565  | 564  | 567    | 565   |
HAp, without the need to increase at higher temperatures, as it has been reported in some papers. That is, it obtained monoclinic HAp in the nanometric scale at a lower temperature. Unlike Ma and Liu [25] who used electron microscopy and electron diffraction techniques to identify the monoclinic HAp, in this research, it used XRD and the Rietveld method to identify and quantify the monoclinic HAp. It also showed that its abundance depends on pH synthesis.

Considering that the main difference between monoclinic and hexagonal HAp consists in the orientations of the hydroxyl groups; for the monoclinic HAp, all of the OH’s in a given column are pointed in the same direction, and

Table 3: Reported results in recent scientific papers using the hydrothermal method to synthesis hydroxyapatite.

| Author            | Year | Reagents                        | Method     | Phase      | pH  | Temperature synthesis | Morphology        |
|-------------------|------|---------------------------------|------------|------------|-----|-----------------------|-------------------|
| Arantes et al. [31] | 2018 | CaCl₂ and (NH₄)₂HPO₄             | Hydrothermal| Hexagonal  | 9   | 100-140°C             | Rods              |
| Hoai et al. [32]   | 2017 | Na₃HPO₄ and CaCl₂                | Hydrothermal| Hexagonal  | —   | 180°C                 | Rods              |
| Yang et al. [10]   | 2014 | CaCl₂ and Na₂P₂O₇·STTP           | Hydrothermal| Hexagonal  | —   | 180°C                 | Rods and semi-spherical |
| Zhu et al. [33]    | 2018 | Ca(NO₃)₂·4H₂O and (H₃PO₄)       | Hydrothermal| Hexagonal  | 8, 10| 200°C                 | Rods              |

Figure 7: Possible growth mechanism of the synthesized particles of Hap depending on pH.
the direction reverses in the next column; while in the hexagonal HAp, the adjacent OH’s point in the opposite direction as mentioned above [25, 34]. This difference induced important modifications in their respective physicochemical properties. Because the monoclinic HAp is structurally more stoichiometric than the hexagonal HAp, the kinetic dissolution and the kinetics of diffusion along the OH-column region are expected to be different. Chemical stability and dielectric properties of HAp are modified because of the structural difference [25, 35].

As it was mentioned above, the physicochemical properties could be changed depending on the quantity of the monoclinic or hexagonal phase in HAp. That is critically important if the synthesized HAp is going to be used, for example, as a coating material for metallic implants. However, these results also open a range of possibilities to design HAp samples for several applications such as cell activation, carrier in drug delivery systems, CO₂ gas sensing, catalysis, and water treatment with much more efficient results.

5. Conclusion

The correlation between XRD, SEM-EDS, Rietveld method, and FTIR results showed an important effect of H⁺ on the morphological and crystallographic characteristics of the hydroxyapatite, demonstrating that the shape and nanoparticle size, as well as the number of crystalline phases, can change depending on the pH during the synthesis. It was observed that there is an increase in the formation of the monoclinic phase and a decrease of the hexagonal phase when the pH value diminishes from 9.6 to 7; that means, the higher concentration of the monoclinic phase was at pH 7. This result offers a simple methodology to obtain monoclinic hydroxyapatite at a lower temperature of synthesis and without precursor residues; besides, it promotes new different applications due to the presence of this HAp crystalline phase with control of the shape and particle size. It was concluded that a decrease of pH from 9.6 to 7, using nitric acid, contributes to the formation of H⁺, which favors the majority formation of the monoclinic phase. Finally, it was demonstrated that it is necessary that the correlation of several characterization techniques to distinguish between the monoclinic and hexagonal hydroxyapatite if both are present in a HAp sample.

Data Availability

All the data results in our article, we can provide them if required by the reviewers.

Conflicts of Interest

The authors declare there are no competing interests.

Authors’ Contributions

S. López-Ortiz made the first draft and prepared all the figures, tables, and designed the experimental work. D. Mendoza-Anaya and V. Rodriguez-Lugo contributed in the discussion and writing of the manuscript. M.E. Fernandez-García contributed in the analysis of the Rietveld method. D. Sánchez-Campos and M. I. Reyes-Valderrama made the research design and the revision of the article.

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