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Synthesis Of Hydroxyapatites And Their Application In Medicine

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Abstract

The objective of this work was initially, it was a new field of research that deals with more advanced ceramic materials used in Biomaterials and Nanotechnologies, the second objective was to synthesize hydroxyapatite of high purity from natural resources for their application in Medicine. We can consider that this double objective has been achieved since on the one hand we have characterized these hydroxyapatites; on the other hand, this material is synthesized from several routes. Several techniques were used; including X-ray diffraction (XRD), scanning electron microscopy coupled with EDX microanalysis (SEM-EDX), differential thermal and gravimetric analyzes (DTA-TGA) and finally the Fourier transform infrared (FTIR) and X fluorescence (XRF). This study concerns the results of the synthesis of hydroxyapatites, in the field of Biomaterials, we mainly encounter ceramics, especially the uses and developments of osseointegration and bioactive ceramics based on calcium phosphate: hydroxyapatite (HAP), there are therefore uses of hydroxyapatite (HAP) in dental implants and filling materials and in orthopedic surgery.

KEYWORDS SYNTHESIS, HYDROXYAPATITE, OSSEOINTEGRATION, DRX, IR, CHARACTERIZATION, POROSITY, OSTEOCONDUCTION

1. INTRODUCTION

The Hydroxyapatite (HAp) - [Ca_{10} $(PO_4)_6(OH)_2$] has a similar chemical composition to bone material, making it the main mineral supplement in bone-making. Due to its high biocompatibility, hydroxyapatite is widely used in the repair of bone deficiencies and in the production of dental or orthopedic implants.[19].

Hydroxyapatite which is one of the most common forms of calcium phosphate with the chemical formula Ca_{10} $(PO_4)_6(OH)_2$, denoted (HAP), the same found in bone tissue (Ca^{2+}) and (PO_4^{3-}) are major players in the regulation of the body's phosphocalcic metabolism [3]. The most important minerals are [4]: -Calcium: the skeleton contains 99% of the body's calcium (1100 to 1200g); -Phosphorus: the skeleton contains 90% of the total the body (about 600g); phosphorus of - Sodium: 18g for an adult skeleton; -Potassium: 6g; - Magnesium: 3g; The inorganic matrix gives the bone its mechanical properties of rigidity, hardness and resistance to compression, but also its role in its functions metabolic and homeostatic [5,7]. It is synthesized in the laboratory by different methods. However, the high cost of the different precursors used for the synthesis prompted researchers to find an alternative method to prepare HAP that can mimic human bone apatites. Given their osteoconduction and bioactivity, hydroxyapatite (HA) coatings promote bone tissue development and contribute to bone cell adhesion and proliferation while preserving the mechanical integrity of the metal prosthetic device. In this study we will focus on the synthesis of HAP by neutralization for its coating on prosthese [2]. Bioceramics are considered one of the best biomaterials, since they are well tolerated by the biological system of the organism. This material has the advantage of being osteoconductive. ¨

2. MATERIALS, METHODS AND RESULTS

2.1 Materials

The hydroxyapatites (HAP) $Ca_{10}(PO_4)_6(OH)_2$ are materials very important inorganic substances in biology and chemistry. Biological HAP are the most common crystalline calcium phosphates, the first constituent mineral of bones, tooth enamel and dentin [8].It seems to be the most suitable ceramic material for the construction artificial bone tissue thanks to its excellent biocompatibility properties [9].

2.2 Methods and Results

2.2.1. Methods of Synthesis (HAP) $Ca_{10}(PO_4)_6(OH)_2$

Given the various applications of hydroxyapatite in several fields, different methods of synthesis of the latter were implemented for its development.

The following figure1 illustrates the different methods of HAP synthesis knowing that the choice of the synthesis method

