

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

186,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Hydroxyapatite-Based Materials: Synthesis and Characterization

Eric M. Rivera-Muñoz

*Centro de Física Aplicada y Tecnología Avanzada,
Universidad Nacional Autónoma de México,
México*

1. Introduction

The use of foreign materials to be used as implants within or outside the human body is not new. There are reports of more than 2000 years old which indicate the replacement of bone material in order to repair seriously damaged tissues. In the mid-nineteenth century it was attempted to repair human body parts using the materials available according to the technological advance of the time, unfortunately, these materials were mainly based on copper or bronze, suffering severe corrosion within the human organism's environment, and causing infections that also endangered the lives of patients. For this reason the prostheses used were basically external. Over the years (the late nineteenth and early twentieth century) were made several attempts to use different materials such as gold, glass and new alloys with better results.

Advances in polymer chemistry and the development of new alloys in modern metallurgy during the second half of the twentieth century gave rise to a variety of materials for reconstruction and replacement of some tissues inside and outside the human body. In the case of ceramic materials, the development of modern technologies has led to new materials with chemical, physical and mechanical properties that make them an excellent choice for applications in dental and orthopedic implants.

There are many ways to define a biomaterial, which has not been easy given the breadth of the term. In the European Society for Biomaterials Consensus Conference in 1986, was given the following definition: "Biomaterial is a material or substance, whether used alone or in making a medical device designed to interact with human tissues to monitor body functions or to treat pathological conditions of the same" (Mattox, 1992; Ravaglioli & Krajewski, 1992). A synonym for this is "biomedical material".

All definitions include the word "material", which usually indicates a solid consistency substance used to manufacture an object, which may consist of living or nonliving materials. If the material is alive, then is called "graft" and those non-living, placed inside the body, are called "implants". With a more limited meaning, the so-called "prostheses" can be considered as "endoprostheses", if they are contained entirely within the body, or "exo-prosthesis"(or "external prosthesis") if they are completely out.

In other hand, the "biocompatibility" of a biomaterial is defined as their ability to successfully fulfill a specific application, with an appropriate response of the host. That is, the biocompatibility means more than the fact that a material is not harmful in the body; it

also includes local interactions of the material and surrounding tissue in both directions. That is, it is vitally important, both the effect of the material on the living tissues as the effect of them on the former one (Hench, 1991).

A material is "not biocompatible" if it is toxic and/or if cause the death of surrounding tissue.

A biocompatible material may be considered "inert" if there is no reaction with tissue and the material is stable for indefinite periods of time (the only answer may be the formation of a fibrous layer around the implant), "bioactive" if there specific interactions with surrounding tissue, "bioabsorbable" if it dissolves into the body through a cellular activity and the vacant space is then filled with tissue, and finally "biodegradable" if the material fails gradually due to biological or specific biochemical activity (Hench 1991; Ravaglioli & Krajewski, 1992).

In general, different types of biomaterials are classified according to their nature and application; polymeric materials are used when complex shapes are required or require high flexibility; metals are used when the implant is subject to high mechanical loads. The applications of ceramics have taken great importance due to its high biocompatibility, corrosion resistance and primarily because the bone tissue is composed largely of mineral phases, which makes them an important option for replacement of bone or to promote regeneration of it. Composite materials are used to improve the interaction between the tissue and the implant (mainly metallic) at the interface (Lemons, 1986; Mattox, 1992; Park, 1984).

The current status of biomaterials is clearly in a state of rapid change, which provide a wide range of opportunities for both conventional materials as well as for the new materials developments (such as in nanotechnology, for example), and improvements in these areas are needed day by day, therefore which not only justified but also they requires the development of new technology in the production of those biomaterials.

While basic research in materials science and engineering, plus physics and chemistry involved in it is of vital importance, we can not ignore the economic aspect of these developments at the moment of entering the market.

It is very difficult to do a count on total sales worldwide biomaterials; however, one could refer to information published by Millennium Research Group on its website in 2002. Considering only the market for orthopedic biomaterials, according to this company was worth US\$ 930 million in 2001 only in the United States, anticipating a growth rate of 25.7% annually over the next five years, increasing the value of that market up to a level of US\$ 3700 million in 2006 (Millennium Research Group [MRG], 2002).

In a latest study conducted by MarketsandMarkets Research (MarketsandMarkets Research, 2010), called Global Biomaterial Market (2010-2015), has been reported that currently the biomaterials market has crossed the US\$ 28 billion worldwide. This study indicates that the total global biomaterials market is expected to be worth US\$ 58.1 billion by 2014, growing at a Compound Annual Growth Rate (CAGR) of 15 % from 2009 to 2014. It also indicates that the U.S. market is the largest geographical segment for biomaterials; and is expected to be worth US\$ 22.8 billion by 2014 with a CAGR of 13.6% from 2009 to 2014. Europe is the second largest segment and is expected to reach US\$ 17.7 billion by 2014 with a CAGR of 14.6% and the Asian market size is estimated to increase at the highest CAGR of 18.2% in the same period. They mention that improvement in fabrication technology and new product development at competitive prices will be the key to future market growth.

Taking into account the above it is clear that the market opportunities for new developments in the area of biomaterials are very promising, there is no doubt that the

production of items and medical devices worldwide is growing rapidly, coupled with this is the fact that this is a highly competitive industry and has a relationship of high cost - low volume, reasons why it is important to develop new technologies to production, because given their high costs are often far from the reach of those most in need.

The manufacture of biomaterials and devices depends on both the application and the availability of raw materials, so if one that manufactures has the potential to provide raw materials and generate the appropriate technology, their production costs, and hence the consumer price, will be decrease.

An important fact to note is that biomedical engineering has enormous potential of development, and that to achieve significant progress is not always necessary to have a dominant technological position because, in many cases, innovation comes from the improvement and integration of already existing technologies.

Among the areas with greatest potential for development are found Bioceramics and Biomechanics, as well as Nano-biotechnology, Microsystems and Micro-Robotics, Biomedical Imaging, Bioinformatics, Medical Instrumentation and Telemedicine.

Given the broad scope in terms of existing types of biomaterials, in this chapter we focus only in the case of bioceramics and more specifically in the case of calcium phosphates, in their characteristics, their importance and methods of synthesis, as well as the various applications that take place at this time.

This chapter will show different progress made by our research group in the area; from the discussion on different methods of synthesis of calcium phosphates (particularly hydroxyapatite), using in some cases unconventional sources as precursors (such as eggshells, for example) as well as the obtaining of nanoparticles and other nanostructures of hydroxyapatite. Also the obtention of shaped articles made from hydroxyapatite-based composite materials with different forms to be used in the manufacture of artificial prosthesis and replacement of bone tissue as well as improvements in their mechanical properties will be shown.

2. Bone tissue

Bone is specialized tissue that characterizes vertebrates. Bones and teeth are living organisms made up of minerals and tissues, the latter consist of cells, fatty substances, natural polymers (such as polysaccharides, collagen and polyphosphates) and other substances. While the properties of bone tissue, and the proportions of the substances that form them, vary according to different parts of the skeleton, we can consider that contain about two thirds of his weight of inorganic material and a third of organic material in average. So, bone tissue is composed of a mineral phase that occupies about 69% of its total weight, about 9% water and about 22% of an organic matrix, which consists, in turn, mainly of collagen (90-96%).

The mineral phase is composed mainly of microscopic crystals of calcium phosphates, in which the hydroxyapatite (HAp), whose chemical formula is $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$, is the most important. Other mineral phases that are present in bone are dicalcium phosphate ($\text{Ca}_2\text{P}_2\text{O}_7$), dibasic calcium phosphate (DCP, CaHPO_4), tricalcium phosphate (TCP, $\text{Ca}_3(\text{PO}_4)_2$) and some amorphous phases of calcium phosphate. There are also other ions such as citrate ($\text{C}_6\text{H}_5\text{O}_7^{4-}$), carbonate (CO_3^{2-}), fluoride (F^-) and hydroxyl ions (OH^-), which can lead to subtle differences in bone microstructure. Finally, there are also some impurities such as magnesium and sodium, traces of chlorine and iron (Park, 1984).

Only both the HAp as well as the DCP are the calcium phosphate phases that are chemically stable at the temperature and pH of the human body (37 ° C and about 7, respectively) (Neuman & Neuman, 1958).

From a biological standpoint, the bones are defined as connective tissue and their function as a structural component of the human body are well known, serves to support, protect delicate parts and organs and provides a connection between the muscles, allowing movement.

From the standpoint of Materials Science, bone tissue is classified as a "composite", in which the mineral phase supports almost all the mechanical loads and the organic phase (collagen) serves as a binding material, also absorbs impacts, providing flexibility to the bone (Miller & Wray, 1971; Natali & Meroi, 1989).

In terms of the microstructure of the mineral phase, the bone can be classified as cancellous (or spongy) or as cortical, resulting in different mechanical properties.

The process of mineralization of bone tissue is very complex and remains largely unknown. The main constituents of the inorganic salts that make bone tissue are present, in the form of aqueous solutions, in the physiological fluid (blood plasma or extracellular fluid) coming from the blood vessels vascularized bone tissue. Under a chemical analysis, the bone has large amounts of complex groups of cations and anions, such as Ca^{2+} , PO_4^{3-} and CO_3^{2-} ; other ions present in lesser amounts are Mg^{2+} , Fe^{2+} , F^- y Cl^- . Due at the cellular exchange, are also found small traces of Na^+ and K^+ , ascorbic acid, citric acid and polysaccharides, as well as some heavy atoms, such as Ba^{2+} , Sr^{2+} y Pb^{2+} (Ravaglioli & Krajewski, 1992).

The phosphorus and calcium ions promote the formation of salts, primarily amorphous hydroxyapatite and calcium triphosphate, which are dispersed within the organic phase, while once crystallized, the inorganic phase is practically hydroxyapatite, which provides the mechanical features of the bones previously mentioned. Because of this, it is obvious the study of ceramics as potential bone substitutes, and in particular calcium phosphates such as hydroxyapatite.

3. Hydroxyapatite

The term "apatite" applies to a group of compounds (not only at calcium phosphates) with a general formula in the form $\text{M}_{10}(\text{XO}_4)_6\text{Z}_2$, where M^{2+} is a metal and species XO_4^{3-} and Z^- are anions. The particular name of each apatite depends on the elements or radicals M, X and Z. In these terms, hydroxyapatite (HAp) has the molecular structure of apatite, where M is calcium (Ca^{2+}), X is phosphorus (P^{5+}) and Z is the hydroxyl radical (OH^-). This is known as stoichiometric hydroxyapatite and its atomic ratio Ca/P is 1.67. Its chemical formula is $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$, with 39% by weight of Ca, 18.5% P and 3.38% of OH.

Hydroxyapatite crystallizes in a hexagonal system, although with some exception in a monoclinic system (Elliot et al., 1973; Kay et al., 1964). The system belongs to the hexagonal space group $\text{P6}_3/\text{m}$, with hexagonal rotational symmetry and a reflection plane and with cell parameters of $a=b=9.418 \text{ \AA}$ y $c=6.884 \text{ \AA}$. Figure 1 shows the unit cell of hydroxyapatite.

