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Crystalline Bioceramic Materials

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A strong interest in the use of ceramics for biomedical engineering applications developed in the late 1960´s. Used initially as alternatives to metallic materials in order to increase the biocompatibility of implants, bioceramics have become a diverse class of biomaterials, presently including three basic types: relatively bioinert ceramics; bioactive or surface reactive bioceramics and bioresorbable ceramics.
This review will only refer to bioceramics "sensus stricto", it is to say, those ceramic materials constituted for nonmetallic inorganic compounds, crystallines and consolidated by thermal treatments of powders to high temperatures. Leaving bioglasses, glass-ceramics and biocements apart, since, although all of them are obtained by thermal treatments to high temperatures, the first are amorphous, the second are obtained by desvitrification of a glass and in them vitreous phase normally prevails on the crystalline phases and the third are consolidated by means of a hydraulic or chemical reaction to room temperature.
A review of the composition, physiochemical properties and biological behaviour of the principal types of crystalline bioceramics is given, based on the literature data and on the own experience of the authors.

Key words: alumina, zirconia, zirconia-toughened alumina, graphite, hydroxyapatite, bioactive silicates, bioeutectic□, tricalcium phosphate

Materiales biocerámicos cristalinos

A finales de los años sesenta se despertó un gran interés por el uso de los materiales cerámicos para aplicaciones biomédicas. Inicialmente utilizados como una alternativa a los materiales metálicos, con el propósito de incrementar la biocompatibilidad de los implantes, las biocerámicas se han convertido en una clase diversa de biomateriales, incluyendo actualmente tres tipos: cerámicas cuasi inertes; cerámicas bioactivas o reactivas superficialmente y cerámicas reabsorbibles o biodegradables.
En la presente revisión se hace referencia a las biocerámicas en sentido estricto, es decir, a aquellos materiales constitutitos por compuestos inorgánicos no metálicos, cristalinos y consolidados mediante tratamientos térmicos a altas temperaturas. Dejando aparte los biovidrios, los vitrocerámicos y los biocementos, puesto que, si bien todos ellos son obtenidos por tratamiento térmicos a altas temperaturas, los primeros son amorfos, los segundos son obtenidos por desvitrificación de un vidrio, prevaleciendo normalmente la fase vítrea sobre las fases cristalinas, y los terceros son consolidados mediante una reacción química o hidráulica a temperatura ambiente.
Así pues, teniendo en cuenta la abundante bibliografía sobre el tema y la experiencia propia de los autores, se presenta una revisión de la composición, propiedades fisicoquímicas, aplicaciones y comportamiento biológico de los principales tipos de biocerámicas cristalinas.

Palabras clave: alúmina, zircona, alúmina-circona, grafito, hidroxiapatito, silicatos bioactivos, bioeutecticos®, fosfato tricálcico.

1. INTRODUCTION

Bioceramics are those engineered materials that find their applications in the field of medicine [1]. Traditionally, the brittleness, the low mechanical fracture toughness and the low resistance to the impact have limited the applications of the ceramic materials. Nevertheless, a strong interest in the use of ceramics for biomedical engineering applications were developed at the end of the years sixty. New ceramics, with very improved properties, contributed to increase the possibilities of using ceramics in biomedicine and their use has extended considerably since then [2,3].

The great chemical inertia of the ceramics, their high compression strength and their aesthetic appearance, made that these materials began to be used in dentistry, mainly in dental crowns. Later their use extended to orthopaedic applications [4-6].

Used initially as alternatives to metallic materials in order to increase the biocompatibility of implants, bioceramics can be classified from different points of views [7, 8]:
(a) According to the type of answer of the living host
(b) According to the application to which they are destined [9]
(c) According to the characteristics of the material [10]

However, in this review, the classification, according to the answer of the living host, is going to be followed, because it is considered more in accordance with the application of the bioceramic materials. Then, according with this, bioceramics can be divided in Bioinert; Bioactive or Surface Reactive and Biodegradable or Resorbable Materials.

2. BIOINERT CERAMICS

Relatively Bioinert ceramics undergo little or no chemical changes when they are exposed to physiological environments. They maintain their physical and mechanical properties while in the host. The answer of the host to these bioceramics is the formation of a very fine fibrous tissue capsule of varying thickness, several micrometers or less, that surround implant materials. The fixation of implants in the body is made through a strong mechanical interlocking, by tissue ingrowth into undulating surfaces [11]. When high strength is required, the bond is made by perforations in the implants using threads, cements, etc. When so high strength are not required can be used porous inert bioceramics, with sizes of pore between 100 and 150 μm, which guarantee the growth of the tissue towards within implants assuring its fixation [12-14].

Typical examples of these bioinert ceramics are: Alumina (α-Al_2O_3); Zirconia (ZrO_2), Alumina-Zirconia and Pyrolytic Carbon.

2.1. Alumina

Alumina of high density and purity (99.5 % in weight of α-Al_2O_3), with an average grain size < 4 μm is probably, the bioinert ceramic material of greater biological interest. This material was developed, as alternative to used metallic alloys in load-bearing hip prosthesis and in dental implants, to display an excellent biocompatibility, good resistance to the corrosion, to form a very fine fibrous capsule, to have a low coefficient of friction and good mechanical properties as much high strength as wear resistance [15-17].

According to the International Standards Organization (ISO), the purity of the alumina that is used in biomedical applications has to be over 99.5 %, being the rest of the impurities (SiO_2, Na_2O, K_2O, CaO, etc.) below 0.1 % in weight, in order to avoid a large grain increase during sintering. An increase of average grain size to ~7 μm can decrease mechanical properties by about 20 %. It is normal the addition of approximately 0.5 wt. % of MgO that acts as inhibitor of the grain growth. Table I shows the characteristics of alumina implants, according to Ratner et al. [17], together with the ISO 6474-81 requirements.