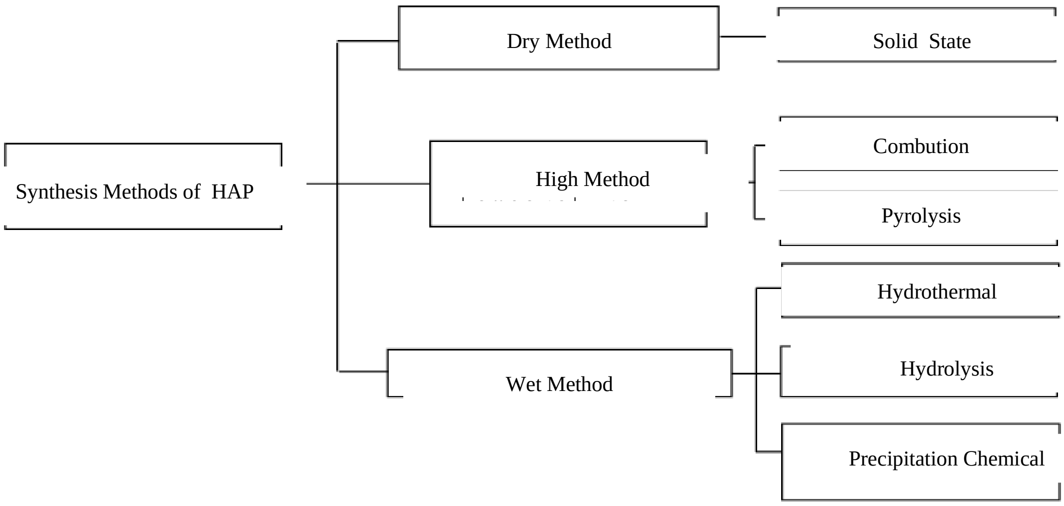


Figure 1. Presentation of the different PAH synthesis methods [21].

influence the morphology, chemical composition and crystallinity of the hydroxyapatite obtained.
in this work we were interested in the (HAP) synthesis method: The wet method by neutralization (precipitation).

1. by neutralization method

It consists in neutralizing a solution of calcium hydroxide $Ca(OH)_2$ commonly called milk of lime, by adding a solution of phosphate monoammonium or dihydrogen ammonium phosphate [11,12].

The reaction involved between the two solutions is the following:

$$10\ Ca(OH)_2 + 6\ NH_4H_2PO_4 \Longrightarrow Ca_{10}(PO_4)_6(OH)_2 + (OH)_2 + 6NH_4OH + 12H_2O \quad \textbf{(1)}$$

This reaction **(1)** makes it possible to quickly obtain large quantities of HAP calcium phosphate with little material [12,13]. After 48 hours, the reaction mixture is filtered in order to recover the white precipitate. The solid is then washed several times with a mixture (water + ethanol) and dried at 80°C in an oven for 24 hours. The material thus obtained is crushed and sieved desired grain size [14].

The hydroxyapatite from coprecipitation and sol-gel methods showed a significant degree of crystallinity compared with that of the microwave route.[20].

2.2.2. Results and Characterization method

2.2.2.1 XRD (X-ray)

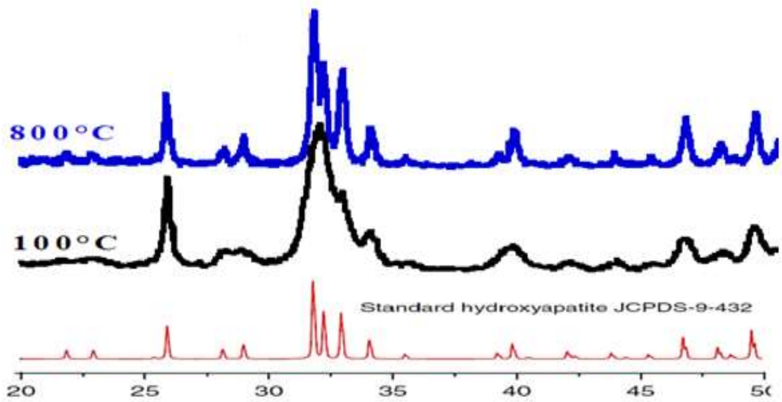


Figure.2.RX Diffractogram of the HAP.

The figure 2 presents the diffractogram of a calcined HA powder. Only the peaks of the apatitic phase (PDF 9-432) are detected and this regardless of the heat treatment applied.
By comparing the diffractograms of the RX spectra of the two hydroxyapatites (standard and synthesized) it can be deduced that we have synthesized a high quality hydroxyapatite with good crystallinity:
-Heating to 100°C resulted in broad diffraction peaks which correspond to poor crystalline apatite.

-Increasing the heating temperature to 800°C results in sharper and narrower diffraction peaks which indicate the increase in crystallinity.