HAp structure is formed by a tetrahedral arrangement of phosphate (PO_4^{3-}), which constitute the "skeleton" of the unit cell. Two of the oxygens are aligned with the c axis and the other two are in a horizontal plane. Within the unit cell, phosphates are divided into two layers, with heights of 1/4 and 3/4, respectively, resulting in the formation of two types of channels along the c axis, denoted by A and B.

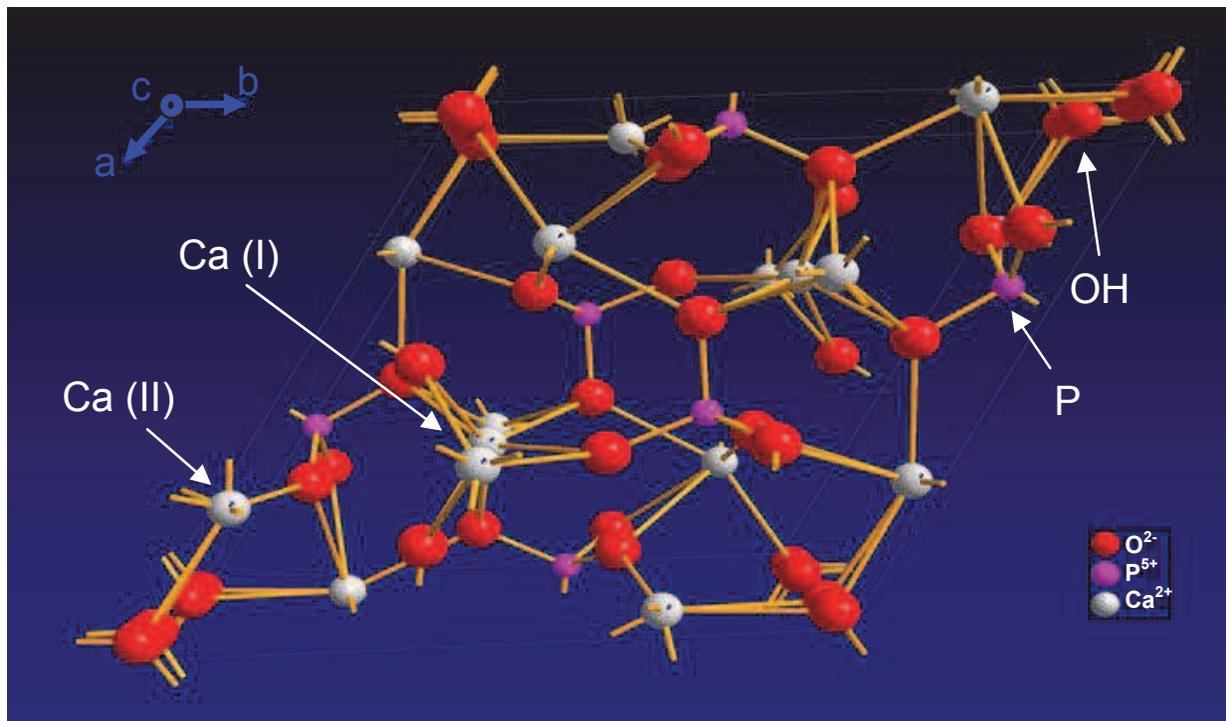


Fig. 1. Crystalline structure of hydroxyapatite.

The walls of channels A type are occupied by oxygen atoms of phosphate group and calcium ions, called calcium ions type II [Ca (II)], consisting of two equilateral triangles rotated 60 degrees relative to each other, at the heights of 1/4 and 3/4, respectively. Type B channels are occupied by other ions of calcium, called calcium ions type I [Ca (I)]. In each cell there are two such channels, each of which contains two calcium ions at heights 0 and 1/2. In the stoichiometric HAp, the centers of the channels type A are occupied by OH radicals, with alternating orientations.

The monoclinic form of HAp is more ordered and thermodynamically stable and is formed at high temperatures, but have never had evidence of its presence in calcified tissues.

Despite being taken to the stoichiometric hydroxyapatite as a model, it is noteworthy that hydroxyapatites produced biologically are much more complicated, they are not stoichiometric, have an atomic ratio Ca/P < 1.67 and does not contain only ions and radicals of the HAp but also traces of CO₃, Mg, Na, F and Cl. These amounts vary according at the specific type of tissue, which is related to the properties and bioactivity of it.

One aspect that is important to note is that, the closer the value of Ca/P to 1.67, the greater the stability of the material inside the human body as they tend to be inert, and on the other hand, if this value decreases (deficient HAp), the better the bioactivity.

Another aspect we must consider is the degree of crystallinity. It has been observed that the crystallinity in the tissues for the tooth enamel is very high, while in the cases corresponding to dentin and bone, it is very poor. This means that the reactivity depends on the degree of crystallinity, since the reactivity in dentin and bone is higher than in tooth enamel.

In order to manufacture articles made of hydroxyapatite, it is necessary to take into account, besides the above, that differences in structure and composition of apatites also depend on the different processing techniques, as well as temperature and atmosphere in which are made.

3.1 Quick review on synthesis methods

Different methods of preparation of HAp have been reported (Khon & Ducheyne, 1991; Park, 1984; Ravaglioli & Krajewski, 1992; Yoshimura & Suda, 1994), which may be classified as follows:

- i. Solid state synthesis at high temperatures.
- ii. Synthesis in aqueous phase.
- iii. Hydrothermal methods.
- iv. Growth from molten salts.
- v. Growth in gels.

Have also been reported other methods, including synthesis by alkoxides, sol-gel and chemical methods, and several procedures for obtaining coatings on various substrates, such as electrochemical deposition, plasma spray methods, etc (Chae et al., 1992; Dhert et al., 1991; Ducheyne et al., 1990).

The solid state synthesis at high temperatures has been generally used for processing ceramic powders and to study the stability of the phases.

Within the aqueous phase synthesis can found hydrolysis, acid-base reactions, in vitro culture, etc. For example, hydrolysis of brushite (DCPD, $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$) at temperatures between 40 and 60 °C and at pH of about 8 (Monma & Kamiya, 1987), or TCP hydrolysis under similar conditions, produce HAp powder. Another method of synthesis of HAp in aqueous phase includes ultrasonic acceleration of the reaction.

With regard to hydrothermal methods, they allow the preparation of well-crystallized powders with homogeneous composition, uniform and easily sintered. This is due to the effects of high temperatures and pressures that are applied to the aqueous solutions ($T > 100^\circ\text{C}$, $P > 1 \text{ atm}$) (Yoshimura & Suda, 1994).

The method of growth from molten salts has been used for the preparation of HAp monocrystals. These crystals grow from the molten phase (with a given composition) at high temperatures, but are severely deformed due to high temperature gradients that occur during growth.

The growth in gels is produced by immersing these in an aqueous system containing Ca^{2+} and PO_4^{3-} ions. The conditions under which it makes are similar to the physiological environment (pH close to 7 and temperatures around 37 °C), although there are reports in which they have used lower or higher temperatures (60 °C) (Castaño et al., 1996; Li, 1992, 1993; Rivera et al., 1997; Rivera-Muñoz et al., 2001, 2011)

Since wet chemistry methods are relatively easy to drive, HAp is synthesized by them often. In particular, since the reactions occur in any living being in aqueous solutions and at low temperatures, many experiments in the preparation of HAp have been performed to investigate the mechanisms of formation of calcium phosphates in vitro and in vivo.

3.2 Applications

Among the main areas of application of calcium phosphates, and particularly the HAp, we have all areas of orthopaedics and orthodontics, where they have to replace, partially or totally, parts of bone tissue.

In the first place we have the applications as filling material for bone. This is where there is greater application mainly because it is not necessary that the material supports high mechanical loads. The idea is to create physicochemical links, between ceramic and surrounding bone tissue, promoting their integration and growth of new tissue (Oonishi, 1991, 1992).

Another factor to consider is the phenomenon called osteoconductive, which occurs in materials with high affinity with bone tissue, which promote the formation of new tissue, but are also capable of directing their growth, depending on the structure they have. It is known that these materials should have high porosity (the order of hundreds of microns) to allow the development of bone within and across them. This property has been used both for filling bone as well as for cement with additives of HAp particles (Castaldini & Cavallini, 1985; denHollander et al., 1991).

Another important application is as a coating of metallic prostheses, which is done to give at the tissues a better suited and recognizable surface, given their characteristics and biocompatibility. Currently it has been working to improve the different techniques to achieve coatings with adequate stoichiometry and thickness. Among these techniques can find: physical and chemical deposition, electro-deposition, radiation treatments on surfaces, plasma spray, electrophoresis, etc. (Ducheyne et al., 1990; Sendax, 1992; Yoshimura & Suda, 1994).

Due to the reduced of both stability and bioactivity of HAp, a large number of applications have been developed in the field of maxillofacial surgery (Block & Kent, 1992; Jarcho, 1992; Kay, 1992; Trager et al., 1992). Although due to their reduced mechanical properties is primarily used in coatings for dental prostheses and metal plates, for the reconstruction of some cranial bones.

In all cases, these materials provide a surface suitable for cell adhesion, which by enzymatic action remains in a long term.

The *in vivo* behavior of calcium phosphate implants depends on several factors, among which the most important are the Ca/P ratio, the crystal structure and porosity. The physiological environment may also have a decisive influence on the biological response.

In the case of porous ceramics made of hydroxyapatite, implants are surrounded by connective tissue and osteoids, developing a network structure accompanied by some degree of collapse around the ceramic, unless osseointegration takes place at the implant site (Ravaglioli & Krajewski, 1992).

One of the most important aspects in the application of these materials is the interaction that may exist at the interface with living tissues, both in terms of toxicity, such as dissolution and the active roles that promote the formation of new bone (Ravaglioli & Krajewski, 1992; Park, 1984; Williams, 1991, 1994).

The development of new ceramics today must take into account the compromise between the above aspects, trying to improve the mechanical properties for a better performance of the implants *in vivo*, and also controlling the level of interaction between the material and surrounding tissue (Hench, 1991).

Taking into account that the devices manufactured with hydroxyapatite for biomedical applications have to withstand mechanical stress, friction and consequently wear, it is necessary to study their mechanical properties as well as its thermal behavior.

Some studies reported that the stoichiometry of HAp plays an important role in the mechanical properties; obtaining better results when the Ca/P ratio is between 1.60 and 1.67. In these studies it reported also that the mechanical strength decreases when the grain size exceeds the 2 microns (Royer, 1993).

Another important aspect is that these properties should be taken into account, both for the synthesis of HAp, as for processing. For this reason, become of vital importance the control of morphology and microstructure during the synthesis process of HAp, as well as the control of manufacture process of parts or objects with mechanical properties suitable for biomedical applications.

4. Some experimental experiences

Different methods of synthesis of hydroxyapatite have been used by our research group. In some cases innovations have been achieved by improving and integrating existing technologies.