TABLE I. CHARACTERISTICS OF AL_2O_3 IMPLANTS

Properties	Al_2O_3 Implants	ISO 6474-81
Al_2O_3 (wt. %)	> 99,8	≥ 99,50
Density (g/cm^3)	> 3,93	≥ 3,90
Average grain size (μm)	3 – 6	< 7
Surface roughness (Ra) (μm)	0,02	
Hardness (Vickers)	2300	> 2000
Compressive strength (MPa)	4500	
Bending strength (MPa)*	550	400
Young modulus (GPa)	380	
Toughness (K_{Ic})(MPa m$^{1/2}$)	5 - 6	
Threshold (K_{I0}) (MPa m$^{1/2}$)	~ 2,5	

The most common application of alumina bioceramics is in the area of orthopaedics as component in hip and knee prostheses. The first clinical use of total hip prosthesis with an alumina head and alumina socket was in 1971. The long-term coefficient of the pair alumina/alumina and the wearing down index decrease with time and approaches the value of a normal healthy joint [18].

The main problem with total hip system is the loosening of the acetabular component, which is caused by wear debris. For this reason alumina is used only in the head of femur since numerous clinical studies indicates that alumina/ultrahigh molecular weigh polyethylene (UHMWPE) pair reduces wear debris by a factor of 10 or greater [19-21]. Figure 1 shows the typical microstructure of an alumina used in the femur head.

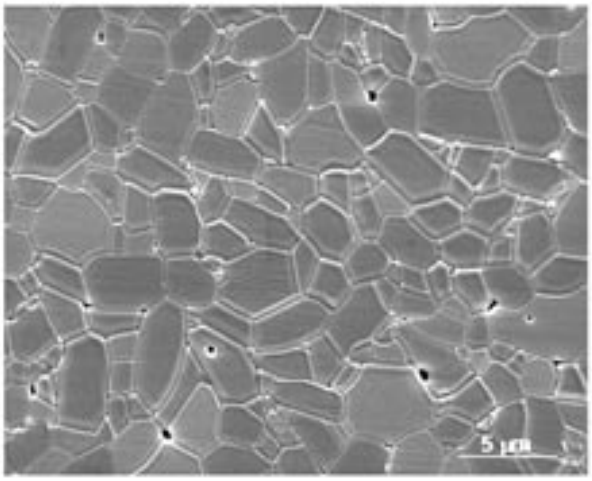

Fig. 1.- Microstructure of an alumina for hip prosthesis obtained by HIP at 1500ºC.

Other clinical applications of alumina are the used for screws, tooth-root implants, orbital walls, implants for maxillofacial reconstructions, dental implants etc. Between these last ones, the most well known application is the Tübingen implant [22-24] employee like substitute dental immediately after the extraction or in edentulous regions. The effectiveness of these implants is of 92.5 %. The cross-sectional fracture is the most frequent failure of these implants, due to relatively low resistance to the flexion, being the main cause of failure. Due to it, the use of alumina single crystals began to used as dental implant [25, 26] with resistance to flexion 3 times over polycrystalline alumina. However, the use of single crystals do no eliminate the basic disadvantage of alumina bioceramics (low fracture toughness), which for alumina single crystals is equal to 4-5 MPa m$^{1/2}$. These alumina single crystals are obtained generally by grown and crystallization from a melt or by the Verneuil method [27].

2.2. Zirconia

It has become a popular alternative to alumina as structural bioinert ceramics because, properly treated, it has a greater resistance to the fracture (greater fracture toughness) of any monolithic ceramics. On the other hand, zirconia is also exceptionally inert in the physiological environment and presents very good static fatigue strength. In addition, the zirconia/UHMWPE pair displays lower coefficient of friction than the alumina/UHMWPE pair, with the consequent diminution of particles to the physiological environment [28 - 30].

Zirconia presents three different crystalline forms: monoclinic, from room temperature to ~ 1100 ºC, tetragonal, from this temperature to ~2372 ºC, and cubic, from this last temperature to the melt at ~2680 ºC. The monoclinic ↔ tetragonal transformation is of martensitic type, and therefore reversible when warming up or to cool down through the transition temperature (~1100 ºC). This happens with an increase of volume of the order of 3 to 5 %, which produces the cracking or fracture of the pieces. In order to avoid this transformation, and even increase the toughness of the zirconia materials, the use of totally or partially stabilized tetragonal or cubic zirconia by suitable additives is recommended. Zirconia of higher toughness is usually obtained by stabilizing its tetragonal phase by doping it with yttria (~3 mol %), followed by a suitable heat treatment, considering the binary system ZrO_2 - Y_2O_3 [31]. In this way the zirconia bioceramic is totally a tetragonal material with a microstructure formed by very small grains of the order of 0.2 to 0.5 μm. The additives most widely used in biomedical applications are the yttria (Y_2O_3) and the magnesia (MgO).

Between all the ceramic materials, zirconia are those where their mechanical properties depend more of the sintering process, because is necessary to have a balance between the density and the average grain size of the bioceramic [32].

Figure 2 shows a typical microstructure of a tetragonal zirconia containing 3 mol % of yttria and Table II illustrates the characteristics of tetragonal zirconia stabilized with yttria (TZP = tetragonal zirconia polycrystals) versus partially stabilized zirconia with magnesia (Mg-PSZ = magnesia partially stabilized zirconia) [33].

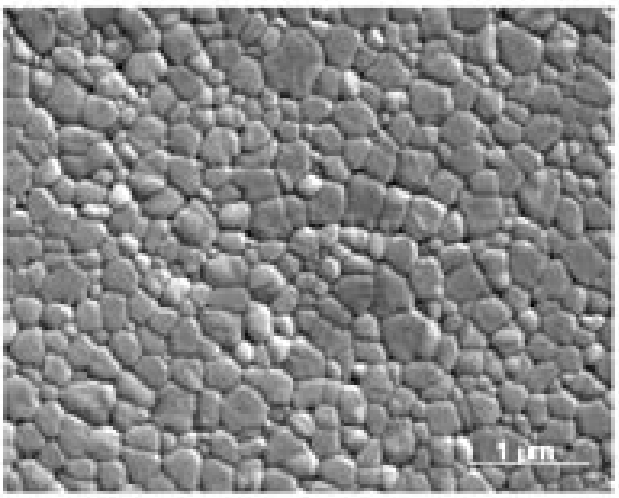

Fig. 2.- Typical microstructure of a tetragonal zirconia containing 3 mol % of yttria

Recently studies on new TZP materials, doped with yttria, tested in simulated body fluids and in animals, have shown slight decreases in fracture toughness and young modulus [34-36]. The observed strength, after two years, is sill much higher that the strength of alumina bioceramics tested under similar conditions. Because the zirconia/zirconia pair displays a wear rate 5000 times greater than the alumina/alumina pair, those do not have to be used in articulated surfaces.