2.2.2.2 Spectroscopy Fourier Transform Infrared (FTIR)

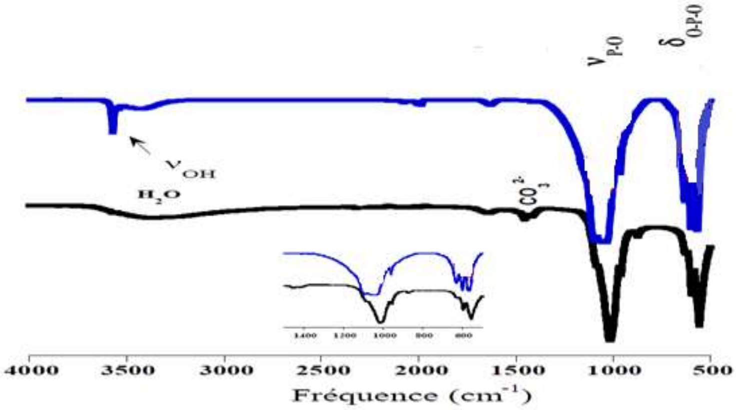
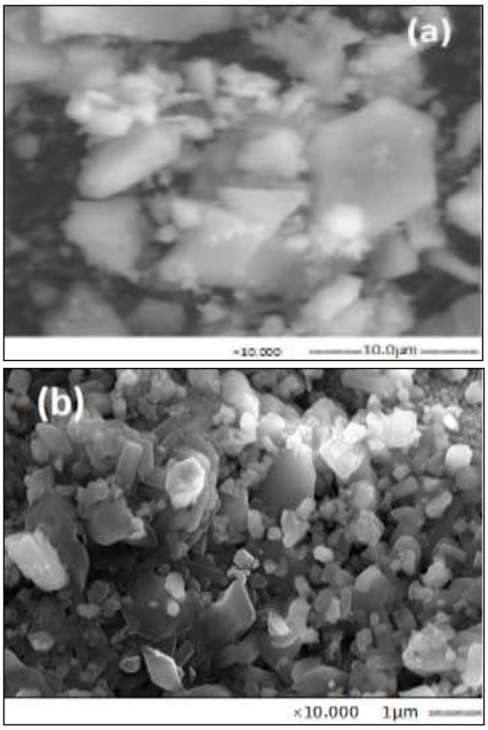


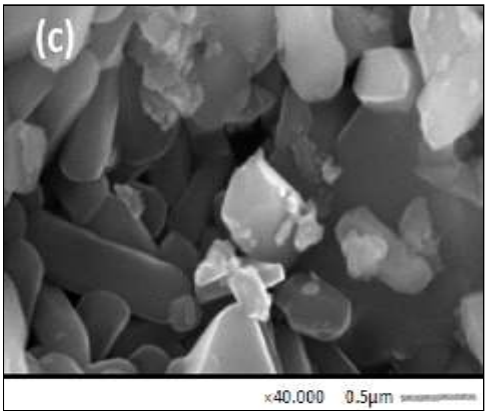
Figure 3.FTIR spectre of the HAP.

From figure 3. There is a symmetric and antisymmetric absorption bands attributable to (PO_4^{3}) groups in the 1100 and 900 cm^{-1} range and those deformation between 600 and 500 cm^{-1}. For the parboiled product, a wide band between 3000-3650 cm^{-1} and another of low intensity at 1649 cm^{-1} corresponding to the stretching vibration of the OH groups of the water molecule. Others bands at 1420 and 870 cm^{-1} were detected characteristic of the presence of carbonates in the powder. Moreover, the characteristic absorption bands to the vibrations of the OH^- hydroxyls of the apatitic lattice are located around 3560 and 630 cm^{-1} are visualized only in the case of hydroxyapatite calcined at 800°C. On these IR spectra, we observe that the bands related to carbonates disappear, which explains the total decomposition of the carbonate residues.

The FTIR results also showed that the intensity of the hydroxyl peak decreased with the water departure into the HAp structure.[21].

2.2.2.3 Elemental Chemical analysis Scanning Electronic Microscope





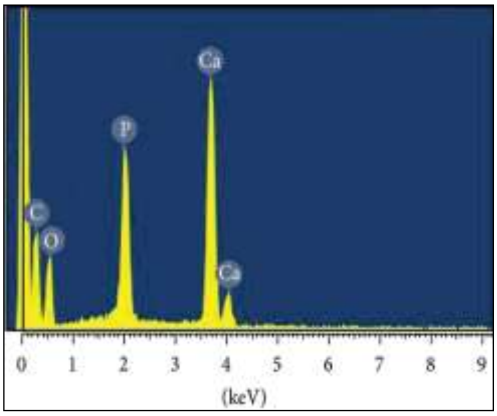


Figure.4.SEM micrographs an (d) nalysis of hydroxyapatite obtained by scanning electron microscopy of the product baked at 100°C (a) and powder calcined at 800°C (two magnifications (x10,000 (b),x40,000 (c)) and Energy dispersive X-ray (d).

The morphology (a), (b) and (c) shows an irregularity of the particles forming the aggregate of hydroxyapatite (HAP) with the major elements of phosphorus and calcium proven by EDX energy spectra (d).

Table 1. Characterization by X Fluorescence of HAP.