As examples, we mention the following:

4.1 Synthesis of hydroxyapatite nanoparticles on silica gels

The method is based on the immersion of silica gels in an aqueous system containing Ca^{2+} and PO_4^{3-} ions. The conditions under which it takes place are similar to the physiological environment (pH close to 7 and temperatures around 37 °C) (Castaño et al., 1996; Li, 1992, 1993).

Silica gels were obtained by the standard method of hydrolysis and condensation of Tetraethyl Orthosilicate (TEOS) in an acidic environment and using different chemical additives for surface modification and control the contraction of the gels during drying process (Rivera et al., 1997; Rivera-Muñoz et al., 2001, 2011).

Chemical additives that were used are monoethylene glycol (MEG), diethylene glycol (DEG) and glycerin. An important aspect is that the catalyst was chosen by considering the application of those gels, i.e. it was used hydrofluoric acid (HF) since the fluoride ion replaces some of the OH^- radicals in the crystal structure of hydroxyapatite, where their positions are not very stable, but since the fluoride ion occupies fixed positions, its chemical stability increases. Besides, it was found that the time of gelation decreases considerably, being the order of minutes, which benefits at the method of synthesis. It is also known that the particle size and pore size is very uniform when the process is carried out under acidic conditions.

Thus, a solution was prepared as a basis for the synthesis of all the gels, dissolved 7 ml of TEOS (Aldrich Chemical Co., analytical grade) in 11 ml of ethanol (EtOH) (Baker Analyzed, reagent grade) and 1.5 ml distilled water under stirring. In this manner, the resulting solution has a composition TEOS: H₂O: EtOH of 1:4:6. At this point, start the hydrolysis reaction and to accelerate the process was added 2 ml of hydrofluoric acid (HF) (Baker Analyzed, reagent grade) to 40% by weight and the additive. Under these conditions, the gelation occurs in about 7 minutes.

In addition, different chemical additives monoethylene glycol (MEG, J. T. Baker), diethylene glycol (DEG, Fluka) and glycerin (J. T. Baker, 99.8%) were used. The optimal concentrations correspond to 35 vol% MEG, 35 vol% DEG and 10 vol% glycerine with respect to the ethanol. After one week of slow drying, silica gels were obtained.

It is noteworthy that the whole process was carried out at room temperature, which has implications for energy savings.

After the drying process of silica gels, Simulated Body Fluid (SBF) was prepared by dissolving NaCl, NaHCO₃, KCl, K₂HPO₄, MgCl₂•6H₂O, CaCl₂•2H₂O and Na₂SO₄ in deionized water and finally it has ion concentrations nearly equal to those in human blood plasma (Rivera et al., 1997; Rivera-Muñoz et al., 2001, 2011). The growth of hydroxyapatite nanoparticles was promoted by immersing small specimens of silica gels in the SBF at 37°C for six weeks. The SBF was replaced every week to keep constant the Ca^{2+} and P^{+5} ion concentrations.

Samples obtained by this method were characterized to confirm the presence of HAp. Representative results of Energy Dispersive Spectroscopy (EDS), Fourier Transform Infra

red Spectroscopy (FTIR) and X-ray Diffraction (XRD) techniques are showed in Figures 2, 3 and 4, respectively.

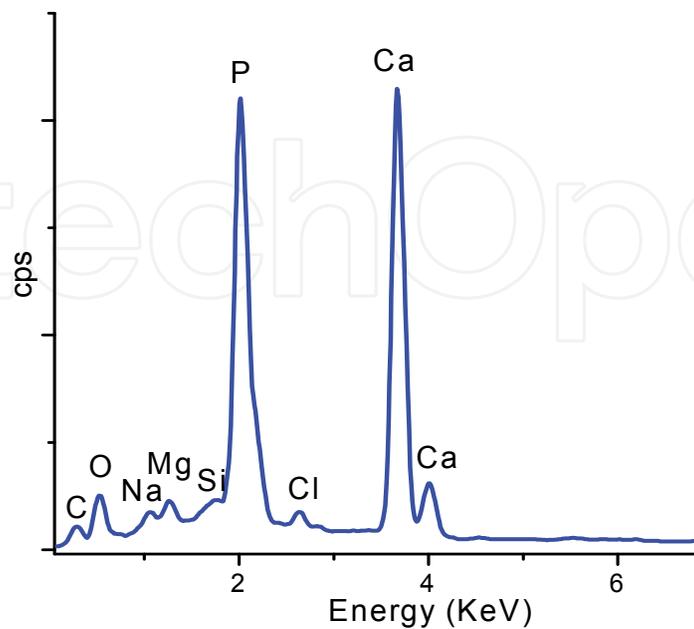


Fig. 2. Determination of the chemical species present in the samples by elemental analysis using energy dispersion spectroscopy (EDS).

Elementary analysis (EDS) results show an average Ca/P atomic ratio of 1.6 and it can be observed the presence of other elementary components in a smaller scale.

A typical Infra Red spectroscopy (FTIR) analysis result is showed in figure 3. Bands at 560-640, 963 and 1028 to 1110 cm^{-1} , correspond to the phosphate group (PO_4^{3-}), and the band at

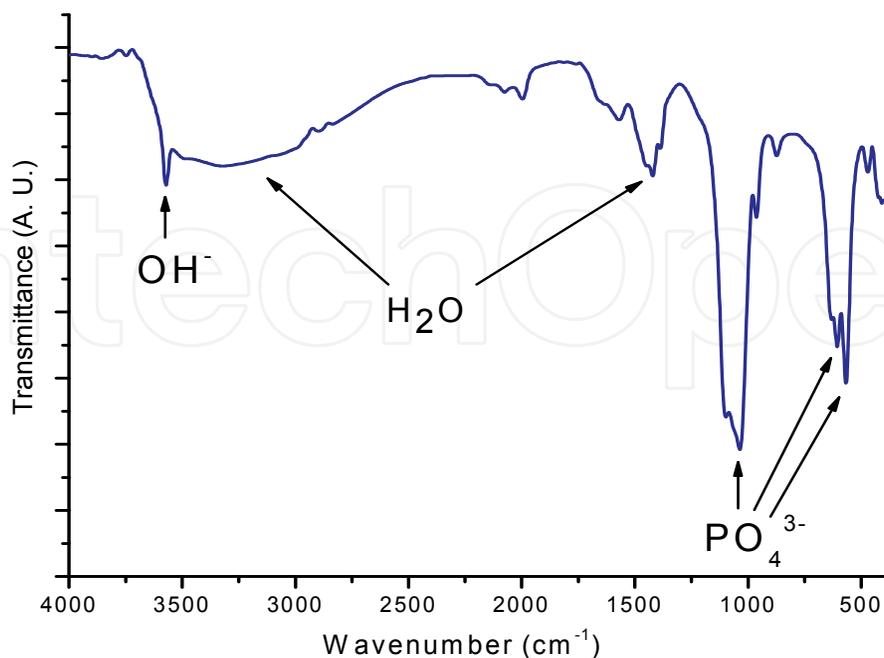


Fig. 3. FTIR spectrum of a sample of silica gel with glycerin extracted from PHS after six weeks. It shows the identification of characteristic bands corresponding to hydroxyapatite.

3572 cm^{-1} corresponds to structural OH^- group; these are typical bands corresponding to the HAp spectrum. These assignments are in agreement with those reported in literature for that phase (Panda et al., 2003).

Figure 4 corresponds to an X - ray powder diffractogram, taken to a sample of silica gel extracted from SBF after six weeks. Reflections corresponding to hydroxyapatite structure are showed and they have been identified by the PDF (JCPDS) file # 09-0432; it also appears a broad peak due to the typical sign of an amorphous material (the silica gel) at an angle 2θ about 22° .

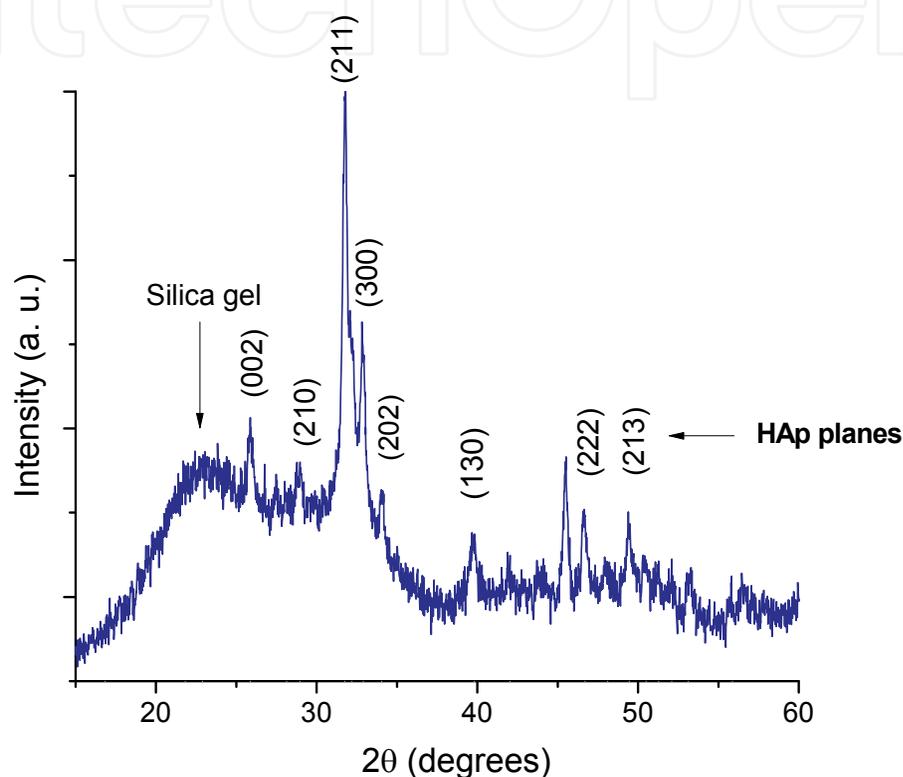


Fig. 4. X-ray diffraction pattern of a silica gel sample removed from PHS after six weeks. It shows the identification of crystalline HAp reflections.

Thus, the results of EDS, FTIR and XRD techniques confirm the presence of hydroxyapatite on the surface of silica gels.

Scanning Electron Micrograph of the surface of silica gel taken after six weeks of soaking into Simulated Body Fluid at 37°C is showed in figure 5. As it can be observed, HAp nanoparticles grow on the surface of the gel. Those nanoparticles present a spherical-like shape with an average diameter of 800 nm. They can also be observed a few crystals of NaCl and the surface of silica gels.

A more detailed image, as in Fig. 6, shows that those particles are not compact spheres but formed by smaller particles. Thus, the particle size must be adjusted depending on the scale and resolution of the measure instrument. This is an important feature, typical of the structures with fractal geometry.