TABLE II. CHARACTERISTICS OF TWO TYPES OF ZIRCONIA MATERIALS

Properties	TZP	Mg-PSZ
Purity	~ 97 %	~ 96.5
% Y_2O_3	3 mol %	
% MgO		3,4 mol %
Density(g/cm^3)	6.05	5.72
Average grain size (μm)	0.2 – 0.4	0.42
Bending strength (MPa)	1000	800
Compressive strength (MPa)	2000	1850
Young Modulus (GPa)	150	208
Hardness(Vickers)	1200	1120
Fracture toughness (K_{IC}) (MPam^{½})	7 – 8	~ 8
Threshold (K_{I0}) (MPam^{½})	~ 3,5 ± 0,2	

On the other hand, the potential radioactivity of the zirconia prosthesis, although the detected activity has been small, the long-term effects of the alpha radioactivity still must be evaluated.

Nevertheless, very recently, French Government has prohibited the manufacture, distribution, export and use of these prostheses in France by decision of the July 22, 2003, because of having detected frequent breakage of femoral heads made in zirconia [37].

2.3. Alumina-Zirconia

Recently, the orthopaedic community reports significant in-vivo failures, due to the slow crack growth, of alumina and zirconia prostheses. Consequently, researches have been made with a new generation of alumina-zirconia nano-composites having a high resistance to crack propagation, which may offer the option to improve lifetime and reliability of ceramic joint prostheses. De Aza et al. [38, 39] have put in evidence that, tailoring the microstructure by refining powder processing using a new colloidal processing synthesis route, is possible to produce alumina-zirconia nano-composites at the top end

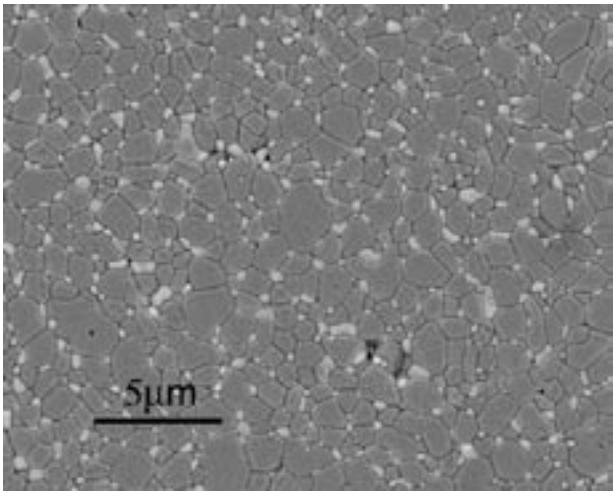

Fig. 3.- Microstructure of an alumina - 10 vol.% zirconia nanocomposite. Dark phase = alumina; clear phase = zirconia

of they strength spectrum. Figure 3 shows a microstructure of one of these composite alumina-zirconia materials. These new composites can display not only a greater toughness (K_{IC}) that the monolithic materials previously mentioned, otherwise, and what it is more important, a greater threshold for the stress intensity factor (K_{I0}), under which crack propagation does not take place (Table III). This threshold represents an intrinsic property for a given material that gives information of its mechanical behaviour more realistic than the widely used toughness, which means only fast crack growth [40-41].

TABLE III.

Material	Fracture threshold K_{I0}(MPam$^{1/2}$)	Tougnhess K_{Ic}(MPam$^{1/2}$)	Hardness H (Vickers)
Alumina (Al_2O_3)	2.5 ± 0.2	4.2 ± 0.2	1600±50
Zirconia (3Y-TZP)	3.5 ± 0.2	5.5 ± 0.2	1290±50
Composite (Al_2O_3-10% ZrO_2)	4.0 ± 0.2	5.9 ± 0.2	1530±50

On the other hand, since hardness and chemical stability are equally important in the orthopaedic field, these composite materials, with relatively low contents of zirconia (10 % in volume), present similar hardness values than alumina (Table II) and are not susceptible to the hydrothermal instability observed in some cases of stabilised zirconia bioceramics (low temperature degradation). These nanomaterials may offer the option to improve the lifetime and reliability of ceramic femoral heads, so contributing to improve the quality of life of a large number of patients. Further, surgical operations and consequently the suffering of people as well as the high cost of such operations will be avoided.

2.4. Carbon

Carbon presents a great variety of forms: amorphous carbon, graphite, diamond, vitreous carbon and pyrolitic carbon. Some of them display the most excellent properties of biocompatibility, chemical inertia and thromboresistance that any other bioceramics. Another advantage of these materials is that their physical characteristics are close to those of the bone [42]. Thus, their densities, according to the type carbon, change between 1.5 - 2.2 g/cm^3, and their elastic modules between 4 - 35 GPa. In spite of all the mentioned varieties, only three types of carbon are used for biomedical devices: the pyrolitic carbon, in its two varieties of low temperature isotropic (LTI) and ultra-low temperature isotropic (ULTI), and the vitreous carbon. The three types of carbon have disordered lattice structures and are collectively referred to as turbostratic carbons. While the microstructure of turbostratic carbon might seem very complicated due to its disordered nature, it is in fact quite closely analogous to the structure of graphite, but with at random oriented layers [43].

Pyrolitic carbon is widely used for implant fabrication. It is normally used as surface coating. Figure 4 shows a pyrolitic carbon deposited on a graphite fibre. Pyrolitic carbon devices are typically made, from a hydrocarbon gas in a fluidized-bed, via a chemical vapour-deposition method.