Element	Ca/P	CaO	PO_4
HAP (Wt %)	1.67	39.6	18.5

The elemental chemical analysis of the hydroxyapatite (HAP) (Table 1) and EDX shows that there is a significant percentage of CaO (39.6%), PO_4 (18.5%), which proves that HAP is rich in calcium and phosphorus.
According to the Ca/P molar ratio in the apatitic structure, the composition chemistry of HAP may vary. A HAP having a Ca/P atomic ratio of the order of 1.67 is said to be stoichiometric whereas the other apatites ($1.5 < Ca/P < 1.67$) are called deficient apatites. [7].
The results showed that the weight ratio of the components strongly influenced the crystal size and crystallinity [21].
Ca/P ratios closer to the stoichiometric ratio due to the use of effective extraction methods such as manipulating aging time or stirring process parameters [22].
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2.2.2.4 Thermal analysis: ATD / ATG

The purpose of thermogravimetric analysis (TGA) is to continuously record the mass variations of a sample during a thermal cycle. This technique is coupled with differential thermal analysis (DTA), which is based on the study of the energy released or absorbed by the material studied when it undergoes physical or chemical transformations. The thermal evolution of the PAH powder by (ATG) and (ATD) from room temperature to 800°C under a stream of argon-air mixture, with a temperature rise rate of 10°C/min.

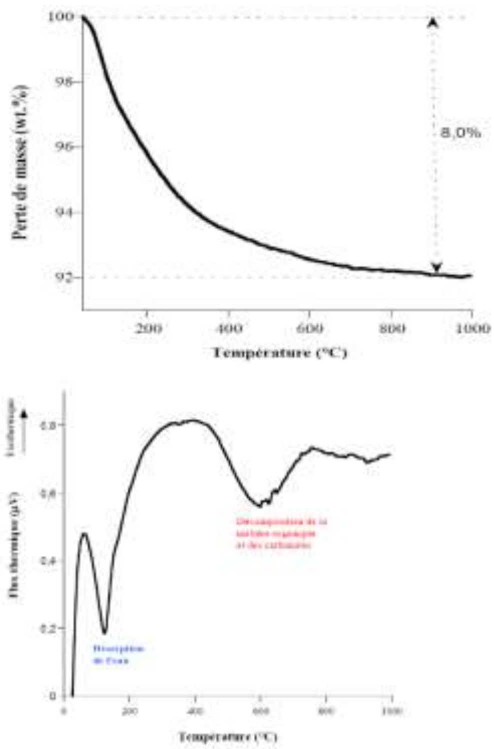

Figure.5. Curves of differential and gravimetric thermal analyses of HAP.

The figure 5 shows a continuous mass loss between room temperature and 800°C.

The first loss of 7.5% in total weight of the material occurs between ambient temperature and 600°C.

=> produced by the increase in temperature is attributed to the desorption of water.

The 2nd loss (> 600°C), of the order of 0.5% by weight, may correspond to the decomposition of residual carbonates, which are detected by infrared spectroscopy.

The absence of endothermic peaks up to 800-1000°C, showing that the hydroxyapatite powder is pure and does not undergo any decomposition phenomenon.

2.2.2.5 Plasma projection torch

The material to be sprayed: HAP Calcium phosphate for validation defined by: chemical composition, cristallinity, ratio Ca/P, porosity, particle size and physico-chemical characteristics, thickness, roughness, adhesion.

As mentioned previously, thanks to the similarity with the component inorganic material of human hard tissue, hydroxyapatite is considered a material suitable for various applications frequently in the field of medicine and pharmacy [6,8].

HAPs are also frequently used as a "coating" on titanium prostheses to facilitate osteointegration [15] or to prevent wear due to oscillatory micro-movements at the interface between the implant and the bone sometimes even leading to rupture of the prosthesis [16].

A hydroxyapatite-based coating improves the fixation of the prosthesis on bone tissue and reduce the release of metal ions from the alloy of the implant to the living organism [17][18].

There are some examples of use as a cement used in facial surgery to replace autogenous bone grafts [19] and a increasing number of applications as a vector of drugs for the direction of the cells.

Thus, synthetic grafts based on hydroxyapatite fit into the human body without being rejected by the host tissue and they facilitate the formation of new bone tissue, by creating bonds with the tissue newly formed [6].

In all these applications, it is ultimately the surface reactivity of the HAP with the biological medium which is the key point.

The results obtained after validation of the coating conditions and clinical tests have shown great satisfaction and are in progress to move on to the application part.

3. CONCLUSION

In the fight to increase the lifespan of the human body, the biomaterial is the alternative most seriously considered by doctors.

The field of materials science is undergoing a great evolution and the field of biomedical science is therefore a field for which the requirements are going to be increasingly important in the race to increase the duration of life of human beings. Choosing the right materials is very important particular. We believed for a long time that it was necessary, above all, to seek materials with the highest possible resistance to deformation. Then, gradually, in many cases, efforts had to be made to seek biomaterials presenting a better compromise between their resistance and their biocompatibility or, more generally, their resistance to fatigue.

The tests must be carried out and interpreted by specialists according to the future clinical use of the biomaterial, this makes it possible to avoid rejecting

biomaterials used successfully for a long time and which would not pass the tests imposed today on modern materials.

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