The presence of those HAp nanoparticles over the surface of silica gels can be explained as follows: it carries out a process of heterogeneous nucleation due to the large surface

area of silica gel as well as abundant and dispersed nucleating centers in the SBF due to the dissolved salts; this process occurs mainly in the liquid and to a lesser extent on the gel surface and this could be attributed to the presence of chemical additives used in the sol-gel process since they affect the liquid-to-solid interface by reducing the interfacial energy as well as stabilizing the gel structure (Brice, 1973; Brinker & Scherer, 1990).

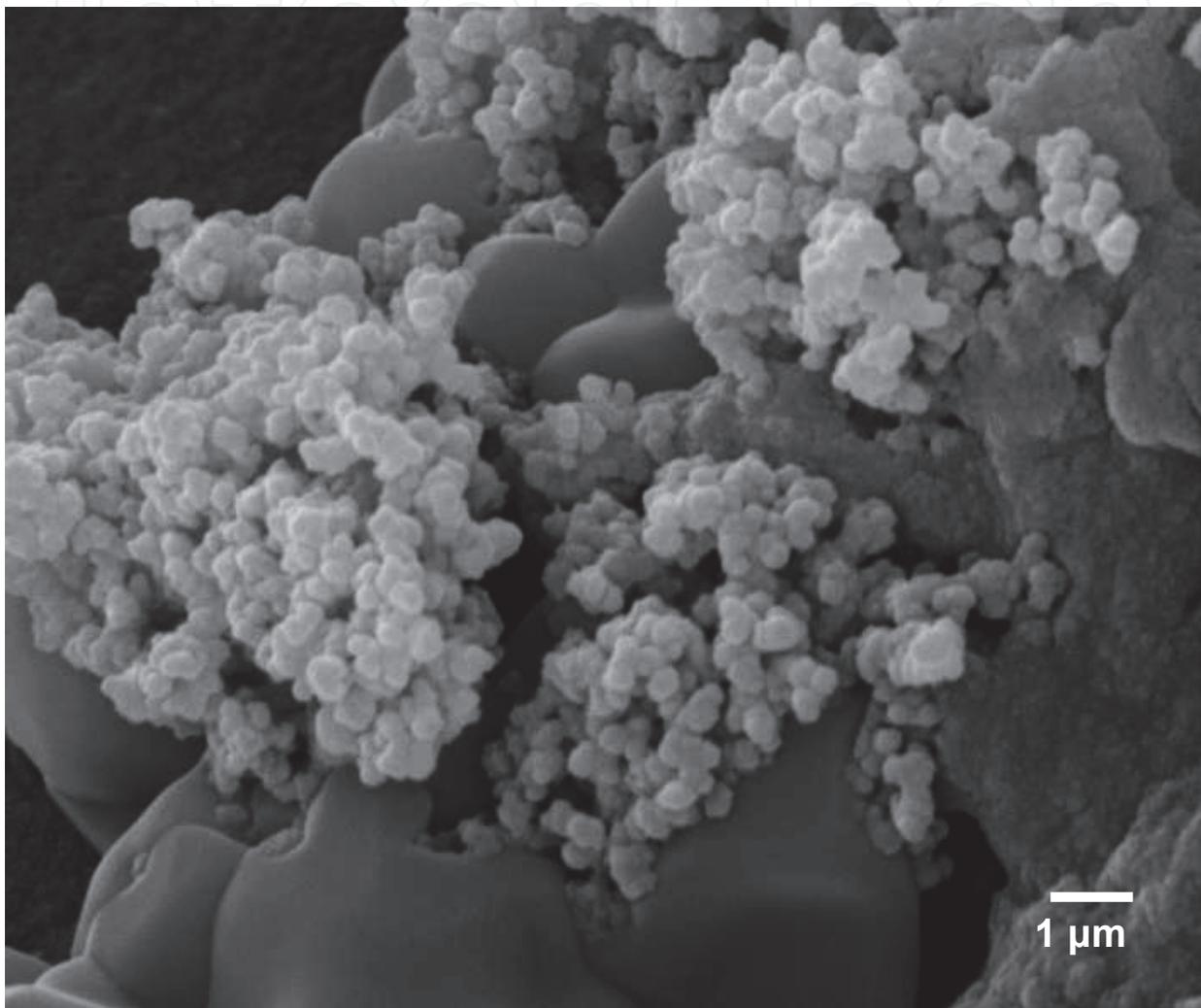


Fig. 5. SEM micrograph of HAp nanoparticles grown on the surface of silica gels.

Finally, the growth of HAp nanoparticles could be carried through a diffusion limited aggregation process (DLA).

In summary, the size and morphology of HAp nanoparticles can be controlled by using chemical additives during the process of obtaining silica gels, as these modify the surface energy of the system, resulting in the nucleation of HAp into the SBF, while growth occurs on the surface of silica gels.

Moreover, since many applications of biomaterials depend, among other factors, of the control of morphology, this work may lead to a wide range of applications in modern biotechnology processes.

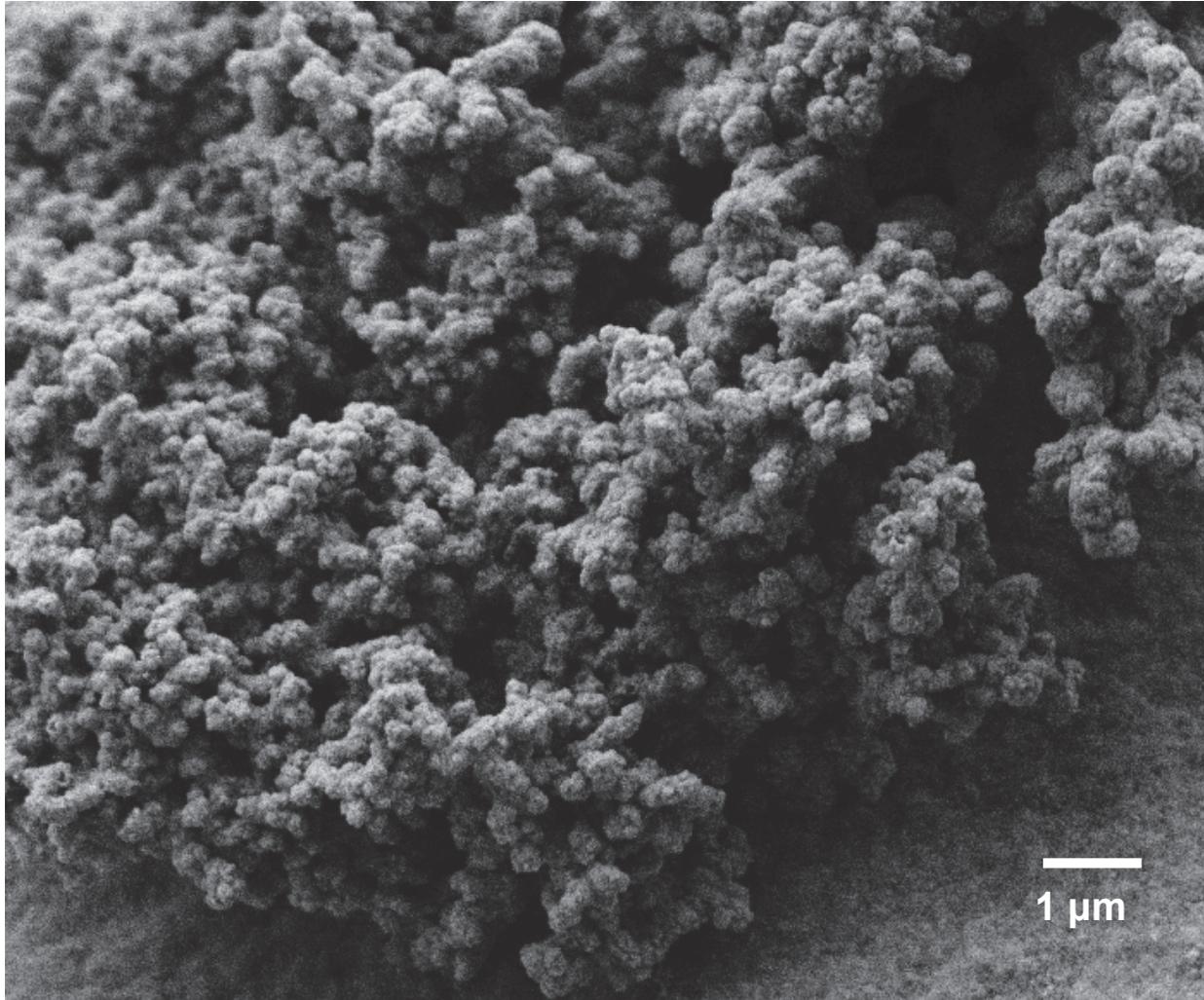


Fig. 6. SEM micrograph of HAp nanoparticles. There is evidence of a texture at an even smaller scale.

4.2 Synthesis of hydroxyapatite from eggshell

An important aspect in the development of methods of synthesis of hydroxyapatite is the use of raw materials from unconventional sources. Here, it is reported the use of eggshells as a calcium source for the synthesis of HAp.

It is estimated that the world's egg production was approximately 6.37×10^7 tons in 2010 (Global poultry trends, 2010). Taking into account that the shell occupies about 11% of the weight of each egg, the amount of eggshells produced in the world in the last year ascends to about 7×10^6 ton.

This material is basically useless after the production of eggs and egg derivatives. Moreover, in many cases, once the egg is used, manufacturers store waste and are then discarded so that it contributes to environmental pollution due to microbial action as a result of the decomposition of organic compounds present in these wastes.

In the best case scenario, the eggshells are used as part of the diet of some animals (chickens) or as fertilizer, although in these cases the benefits are scarce.

This underscores the importance of using these eggshells as a calcium source for the obtention of a useful material, giving an added value to both the material obtained, as well as to the waste coming from human daily activity.

As mentioned, eggshells represent the 11% of the total weight of the egg and it is composed by crystals of calcium carbonate (94%), organic matter (4%), calcium phosphate (1%) and magnesium carbonate (1%).

Figure 7 (a) corresponds to a Scanning Electron Micrograph of the cross section of an eggshell. It shows the spatial arrangement of crystals of calcium carbonate (CaCO_3) and its size. It is also noted, in figure 7 (b), that these crystals grow with a preferential crystal orientation in the direction corresponding to the c axis of the unit cell of CaCO_3 , perpendicular to the surface of the shell; this is because the structure is more stable mechanically in that direction.