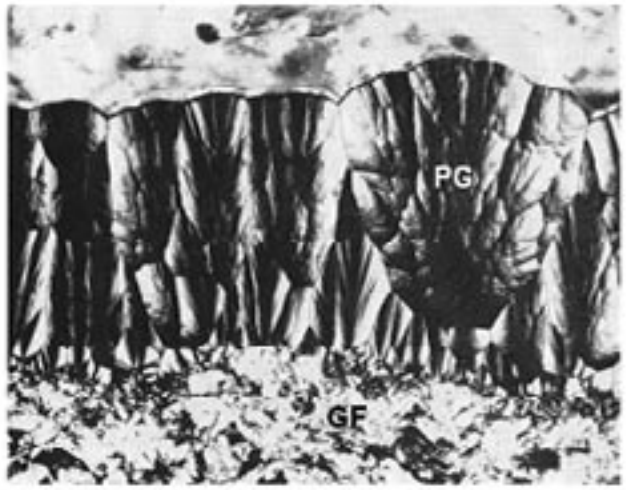

Fig. 4.- Pyrolitic graphite (PG) deposited on a graphite fiber (GF)[45]

Its great cellular biocompatibility with the blood and the soft tissue as well as its excellent thromboresistance, does carbon material to be used fundamentally in applications of the circulatory apparatus, blood vessel and mechanical cardiac-valve prosthetic devices, being this last the most extended application. Nowadays, most of the modern heart valves are made with a coating of LTI on a polycrystalline graphite substrate or like a monolithic material [44].

In both cases is frequently added up to 10 wt.% of silicon, often in the form of discrete sub-micron β-SiC particles randomly dispersed in a matrix of roughly spherical micron-size subgrains of pyrolitic carbon. The doping with silicon improves the mechanical properties of pyrolitic carbons, issue of great importance in the heart valves, where the joint is subject to degradation by cyclic fatigue or stress corrosion and possible cavitations by erosion during the life of the patient.

Some structural and mechanical properties of graphite and biomedical turbostratic carbons is shown in Table 4 [45].

TABLE IV. STRUCTURAL AND MECHANICAL PROPERTIES OF GRAPHITE AND BIOMEDICAL TURBOSTRATIC.

Properties	Polycrystalline Graphite Substrate	Silicon Alloyed LTI Pyrolitic Carbon	ULTI Vapor Deposited Carbon
Density (kg. m^{-3})	1,500 – 1,800	1,700 – 2,200	1,500 – 2,200
Crystalline Size (nm)	15 – 250	3 – 5	8 - 15
Expansion Coefficient (10^{-6} K^{-1})	0,5 – 5	5 – 6	---
Hardness (DPH)	50 – 120	230 – 370	150 – 250
Young´s Modulus (GPa)	4 – 12	27 – 31	14 – 21
Flexural Strength (MPa)	65 – 300	350 – 530	345 - 690
Fracture Strain (%)	0.1 – 0.7	1.5 – 2.0	2.0 – 5.0
Fracture Toughness (MPa m$^{1/2}$)	~1.5	0.9 – 1.1	---

Whereas the pyrolitic carbons coating have been applied in zones in contact with the blood, due to their excellent thromboresistance, the vitreous carbons have been studied mainly to bond to soft and hard tissues, without inflammatory

answer in the adjacent tissues. Similar behaviour has been registered for pyrolitic carbons LTI and ULTI.

Apart from of the mistral and aortic heart valves, there are applications in dental field [46] and middle ear reconstruction and in devices of LTI coating on titanium to make easy the circulation of the blood. Recently, success was achieved in coating ULTI onto the surfaces of blood vessel implants made of polymers. The coating has excellent compatibility with blood and is thin enough not to interfere with the flexibility of the grafts [47].

3. BIOACTIVE CERAMICS

Generally, when an artificial material is implanted in the body, it is encapsulated by uncalcified fibrous tissue that isolates it from the surrounding. This is a normal reaction intended to protect the body from foreign substances. However, in the early 1970s, Hench et al. [48] found that a glass, called Bioglass®; of the complex system Na_2O-CaO-SiO_2-P_2O_5, induced the formation of no fibrous tissue, but rather came into direct contact with the surrounding bone and formed a tight chemical bond with it.

Since then, other types of glasses and glass-ceramics have also been found to bind to living bone [49-51], Hench et al.[52-53], Gross et al. [54-55], Karlon et al. [56-57] and Kokubo et al. [58-59]. These bone-binding materials are called bioactives materials.

The appearance of this type of bioceramics born of the need to eliminate the interfacial movement that takes place with the implantation of bioinert ceramics. Consequently, L. L. Hench proposes in 1967 to the U.S.A. Army Medical Research and Development Command, a research based on the modification of the chemical composition of ceramics, and glasses so that they have chemical reactivity with the physiological system and form chemical bond between the surfaces of implant materials and the adjacent tissue.

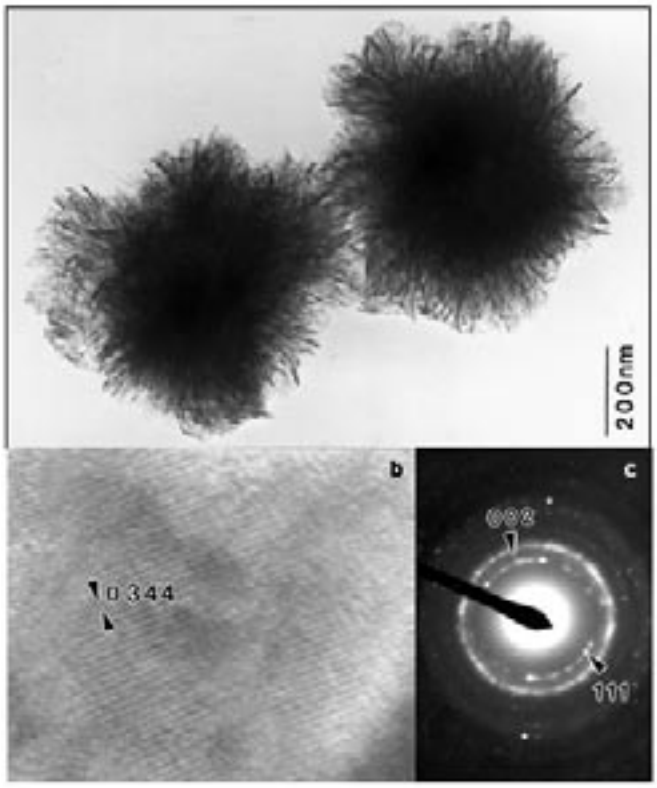

Fig. 5.- (a) TEM image showing overall morphology of the HA crystals. (b) High-resolution TEM image of HA crystals and (c) Selected-area diffraction pattern of the region. HA acicular crystals change to rods to equi-axed crystals with increasing carbonate content

Upon implantation in the host, bioactive ceramics form a strong bond with adjacent tissue. Except hydroxyapatite, which bond directly to living bone, the rest of bioactive materials bond to bone through a carbohydroxyapatite layer (CHA) biologically active, which provides the interfacial union with the host. This phase is chemical and structurally equivalent to the mineral phase of the bone, and the responsible of the interfacial union.