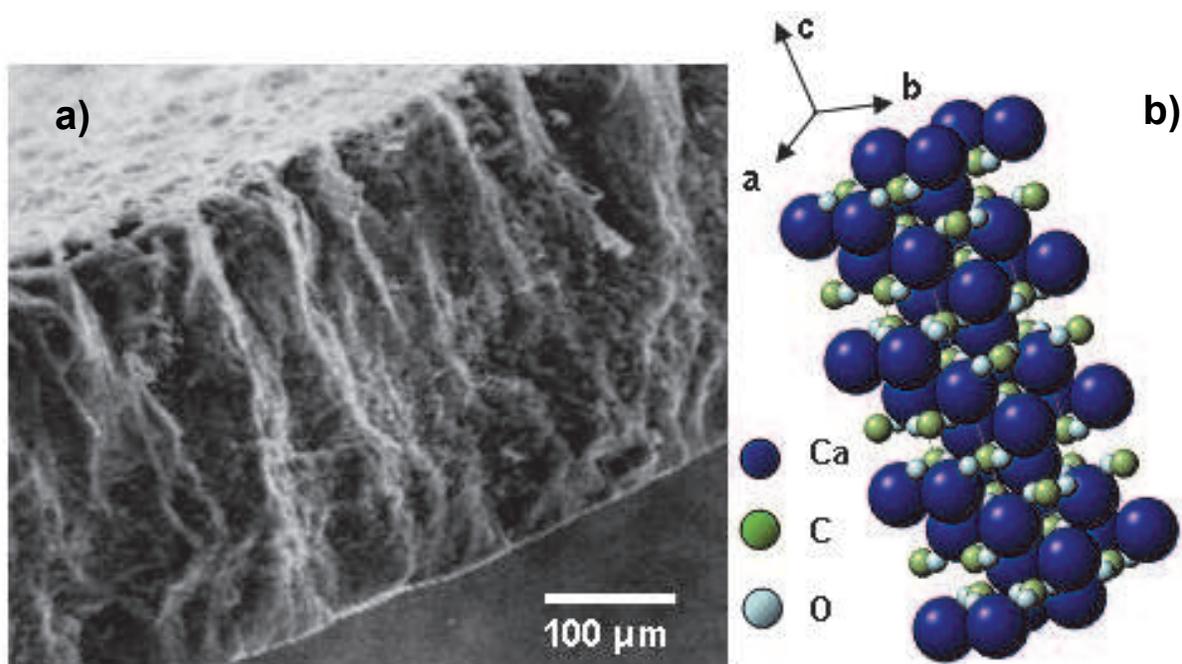


Fig. 7. a) SEM image of the cross section of an eggshell. b) Unit cell of CaCO_3

The synthesis method is described in previous works (Rivera et al., 1999; Rivera-Muñoz et al., 2003) and can be summarized as follows: after collecting and mechanically cleaned eggshells, they were subjected to a heat treatment in two stages: the first consisted of heating at a rate of 5 °C per minute to reach a temperature of 450 °C, maintained for 2 hours. At this stage eliminates the organic phase that could be present in the sample. The second stage consisted of heating the samples to reach 900 °C at a rate of 0.5 °C per minute and maintaining this temperature for 2 hours. At this temperature the calcium carbonate transform into calcium oxide through the freeing carbon dioxide according to the following equation:



This was confirmed by X - ray Diffraction analysis (DRX).

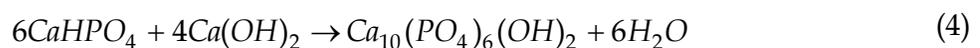
The concentration of reagents was calculated taking into account that the Ca/P in the stoichiometric hydroxyapatite is 1.67, so the CaO was transformed into HAp by reaction

with tricalcium phosphate (TCP, $\text{Ca}_3(\text{PO}_4)_2$). The reaction was carried out at 1100 °C for 3 hours in a moist atmosphere using different heating rates to have control of the species obtained.

In the first place, when the calcium oxide is mixed with water, a reaction between CaO and H_2O takes place to obtain $\text{Ca}(\text{OH})_2$. Therefore, this phase is present as initial reactant, as well as during reaction and then hydroxyapatite can be obtained according to the following equation:



At end of process, HAp is obtained and small amounts of monetite (CaHPO_4) and unreacted CaO. This was confirmed by performing X - ray Diffraction analysis (DRX). The relative amount of HAp obtained can be controlled depending on the heating rate during heat treatment and the presence of monetite as an impurity can be explained by the simultaneous occurrence of the following reactions:



In summary, it is possible to obtain hydroxyapatite from eggshell as unconventional source of raw material. It is also possible to control the relative amount of different calcium phosphate species by controlling the heating rate during the reaction.

Finally, it is important to highlight the fact that it was used a waste material to produce a useful material with great potential for the biomedical industry, adding a high value to the process described and a valuable alternative, both in egg product-derived industry (in waste management and also by reducing environmental pollution), as well as in the industry of biomaterials.

4.3 Molding of objects with different shapes and improvement of their mechanical properties

As previously mentioned, in addition to the development and improvement of different methods of synthesis of hydroxyapatite, is important to develop new processing methods to obtain HAp-based objects with specific shapes for use as potential bone tissue substitutes or in the manufacturing of prostheses.

In addition, once shaped, these objects must have adequate mechanical strength according to the appropriate application, so that it becomes necessary to develop innovative technologies for improving their mechanical properties.

There are different methods in the processing of ceramics, which can be divided in general into three stages: a mixing step, a step of cold-molding and consolidation phase. Within the cold-molding step it can be include pressure molding, slip casting, electrophoresis, extrusion and injection, among others.

One method, called "gelcasting", has been developed to obtain objects with almost any geometry when working at low temperatures and high load of solids (up to 60%), with low amounts of solvents and polymers (Omatete et al., 1991).

The gelcasting method is based on the synthesis of ideas from the traditional processing of ceramics and polymer chemistry. The basis of the process is the use of a monomeric solution, which can be polymerized *in-situ* to form a strong crosslinked structure in the form

of gel, the monomeric solution provides a low viscosity vehicle which supports the ceramic powders and allows their handling. The crosslinking provides a mechanism for permanent immobilization of the ceramic mixture into the desired shape after being poured into a mold. Because the vehicle consisting of monomer solution to form the gel contains only 10 to 20% by weight of polymer, the solvent can be easily removed from the structure through a drying process and the crosslinked polymer can not migrate with him. The part corresponding to polymer can then be removed by burning at temperatures between 400 and 900 °C, depending on the product used, and finally, the obtained green body is subjected to sintering and densification process by various heat treatments.

Gelcasting method has several advantages over the traditional (such as slipcasting): the process is faster in green body formation, the polymerization can be performed *in situ*, the molds used may be metal, glass, plastic or wax and need not be scrupulously cleaned before reuse, and finally, the green body obtained is consistent enough to be easily handled.

The essential components of gelcasting method are: ceramic powders, organic monomers, a polymerization initiator, a dispersant and a solvent. With ceramic powders, solvent, dispersant and the binder is prepared a mixture of liquid consistency. The binder usually consists of organic monomers, the initiator or catalyst is added to the mixture before the molding stage. Then the mixture is poured into the mold and it takes place the gelation process, after which the ceramic keeps the final shape. At this point is obtained a green body and the solvent is removed by drying. The plastifier is then burned and finally the ceramic is subjected to a process of densification by thermal treatment.

The principal modifications to the gelcasting method, which led to the "modified gelcasting process", reported by our research group (Rivera-Muñoz et al., 2001b, 2003, 2007) consists of: 1) The use of polymers to form an interpenetrated network, that supports HAp ceramic particles and takes the form of the mold, and 2) The introduction of a pore-forming agent to promote controlled porosity, without changing the structural characteristics of the finally molded article.

Modified gelcasting process (MGCP), described in previous works (Rivera-Muñoz et al., 2001b, 2003, 2007) can be summarized in figure 8.

As shown in figure 9, it can be molded objects with almost any kind of shape through this method. In fact, we have previously reported the production of porous HAp spheres for use as prosthetic eyeball (Rivera-Muñoz et al., 2001b).

Once obtained porous HAp objects, molded with different shapes, as mentioned in section 3.2., it is vitally important to have control of manufacture processes of parts or objects so they have mechanical properties suitable for biomedical applications.

According to the previously mentioned, from the standpoint of Materials Science, bone tissue is classified as a "composite material", in which the mineral phase supports almost all the mechanical loads and the organic phase (collagen) serves as a binding material, also absorbs impacts, providing flexibility to the bone. So we introduce an organic phase to the system to mimic the conformation of actual bone tissue.

With the inclusion of the second phase was obtained an organic-inorganic composite material in which the inorganic part form a porous structure (made of HAp), while the organic phase is chemically attached to it, forming a flexible matrix.

Figure 10 corresponds to a SEM micrograph of a porous sample, made of HAp through the MGC process. Micro (and interconnected) porosity can be observed, as well as the sintered HAp particles used to obtain the molded object.

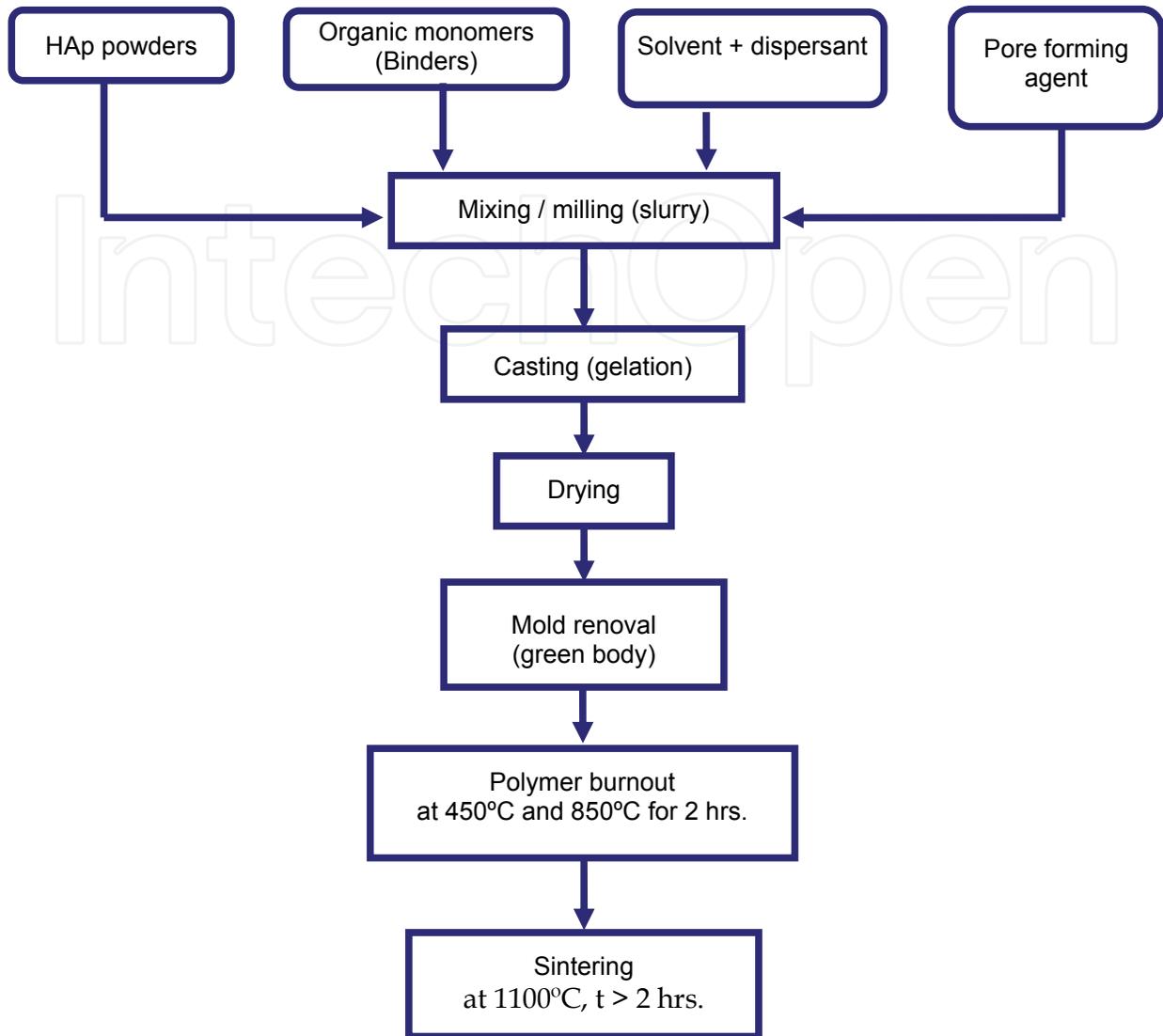


Fig. 8. Modified Gelcasting Process (MGCP) to produce controlled pore size HAp objects.

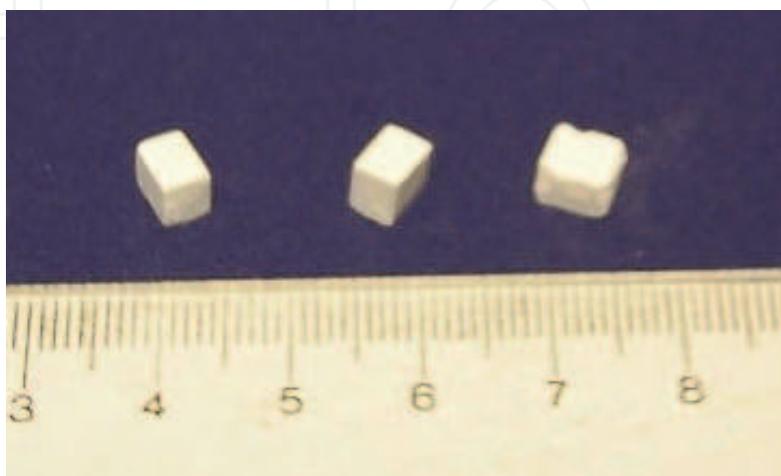


Fig. 9. Molded objects of porous HAp obtained by MGCP (Scale in cm).

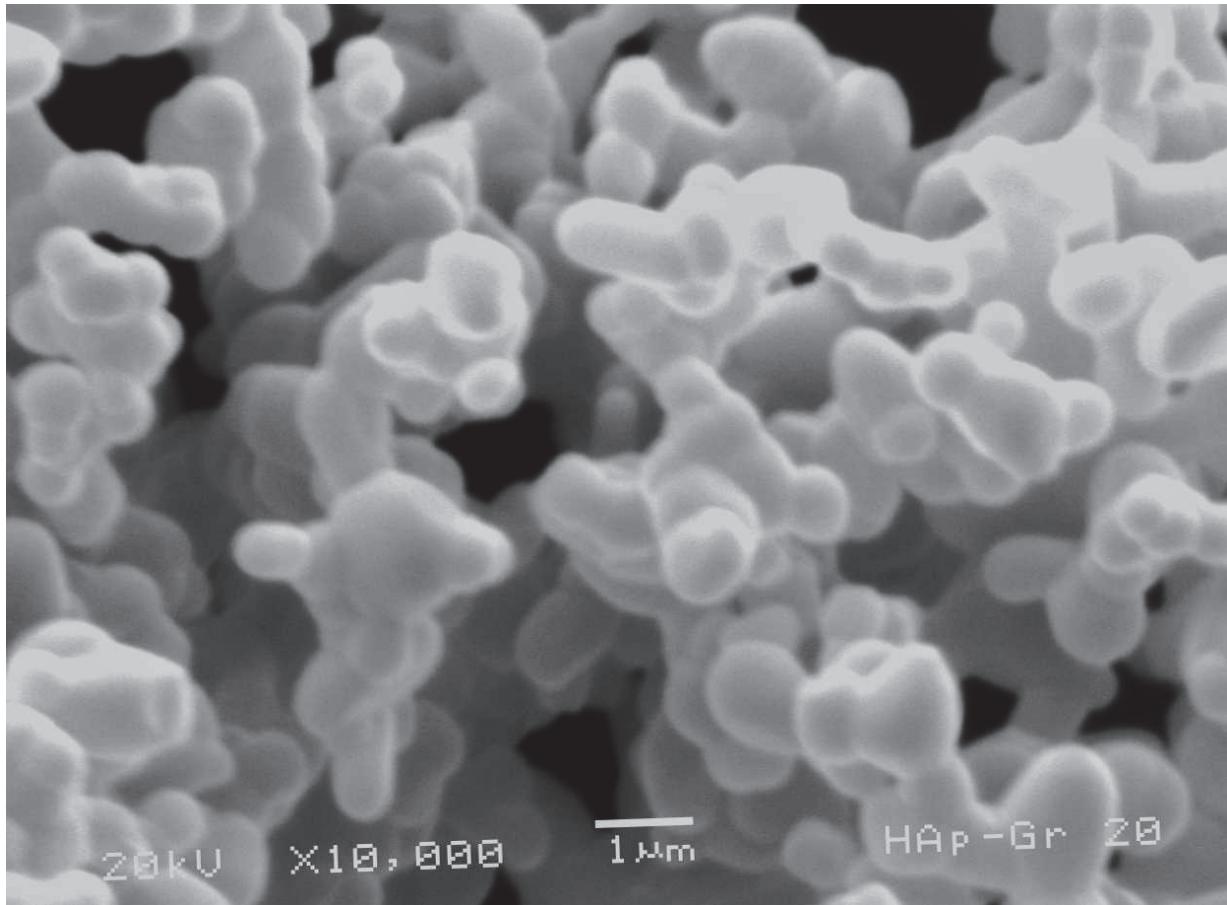


Fig. 10. Scanning Electron Micrograph of a porous sample, made from HAp powders through the Modified Gelcasting Process.

Gelatin was used as the organic phase, primarily because of its similarity to the structure and chemical composition of collagen (as derived from the latter), also due to its ease of handling and processing and, finally, because it is economically affordable.

Figure 11 shows a SEM micrograph of a sample taken after addition of the organic phase. It is observed the integration of the two phases to form an organic-inorganic composite material based on hydroxyapatite.

It is noteworthy that the inorganic structure formed by interconnected pores is connected to one another through the organic phase, showing a cellular-type structure, as in the case of a Voronoi foam, where there are interconnected pores of different sizes in three dimensions.

Once obtained the composite material, it was carried out mechanical testing in compression to study the mechanical behavior of the samples. It was found that the presence of the organic phase significantly improve the compressive strength of the samples. The improvement in these properties was of two orders of magnitude, which indicates a synergistic behavior between the two phases.

Moreover, Figure 12 shows a graph of stress-strain corresponding to a typical result of mechanical compression test performed on composite materials. It notes that the behavior is consistent with a typical non-linear elastic behavior showed by cellular materials and agrees completely with the observations of SEM images showed in figure 11.

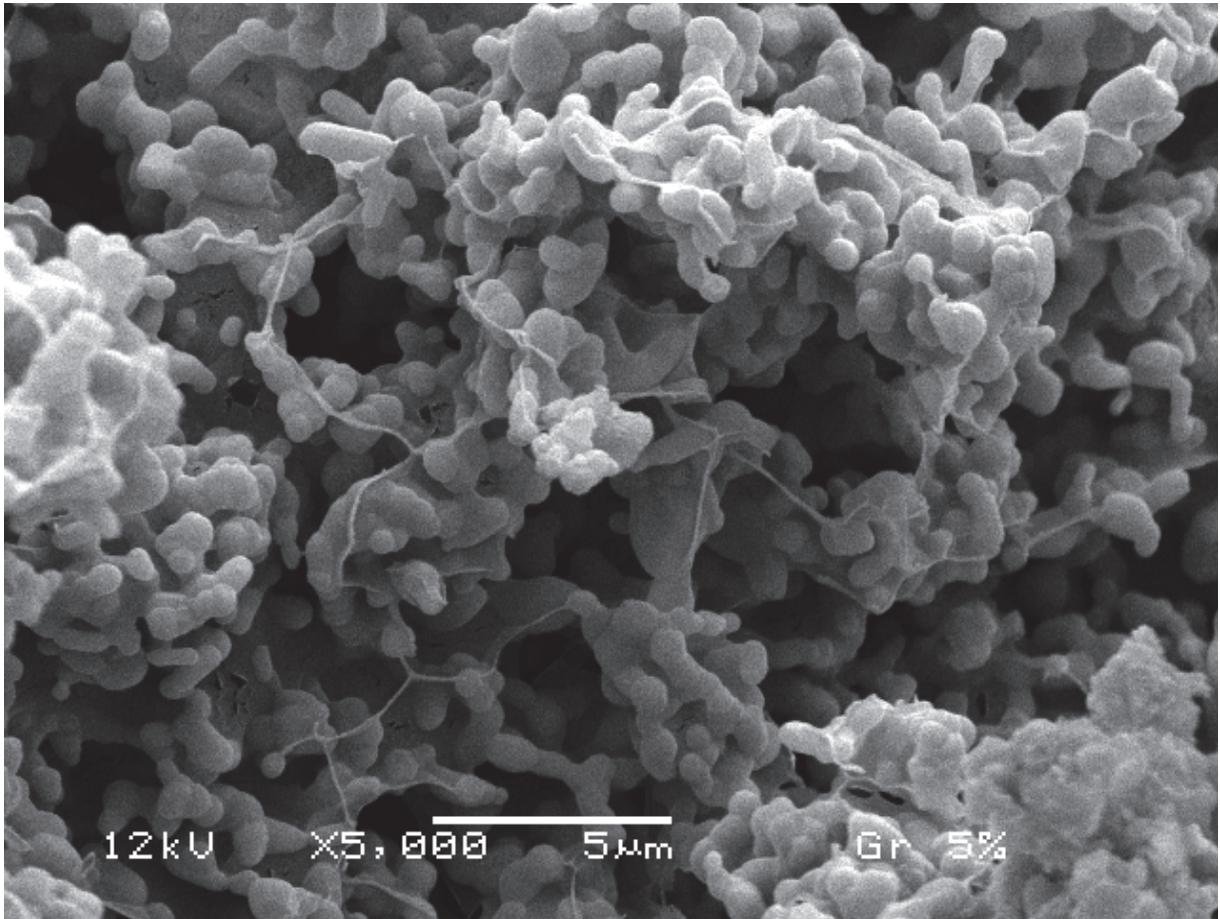


Fig. 11. Scanning Electron Micrograph of a HAp-based, organic-inorganic composite material.