The interface of union between bioactive materials and tissue is usually extremely strong. In many cases, the interfacial strength of adhesion is equivalent to or greater than the cohesive strength of the implant material or the tissue bonded to the bioactive implant. Generally, the break takes place in the implant or in the bone but almost never in the interface [60-63].

However, not only certain types of glasses and glass-ceramics are bioactives. Other ceramic materials "sensus stricto" are also bioactives. The typical example is the hydroxyapatite, which is the only one that bond directly to bone and other examples are: certain silicates (diopside and wollastonite) and a new group of ceramic materials denominated Bioeutéctics®, as it will be exposed next.

3.1. Hydroxyapatite

Hydroxyapatite (HA) is the primary mineral content of bone representing ~43 wt.%. HA is a calcium phosphate whose stoichiometric formula corresponds to a: $Ca_{10}(PO_4)_6(OH)_2$, with a Ca/P molar ratio = 1.67. HA belong the mineral family of Apatites whose name derived from Greek "απαταω" means deception or deceit, due to the facility it was confused with other mineral species like the beryl or the tourmaline [64].

HA displays ionic character, and its crystalline structure can be describe like a compact hexagonal packing of oxygen atom with metals occupying the tetrahedral and octahedral holes of the periodic network. The basic apatite structure is hexagonal with space group $P6_3/m$ and approximate lattice parameters a=9.4 and c=6.9 Å, being the fluorapatite ($Ca_{10}(PO_4)_6F_2$) the representative example of this structure. Nevertheless, HA presents a low symmetry, monoclinic, due to the distortion of the ion OH^- with respect to the ideal model that would represent the position of spherical ion F^- in the fluorapatite. Nevertheless, in most of the works in the field of biomaterials it assumed that HA has a fluorapatite structure but with lattice parameter a=b=9,418 Å and c=6,884 Å. α=ß=90° and γ=120°, Z=2. The unit cell contains 10 Ca^{+2}, 6 PO_4^{3-} and 2 groups OH^- [65].

HA allows the substitution of many other ions in their structure. These substitutions can take place in the positions of the calcium ions (Ca^{2+}) or in the phosphate groups $(PO_4)^3$ or hydroxyls groups $(OH)^-$. Consequences of these substitutions are changes in its properties like lattice parameters, morphology, solubility etc., without significant change in the symmetry. Thus for example, the substitution of F^- by OH^- involve a contraction in the a axis without change in the c axis, associated to an increase in the crystallinity and imparts greater stability to the structure. On the other hand, this imply that the fluorapatite is less soluble than the HA and that all

F^- free apatites, including biological apatites. Many other ions can enter in the HA network, affecting the properties, crystallinity, thermal stability, rate of dissolution etc.

The mechanical properties of the HA are similar to those of the most resistant components of the bone. HA has an elastic modulus of 40-100 GPa; dental enamel: 74 GPa, the dentine: 21 GPa, and the compact bone: 18-12 GPa. Nevertheless, dense bulk compacts of HA have mechanical resistances of the order of 100 MPa versus the 300 MPa of the human bone, diminishing drastically their resistances in the case of porous bulk compacts..

HA differs from biological apatites (enamel, dentin, bone, etc.) in physical and mechanical properties, stoichiometry, composition, crystallinity and other properties. Biological apatites are usually calcium-deficient and are always carbonate substituted. It is therefore more appropriate that biological apatites be referred as carbonate apatite (carbohydroxyapatites) a not as hydroxyapatite or HA, where groups $(CO_3)^{2-}$ replace group $(PO_4)^{3-}$ and where the Ca^{2+} is replaced by Na^+ to balance the charges [66, 67].

The methods of obtaining HA are very varied, including hydrothermal systems, precipitation methods, hydrolysis, solid-state reactions and hydrothermal reactions (68–70). However, when prepared from aqueous reactions either by precipitation or hydrolysis methods, the HA obtained is usually calcium deficient (Ca/P molar ratio lower than the stoichiometric value of 1.69). When the precipitation reaction is carried out under very basic conditions, the precipitate will contain carbonate, which makes the Ca/P molar ratio higher than the stoichiometry value. Figure 5 shows an electron image of CO_3-apatite crystals.

The interest as biomaterial of HA comes clearly by its similarity with the mineral phase of the bone tissue. In principle, HA would be the most suitable material as much for the restoration as for the substitution of the bone. However, the relatively low strength and toughness of HA arouses little interest among researchers when the focus of attention is on dense structural samples. Therefore, its use is restricted to all those applications where mechanical efforts are not required, finding its application mainly as coating on metallic substrata, with the object to accelerate and to increase the fixation of prostheses to the bone [71, 72].

Industrial and laboratory techniques, used for HA coating onto metallic substrates, include plasma spraying, laser ablation, electrophoretic deposition, sputtering and hot isostatic pressing. Being the first one, the most used, mainly in the coating of hip prostheses, being achieved, in this way, what has been called biological fixation of the prosthesis. [73, 74]. Among other applications are: a) coating of dental and maxillofacial prosthesis; b) dental implants; c) middle ear reconstruction; d) augmentation of alveolar ridge; e) periodontal defects; f) spinal surgery; g) pulp-capping materials [75].

3.2. Bioactive Silicates

It has been considered that to show bioactivity, glasses and glass-ceramics must contain both CaO and P_2O_5, which are the main components of the hydroxyapatite [76, 77]. Conversely, Ohura et al. [78] have recently observed that CaO-SiO_2 glasses, free of P_2O_5 as well as those containing very small amounts of P_2O_5, form the HA layer on their surfaces (bioactivity), when they are soaked in simulate body fluid (SBF), whereas CaO-P_2O_5 glasses free of SiO_2 do not form HA layer in SBF. This seems to indicate that bioactive materials can be obtained with compositions based on the CaO-SiO_2 system rather than in the CaO-P_2O_5. Taking into account these observations, Noami et al. [79, 80] and De Aza et al. [81-92] have shown that two polycrystalline chain silicate materials: diopside and wollastonite are also bioactives.