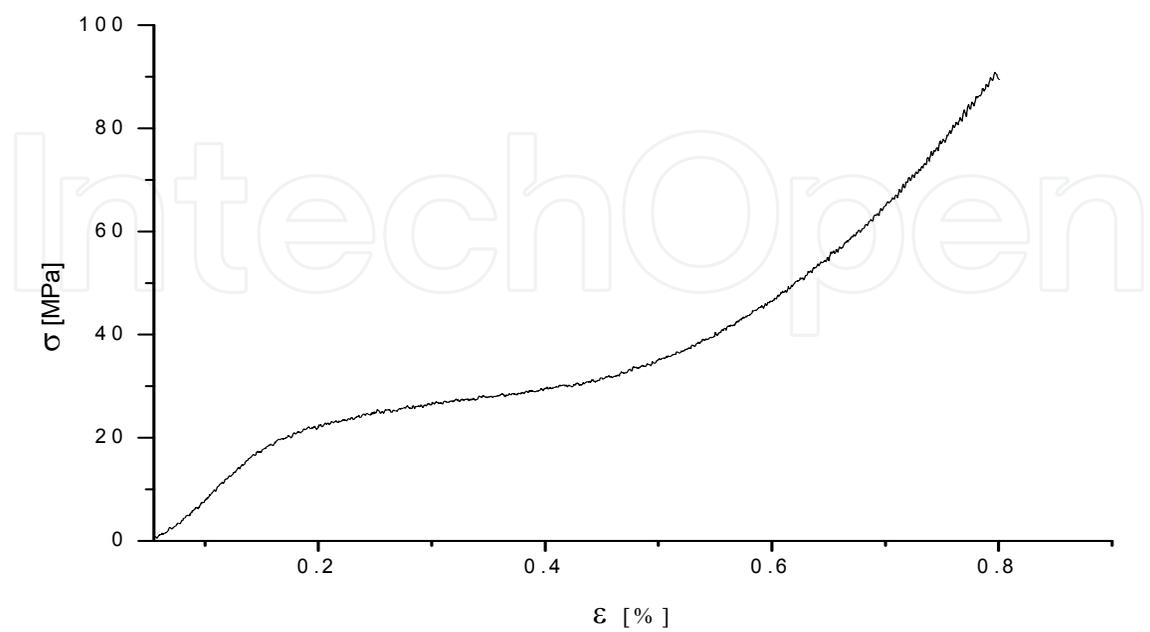


Fig. 12. Typical non-linear elastic behavior of HAp-based, organic-inorganic composites.

Mechanical characterization was performed on samples after MGCP as well as on composite samples with different gelatin concentrations. A dramatic improvement of two magnitude order in compressive strength can be observed in figure 13.

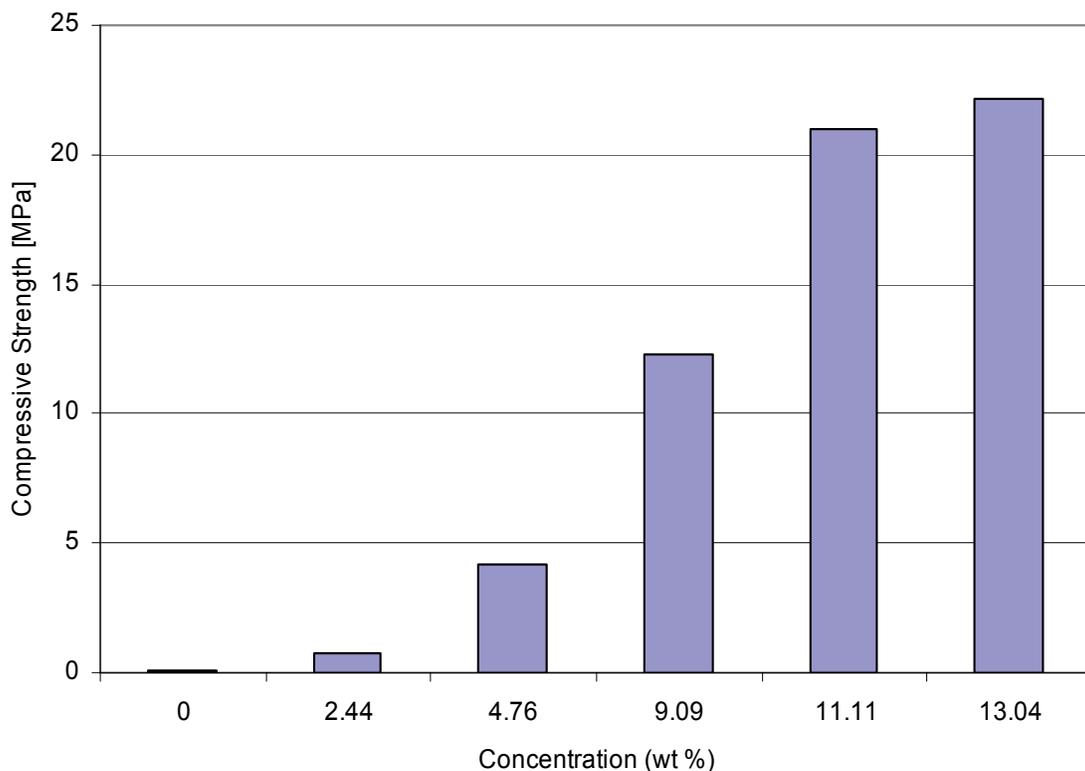


Fig. 13. Improvement of compressive strength with organic phase concentration.

In fact, compressive strength increases with increasing the concentration of the organic phase up to a maximum limit. At that point, the mechanical strength of the composite material is almost 200 times greater than that of the porous material obtained through the MGCP, in which no was added the organic phase. This again is due to a synergistic behavior between the two phases, as occurs in natural bone tissue.

Finally, given some published results on the mechanical strength of natural bone samples, performed under the same conditions as in our samples, we observed: The values reported by Ravaglioli & Krajewski (Ravaglioli & Krajewski, 1992) are: for the compressive strength of trabecular or cancellous bone, of 5.62 ± 2.37 MPa, for cancellous-cortical bone of 15.1 ± 12.6 MPa, while for the cortical bone of 171.67 ± 17.53 MPa. In the case of our samples, they showed a maximum compressive strength of 22.2 ± 5.9 MPa, ie about four times higher than for the trabecular bone and in the same order than the cancellous-cortical bone.

This is a remarkable result, since it opens the door to important applications because we are at a point where it is possible the manufacture of hydroxyapatite-based porous objects, with different shapes using an innovation developed by our group, besides the control, to a large extent, of its mechanical properties. Moreover, the results show that both the structure and mechanical behavior of these composites resemble, to some extent, to the natural bone tissue.

5. Summary

Hydroxyapatite nanoparticles were synthesized on silica gel using various chemical additives introduced during the sol-gel process. Chemical additives used affect the solid-to-liquid interface by reducing the interfacial energy and by stabilizing the structure of the gel. This suggests that the nucleation of hydroxyapatite occurs mainly in the SBF and that growth occurs through a diffusion limited aggregation process (DLA) on the surface of silica gel. By modifying the concentration and type of additive is possible to control both the morphology and the size of the nanoparticles. It was found that these particles show spherical-like shapes, always within the nanometric scale and through smaller-scale observations, shows that consist of even smaller particles, suggesting a fractal-like behavior.

Since many applications of biomaterials depends, among other factors, of the control of morphology, this work may lead to a wide range of applications in modern biotechnology processes, as in the area of dentistry, orthopedics etc., and which highlights the originality of this method, developed in our labs.

In other hand, hydroxyapatite was synthesized successfully by solid state reactions and high temperatures, using eggshells as a calcium source. It was established the optimum conditions for obtaining that calcium phosphate, such as concentration of reagents, reaction temperatures and times, as well as appropriate heating rates in the thermal treatments.

It is important to highlight the fact that it was used a waste material to produce a useful material with great potential for the biomedical industry, adding a high value to the process described and a valuable alternative, both in egg product-derived industry (in waste management and also by reducing environmental pollution), as well as in the industry of biomaterials.

Finally, it was established a procedure for obtaining organic-inorganic composites based on hydroxyapatite with controlled porosity and adequate mechanical strength for use in the manufacture of bioceramics. This innovation was the result of the modification of an existing technology which has been applied to other materials. It was integrated an organic phase so that the composite material obtained has characteristics similar to natural bone tissue: is composed of an inorganic phase consisting of a three-dimensional interconnected pore structure (which supports most of the mechanical loads) embedded in an organic matrix (which gives flexibility to the structure and which also absorbs mechanical energy), showing a synergistic behavior between both phases.

In summary, it has been shown different progress made by our research group in the area of bioceramics; from the discussion on different methods of synthesis of hydroxyapatite, using in some cases unconventional sources as precursors (such as eggshells) as well as the obtaining of nanoparticles of hydroxyapatite. Also the obtention of shaped articles with different forms, made from hydroxyapatite-based composite materials, to be used in the manufacture of artificial prosthesis and replacement of bone tissue as well as improvements in their mechanical properties.

Also important is the fact that any improvement, innovation or development in the area of biomaterials has a positive impact, both from the standpoint of basic science and from the point of view of biomedical applications. That is, there are many beneficiaries: those who are involved in basic science, those who are engaged to research in biotechnology or biomedical

engineering, but also the industry and ultimately the greatest beneficiaries will be patients who will be the ones that wear these materials.

6. Acknowledgment

Author wants to thank Dr. Beatríz Millán Malo for technical assistance in X-ray Diffractometry, M. Q. Alicia del Real López for technical assistance in Scanning Electron Microscopy and Dr. Genoveva Hernández Padrón for technical assistance in Infrared Spectroscopy. Also acknowledges the help of Claudia Medina Ríos and Alejandra Cortez Pérez, students of Biotechnology at the Universidad Autónoma de Querétaro, México. Finally, author thanks the financial support of Project DGAPA-UNAM PAPIITIN107311-3.