3.2.1. Wollastonite

Pseudowollastonita ($CaSiO_3$), the high temperature form of wollastonite, displays in its structure calcium ion chains easily removals by protons, as Bailey and Reesman [93] showed it in the study of the kinetic of dissolution of the wollastonite in H_2O-CO_2 systems. This fact suggests the possibility of extraction of calcium ions, from the wollastonite structure, by protons from the SBF, facilitating therefore the precipitation and formation of a HA layer on the surface of the material.

De Aza et al. have demonstrated the formation of a HA-like layer on the surface of pseudowollastonite ceramic both in vitro" [81-83, 85, 90] and "in vivo" [86,87]. Experiments "in vitro" involved immersion of the material in SBF with an ion concentration, pH and temperature virtually identical to human blood plasma, and in human parotid saliva (HPS).

Figure 6 shows the overall microstructure of a polished cross-section of the pseudowollastonite sample after one-month immersion in simulated body fluid and its relevant X-ray maps for calcium, silicon and phosphorous elements. This microcharacterisation of the interface showed that the reaction zone was composed of two chemically dissimilar layers formed on the pseudowollastonite surface. The outer layer was composed of a CaO/P_2O_5-rich phase, identified as HA-like phase by thin-film X-ray diffraction [83], while the underlayer, in direct contact with the pseudowollastonite substrate, was rich in amorphous silicon as was characterized by TEM, selected-area diffraction pattern and EDS analysis [83].

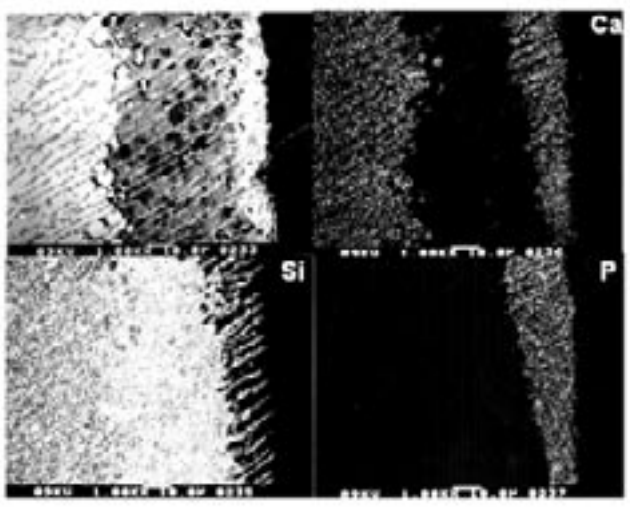

Fig. 6.- SEM image of a cross-section of pseudowollastonite after one month immersion in SBF and X-ray elemental maps of Ca, Si and P

The mechanism involved in the HA layer formation was described by De Aza et al.[94] as follows: at pH 7.25 of the SBF, the reaction mechanism start through an ionic exchange of H_3O^+, from the SBF, by labile calcium ions. This induces

the formation of an amorphous hydrogel silica layer and a sudden increase in pH from 9.0 to 10.5 at the wollastonite/SBF interface. This condition determines the partial dissolution of amorphous silica and the subsequent precipitation of HA. According to De Aza et al., this mechanism is common for both amorphous and crystalline silica-based bioactive material.

The authors also have evaluated the cytotoxicity of the pseudowollastonita [89] and the suitability of the material as a substratum for cell attachment and the ability to affect osteoblast at a distance from the material surface [91, 92]. These experiments demonstrate that extracts of pseudowollastonite do not show any significant cytotoxic effects and confirm the biocompatibility of this material. On the other hand, osteoblastic cells attached and proliferated on the surface to the ceramic. In addition, osteoblastic cells, at a distance form the material, exhibited a dramatic alteration on their appearance. This reinforces the suggestion that the release of soluble factors, silicon and calcium from the wollastonite, is responsible for much of the biological activity of this material.

"In vivo" experiments were consisted of implanting small cylinders of pseudowollastonite into rat tibias [86, 87]. Histological observations twelve weeks after implant show that the bone in contact with the surface of the pseudowollastonite appeared to be progressively replaced by bone with laminar arrangement. The new bone was growing in direct contact with the pseudowollastonite implants after only 3 weeks. Figure 7 shows SEM micrograph of polished cross-sections of pseudowollastonite implant after six weeks of implantation. The individual X-ray maps of the silicon, calcium and phosphorous distribution are also included. The calcium phosphate phase corresponds to new bone tissue as reported by histological examination. At twelve weeks of implantation, new bone was still growing at the interface.

Overall, these results suggest that pseudowollastonite is biocompatible and osteoconductive and it can be used for substitution or repair of bone tissues in places where mechanical solicitations are not high.

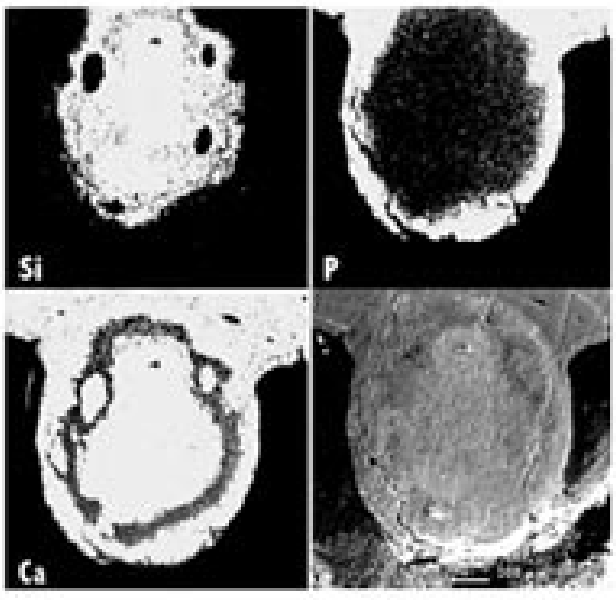

Fig. 7.- SEM image of a cross-section of pseudowollastonite implant after six weeks of implantation and X-ray elemental map of Si, Ca and P

3.3. Wollastonite-Tricalcium Phosphate (Bioeutectic®)

Natural and synthetic materials have been used clinically for many years to reconfigure anatomic structures for aesthetic and therapeutic reasons in several different surgical situations, however many outstanding problems remain unsolved. The most important is the process of total osteointegration of ceramic implants in the human body. When bioactive materials are implanted in a living body, the interaction between the bone tissue and these materials usually take place only on their surfaces, with the remaining bulk of the material unchanged, often causing a harmful shear stress.