7. References

- Block, M.S. & Kent, J.N. (1992). "Prospective review of integral implants", In: *The dental clinics of north america, Hydroxyapatite-coated implants*, Vol. 36, No. 1. V.I. Sendax (Ed.), W.B. Saunders Co., Philadelphia, USA.
- Brice, C. (1973). *The growth of crystals from liquids, Selected Topics in Solid State Physics*, Vol. XII. North-Holland Publishing Co., USA.
- Brinker, C. J. & Scherer, G. W. (1990). *Sol-Gel Science: The Physics and Chemistry of Sol-Gel Processing*, Academic Press, Boston, USA.
- Castaldini, A. & Cavallini, A. (1985). "Setting properties of bone cement with added synthetic hydroxyapatite", *Biomaterials*, 6, 50-56.
- Castaño, V.M., Suárez, D., Rivera, E., Estévez, M. and Hernández, J.C. (1996). "Growth of hydroxyapatite on silica gels", *Ceram. Trans.*, 53, 49-56.
- Chae, J.C., Collier, J.P., Mayor, M.B., Suprenant, V.A. and Dauphinais, L.A. (1992). "Enhanced ingrowth of porous-coated coccr implants plasma-sprayed with ticalcium phosphate", *J. Biomed. Mater. Res.*, 26, 93-101.
- den Hollander, W., Patka, P., Klein, C.P.A.T. and Heidendal, G.A.K. (1991). "Macroporous calcium phosphate ceramics for bone substitution: a tracer study on biodegradation with ⁴⁵Ca tracer", *Biomaterials*, 12, 569-573.
- Dhert, W.J.A., Klein, C.P.A.T., Wolke, J.G.C., van der Velde, E.A. and deGroot, K. (1991). "A mechanical investigation of fluorapatite, magnesium whitlockite and hydroxyapatite plasma-sprayed coatings in goats", *J. of Biomed. Mat. Res.*, 25, 1183-1200.
- Ducheyne, P., Beight, J., Cuckler, J., Evans, B. and Radin, S. (1990). "Effect of calcium phosphate coating characteristics on early post-operative bone tissue ingrowth", *Bimaterials*, 11, 531-540.
- Elliot, J.C., Mackie, P.E. and Young, R.A. (1973). "Monoclinic hydroxyapatite", *Science*, 180: 1055-1057.
- Global poultry trends, 2010 (2010), *The poultry site*, www.thepoultrysite.com
- Hench, L.L. (1991). Bioceramics; from concept to clinic. *J. Am. Ceram. Soc.*, 74: 1487-1510.
- Jarcho, M. (1992). "Retrospective Analysis of hydroxyapatite development for oral implant applications", In: *The dental clinics of north america, Hydroxyapatite-coated*

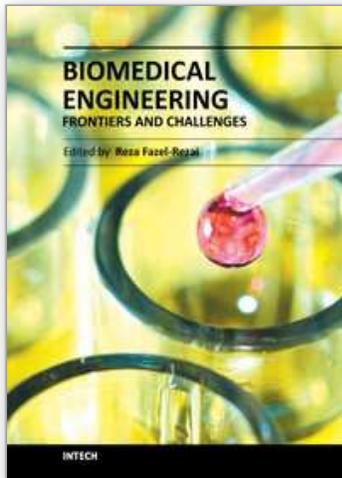
- implants*, Vol. 36, No. 1. V.I. Sendax (Ed.), W.B. Saunders Co., Philadelphia, USA.
- Kay, J.F. (1992). "Calcium phosphate coatings for dental implants: Current status and future potential", In: *The dental clinics of north america, Hydroxyapatite-coated implants*, Vol. 36, No. 1. V.I. Sendax (Ed.), W.B. Saunders Co., Philadelphia, USA.
- Kay, M.I., Young, R.A. and Posner, A.S. (1964). "Crystal structure of hydroxyapatite", *Nature* 204: 1050.
- Kohn, D.H. & Ducheyne, P. (1991). "Materials for bone and joint replacement" In: *Materials Science and Technology. A comprehensive Treatment., Medical and Dental Materials*, Vol.14. R.W. Cahn, P. Haasen, E.J. Kramer, D.F. Williams (Eds.) VCH, USA.
- Lemons, J.E. (1986). "General Characteristics and Clasifications of Implant Material" In: *Pesrpectives on Biomaterials, Materials Science Monographs*. No. 33. O.C. Lin & E.Y.S. Cho, (Eds.). Elsevier, Amsterdam.
- Li, P., Ohtsuki, C., Kokubo, T., Nakanishi, K. and Soga, N. (1992). "Apatite formation induced by silica gel in a simulated body fluid", *J. Am. Ceram. Soc.*, 75 {8}, 2094-2097.
- Li, P., Ohtsuki, C., Kokubo, T., Nakanishi, K., Soga, N., Nakamura, T., and Yamamuro, T. (1993). "Process of formation of bone-like apatite layer on silica gel", *J. of Mat. Sc. Med.*, 4, 127-13.
- Mattox, K. (1992). "The Global Biomaterials Market Where Hard Tissue Biomaterials Fit In" In: *BIOMATERIALS - Hard Tissue Repair and Replacement*. Vol. 3, D. Muster, (Ed.), Elsevier, Amsterdam.
- MarketsandMarkets (2010), Global Biomaterial Market (2010 - 2015) <http://www.marketsandmarkets.com/Market-Reports/biomaterials-market-report-131.html>
- Millennium Research Group (2002). "U.S. Markets for Orthopedic Biomaterials 2002", <http://mrg.net>
- Miller, A. & Wray, J.S. (1971). Molecular packing in collagen, *Nature*, 230: 437-439.
- Monma, H. & Kamiya, T. (1987). "Preparation of hydroxyapatite by the hidrolisis of brushite", *J. of Mat. Sci.*, 22, 4247-4250.
- Natali, A.N. & Meroi, E.A. (1989). "A review of the biomechanical properties of bone as biomaterial", *Biomaterials*, 11: 266-276.
- Neuman, W.F. & Neuman, M.W. (1958). *The chemical dynamics of bone mineral.*, The University of Chicago Press., Chicago.
- Omatete, O.O., Janney, M.A. and Strehlow, R.A. (1991). "Gelcasting - A new ceramic forming process", *Ceram. Bull.*, 70: 10, 1641-1649.
- Oonishi, H. (1991). "Orthopaedic applications of hydroxyapatite", *Biomaterials*, 12, 171-178.
- Oonishi, H. (1992). "Development and application of bioceramics in orthopaedic surgery" In: *BIOMATERIALS - Hard Tissue Repair and Replacement*. Vol. 3. D. Muster (Ed.), Elsevier, Amsterdam.
- Panda, R. N., Hsieh, M. F., Chung, R. J. and Chin, T. S. (2003). "FTIR, XRD, SEM and solid state NMR investigations of carbonate-containing hydroxyapatite nano-

- particles synthesized by hydroxide-gel technique" *J. Phys. Chem. Solids.* 64, 193-199.
- Park, J.B. (1984). *Biomaterials Science and Engineering*, Plenum Press, New York, USA.
- Ravaglioli, A. & Krajewski, A. (1992). *Bioceramics; Materials Properties and Applications*, Chapman & Hall, London.
- Rivera, E., Bonilla, M., Hernández, R., Rodríguez, R. and Castaño, V.M. (1997). "Effect of chemical additives on the growth of hydroxyapatite on silica gels", *Journal of Materials Synthesis and Processing*, 5, 2, 153-167.
- Rivera, E., Brostow, W., Díaz, J. R., Araiza, M., Rodríguez, R., Hernández, R. and Castaño, V.M. (1999). "Synthesis of hydroxyapatite from eggshell", *Materials Letters*, Vol. 41 (3) 128 - 134.
- Rivera-Muñoz E., Brostow, W. Rodríguez, R. and Castaño, V.M. (2001). "Growth of hydroxyapatite on silica gels in the presence of organic additives: kinetics and mechanism" *Mat. Res. Innovat.* 4: 222-230
- Rivera-Muñoz E., Velazquez R. and P. Muñoz-Álvarez (2007) "Mechanical characterization of hydroxyapatite-based, organic-inorganic composites", *Materials Science Forum*, Vol. 539-543: 583-588.
- Rivera-Muñoz E., Velazquez R. and Rodriguez R. (2003) "Improvement in mechanical properties of hydroxyapatite objects with controlled porosity made by modified gelcasting process", *Materials Science Forum*, Vol. 426-432: 4489-4494.
- Rivera-Muñoz, E. M., Huirache-Acuña, R., Velázquez, R., Alonso-Núñez, G. and Eguía-Eguía, S. (2011). "Growth of Hydroxyapatite Nanoparticles on Silica Gels", *Journal of Nanoscience and Nanotechnology*, Vol. 11, No. 6, 5592 - 5598
- Rivera-Muñoz, E., Curiel, R. and Rodríguez, R. (2003). "Selectivity in the hydroxyapatite synthesis from eggshell using different thermal treatments", *Materials Research Innovations*, Vol. 7, 85-90.
- Rivera-Muñoz, E., Díaz, J. R., Rodríguez, R., Brostow, W. and Castaño, V.M. (2001). "Hydroxyapatite spheres with controlled porosity for eye ball prostheses: processing and characterization", *Journal of Materials Science: Materials In Medicine*, 12, 305-311
- Royer, A., Vigure, J.C., Heughebaert, M. and Heughebaert, J.C. (1993). "Stoichiometry of hydroxyapatite: influence of flexural strength", *J. Mater. Sci.: Materials in Medicine.*, 4: 76-82.
- Sendax, V.I. (1992). "Postscript: Hydroxyapatite-coated implants", In: *The dental clinics of north america, Hydroxyapatite-coated implants*, Vol. 36, No. 1. V.I. Sendax, (Ed.), W.B. Saunders Co., Philadelphia, USA.
- Trager, T., Matrai, J., Gyorgy, J. and Szabo, G. (1992). "Ceramics for dental and maxillo-facial use", In: *BIOMATERIALS - Hard Tissue Repair and Replacement*. Vol. 3. D. Muster (Ed.), Elsevier, Amsterdam.
- Williams, D.F. (1991). "Biofunctionality and Biocompatibility" In: *Materials Science and Technology. A comprehensive Treatment., Medical and Dental Materials*, Vol.14. R.W. Cahn, P. Haasen, E.J. Kramer, (Eds.), D.F. Williams, vol. (Ed.) VCH, USA.

- Williams, D.F. (1994). "The Science and Applications of Biomaterials", *Adv. Mater. Tech. Monitor*, Vol 1, No. 2.
- Yoshimura, M. & Suda, H. (1994). "Hydrothermal processing of hydroxyapatite: Past, present, and future", In: *Hydroxyapatite and Related Materials*, P.W. Brown, B. Constantz (Eds.), CRC Press, Boca Raton.

IntechOpen

IntechOpen



Biomedical Engineering - Frontiers and Challenges

Edited by Prof. Reza Fazel

ISBN 978-953-307-309-5

Hard cover, 374 pages

Publisher InTech

Published online 01, August, 2011

Published in print edition August, 2011

In all different areas in biomedical engineering, the ultimate objectives in research and education are to improve the quality life, reduce the impact of disease on the everyday life of individuals, and provide an appropriate infrastructure to promote and enhance the interaction of biomedical engineering researchers. This book is prepared in two volumes to introduce recent advances in different areas of biomedical engineering such as biomaterials, cellular engineering, biomedical devices, nanotechnology, and biomechanics. It is hoped that both of the volumes will bring more awareness about the biomedical engineering field and help in completing or establishing new research areas in biomedical engineering.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Eric M. Rivera-Muñoz (2011). Hydroxyapatite-Based Materials: Synthesis and Characterization, Biomedical Engineering - Frontiers and Challenges, Prof. Reza Fazel (Ed.), ISBN: 978-953-307-309-5, InTech, Available from: <http://www.intechopen.com/books/biomedical-engineering-frontiers-and-challenges/hydroxyapatite-based-materials-synthesis-and-characterization>

INTECH

open science | open minds

InTech Europe

University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

© 2011 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike-3.0 License](#), which permits use, distribution and reproduction for non-commercial purposes, provided the original is properly cited and derivative works building on this content are distributed under the same license.

IntechOpen

IntechOpen