To improve the ingrowth of new bone into implants (osteointegration), the use of materials with an appropriate interconnected porous structure has been recommended [95-100]. The design of a porous ceramic implant material has the potential of controlling the bone ingrowths. However, porous materials have very poor mechanical properties.

A new approach to overcoming this problem was proposed by De Aza et al [101-106].This is based on designing dense bioactive ceramic materials with the ability to develop an in situ porous hydroxyapatite-like (HA) structure when they are implanted into a living body. The material was composed of

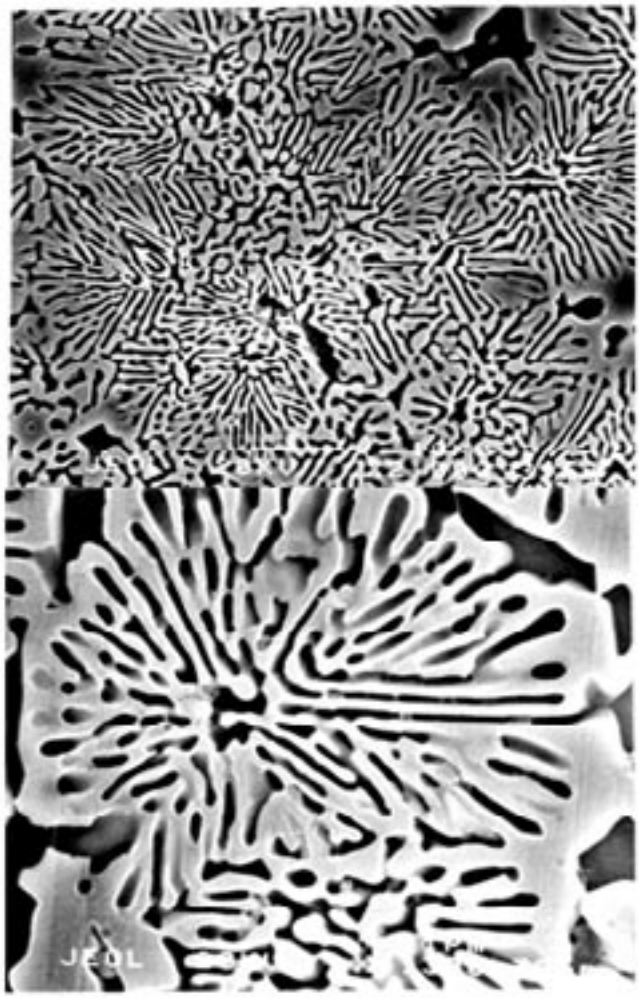

Fig. 8.- SEM image of the microstructure of the eutectic material (Bioeutectic□) and detail of a colony. White and black lamellae pseudowollastonite and □-tricalcium phosphate respectively. Sample etching with dilute citric acid.

two phases, pseudowollastonite ($CaSiO_3$ = psW) of bioactive character and resorbable α-tricalcium phosphate (α-TCP). Taking into account the bone structure, the microstructure of the material was developed by slow solidification of the eutectic composition of the system wollastonite-tricalcium phosphate (60 wt% psW and 40 wt% α-TCP)[107].

Figure 8 shows a SEM image of the microstructure of the eutectic material (Bioeutectic®), which consists of quasi-spherical colonies formed by alternating lamellae of psW and α-TCP with a morphology which correspond to irregular eutectic structure [108-110].

The material, exposed to simulated body fluid (SBF) for one week, transforms partially dissolving the pseudowollastonite lamellae and forming a porous structure of HA-like that mimic porous bone by a pseudomorphic transformation of the α-TCP, according to the reaction:

$$3[Ca_3(PO_4)_2] + Ca_2^+ + 2(OH)^- \rightarrow Ca_{10}(PO_4)_6(OH)_2$$

Figure 9 shows clearly the partial dissolution and transformation of the Bioeutectic® after one week soaking in SBF.

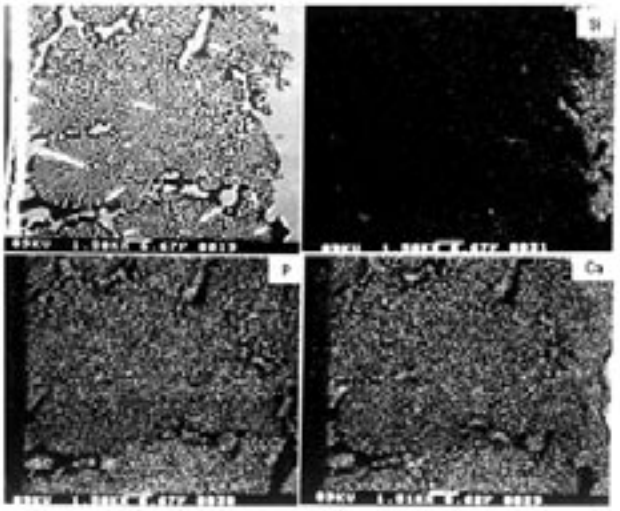

Fig. 9.- SEM image of a cross-section of the Bioeutectic after one week soaking in SBF and Si, P, and Ca X-ray maps.

Conversely, when the material is immersed in a slow stream of SFB (50 cm^3/h) instead of using a static solution, them a complete transformation of the material takes place given rise to a HA artificial porous bone as is shown in Figure 10.

Therefore, the Bioeutectic® material is the only bioactive material, at present, which is totally colonized in SBF. Consequently, it is expected it behaves similarly in *in vivo* experiments facilitating the osteointegration of the implant. These studies are actually carried out.

4. BIODEGRADABLE OR RESORBABLE MATERIALS

The resorbable ceramics began to be used in 1969. These types of bioceramics are dissolved with time and are gradually replaced by natural tissues. A very thin or non-existent interfacial thickness is the final results. They would be the

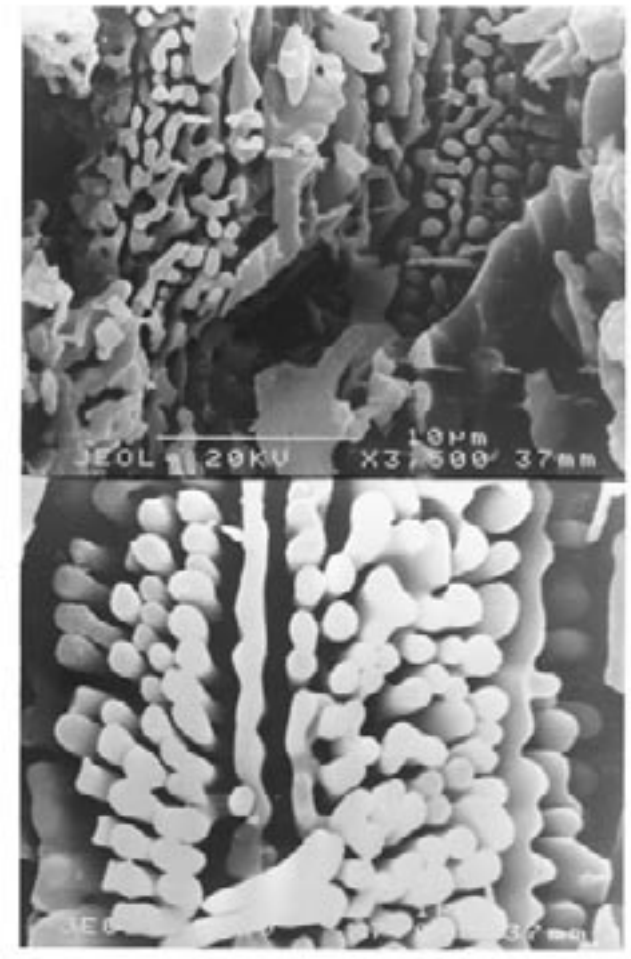

Fig. 10.- SEM images of a fresh fracture of the Bioeutectic after immersion in a stream of SBF for three weeks. (A) General view of the material completely transformed into a porous HA structure similar to porous bone. (B) Detail of a colony after transformation.

ideals implants, since only remain in the body while their function is necessary and disappear as the tissue regenerates. Their greater disadvantage is that their mechanical strength diminishes during the reabsorption process.

Consequently, the function of these materials is to participate in the dynamic process of formation and reabsorption that takes place in bone tissues; so they are used like scaffolding or filling spaces allowing to the tissues their infiltration and substitution [111].

All the resorbable ceramics, except plaster ($CaSO_4 \cdot ½H_2O$), are based on calcium phosphates, varying their biodegradability in the sense:

$$\alpha\text{-TCP} > \beta\text{ TCP} >>>> \text{HA}$$

The biodegradation rate is increased, as it is logical, as: a) specific surface increases (powders are more quickly biodegraded that porous solids and these more quickly than dense solids); b) when crystallinity decreases; c) when grain and crystal size decrease; d) when e.g. there are ionic substitutions of CO_3^{2-}, Mg^{2+} and Sr^{2+} in HA.

The factors that tend to decrease the rate of biodegradation include e.g.: a) F^- substitution F^- in HA; b) Mg^{2+} substitution in β- TCP and c) lower β- TCP/HA ratios in biphasic compounds.

The biodegradation or reabsorption of calcium phosphates is caused by three factors:

1) Physiochemical dissolution, which depends on the solubility product of the material and local pH of its environment. New phases may be formed, such as amorphous calcium phosphates, dicalcium phosphate dihydrate, octacalcium phosphate, and anionic substituted HA.

2) Preferential attack of the grain boundaries and physical disintegration in small particles.

3) Biological factors, such as phagocytosis, which causes a decrease in local pH concentration, the cellular activity and the site of implantation.

One of the few bioceramics that satisfy partially these requirements is the tricalcium phosphate (TCP).

4.1. Tricalcium phosphate

The tricalcium phosphate (TCP) is the biodegradable phosphate par excellence. TCP has a stoichiometric formula $Ca_3(PO_4)_2$ with a Ca/P molar ratio = 1.15. The TCP is a neutral compound in which the 6 positive charges of the Ca^{+2} ions are compensated by 6 negative charges of the anions PO_4^{3-}. It belongs to the family of the Whitlockites that respond to general formulate $(Ca,Mg)_3 (PO_4)_2$, so that the calcium can be replaced partial or totally by magnesium.

The TCP is a material that displays polymorphism. Three polymorphs are known: β, α and α` phases, from low to high temperature of stability respectively [112,113].

The β phase crystallizes in the hexagonal system, and their lattice parameters are: a = 10.429Å and c = 37.38Å. α=β= 90° and γ=120°. The α phase crystallizes in the orthorhombic system with lattice parameters: a = 15,22 Å, b = 20,71 Å and c = 9.109Å. α=β= γ= 90° and finally the α´phase crystallize in the monoclinic system, with lattice parameters: a = 12.887Å, b = 27.280Å and c = 15.219Åα=γ= 90° and β=126.2° [114].

The β phase is stable from room temperature up to 1150 ± 10 ºC ºC to which transforms into the α phase. This is stable from this temperature up to 1475 ± 5 ºC to which transforms into the α´ phase which is stable up to the melting temperature. The α ↔- α´ transition is completely reversible in both senses. Equally it happens with the α ↔ β transition, although if the α phase is abruptly quenched it can be mestastably preserved at room temperature.

As the synthesis of HA, the synthesis of β-TCP, in aqueous solution, is affected by many physical and chemical parameters, what presents great difficulty to obtain a product 100% pure [115-116]. However, pure β-TCP can be easily obtained by solid state reaction of calcium and phosphorus compounds with relationships Ca/P = 1,5.

Applications are temporary fillings and periodontal defects.

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