



Bioactive glasses and glass-ceramics

P.N. DE AZA,* A.H. DE AZA, P. PENA AND S. DE AZA

* Instituto de Bioingeniería, Universidad Miguel Hernández, 03202, Elche, Alicante (Spain)

Instituto de Cerámica y Vidrio, CSIC, C/ Kelsen 5, 28049, Madrid (Spain)

Since the late 1960's, a great interest in the use of bioceramic materials for biomedical applications has been developed. In a previous paper, the authors reviewed crystalline bioceramic materials "sensus stricto", it is to say, those ceramic materials, constituted for non-metallic inorganic compounds, crystallines and consolidates by thermal treatment of powders at high temperature. In the present review, the authors deal with those called bioactive glasses and glass-ceramics. Although all of them are also obtained by thermal treatment at high temperature, the first are amorphous and the second are obtained by devitrification of a glass, although the vitreous phase normally prevails on the crystalline phases.

After an introduction to the concept of bioactive materials, a short historical review of the bioactive glasses development is made. Its preparation, reactivity in physiological media, mechanism of bonding to living tissues and mechanical strength of the bone-implant interface is also reported. Next, the concept of glass-ceramic and the way of its preparation are exposed. The composition, physicochemical properties and biological behaviour of the principal types of bioactive glasses and glass-ceramic materials: Bioglass®, Ceravital®, Cerabone®, Imaplant® and Bioverit® are also reviewed. Finally, a short review on the bioactive-glass coatings and bioactive-composites and most common uses of bioactive-glasses and glass-ceramics are carried out too.

Keywords: Bioactive-glasses, Glass-ceramics, Bioglasses, Bioactive-glass coatings, Bioactive-composites.

Vidrios y Vitrocerámicos Bioactivos

Desde finales de los años sesenta, se ha despertado un gran interés por el uso de los materiales biocerámicos para aplicaciones biomédicas.

En un trabajo previo, los autores hicieron una revisión de los denominados materiales biocerámicos cristalinos en sentido estricto, es decir, de aquellos materiales, constituidos por compuestos inorgánicos no metálicos, cristalinos y consolidados mediante tratamientos térmicos a altas temperaturas. En el presente trabajo, los autores revisan el desarrollo de los vidrios bioactivos (biovidrios) y de las vitrocerámicas bioactivas. Si bien todos ellos son obtenidos también por tratamiento térmico a altas temperaturas, los primeros son amorfos y los segundos son obtenidos por desvitrificación de un vidrio, si bien la fase vítrea normalmente predomina sobre las fases cristalinas.

Después de una introducción al concepto de material bioactivo, se expone una breve revisión histórica del desarrollo de los vidrios bioactivos. A continuación se describe su obtención, reactividad en suero fisiológico artificial, mecanismo de unión al tejido vivo y resistencia mecánica de la interfaz hueso-implante. Posteriormente, se expone el concepto de material vitrocerámico y el proceso de su obtención así como también se describen los principales tipos de vidrios y vitrocerámicos bioactivos (Bioglass®, Ceravital®, Cerabone®, Imaplant® and Bioverit®), sus composiciones, sus propiedades físico-químicas y sus comportamientos biológicos. Finalmente, se lleva a cabo también una corta revisión de los recubrimientos con vidrios bioactivos y de los materiales compuestos (composites) bioactivos así como de los usos más comunes de los vidrios y vitrocerámicos bioactivos.

Palabras clave: Vidrios bioactivos, Biovidrios, Vitrocerámicos bioactivos, Recubrimientos bioactivos, Composites bioactivos.

1. INTRODUCTION

The concept of bioactive material is midway between those of inert material and resorbable material. Although a number of definitions of bioactivity have been reported, one by Hench (1, 2) is especially simple: the property of an implanted material that allows it to bond to living tissue.

As stated in dealing with crystalline bioceramic materials in a previous paper (3), bioactive materials, which include ceramics, glasses and glass-ceramics, can attach directly to bone tissue via a biologically active carboxyapatite (CHA) layer, which provides the interfacial bonding. Such a layer is chemically and structurally equivalent to the mineral phase of bone.

Bioactive glasses and glass-ceramics have been developed in response to the need to suppress interfacial mobility in implanted bioinert ceramics. Thus, in 1967, Hench proposed, to the US Army Medical Research and Development Command, to conduct research with a view to change the chemical composition of glasses, in order to enable their interaction with the physiological system and provide chemical bonding between living tissue and the implant surface. This way, in 1971, Hench et al. (4) showed, for the first time, that a material made by the man could bond to bone. The invention, named Bioglass®, was the first bioactive glass material ever developed.

According to Hench and Wilson (5), bioactive materials include hydroxyapatite (HA) ceramics, glasses, glass-ceramics and surface-active composite materials. Since hydroxyapatite ceramics were dealt with in a previous paper about crystalline bioceramic materials (3); in this work will only be made reference to the bioactive glasses and glass-ceramics.

2. BIOACTIVE GLASSES

The finding by Hench et al. (4) in the early 1970s that some SiO₂-CaO-Na₂O-P₂O₅ glasses induce the formation of no fibrous tissue on contact with living tissue, but rather bond chemically to it, arouse much interest in the development of bioactive glasses and glass-ceramics, and their use as biomedical materials.

The primary requirements to be met by a bioactive glass is that it should contain no extraneous or hazardous elements for the living body but contain calcium and phosphorus, which are the major constituents of the mineral phase in bone tissue. As stable vitreous network builder silica was selected, what allow to develop phosphate glasses with a silica-rich matrix.

The first bioactive glass (Bioglass®), which was developed by Hench et al. (6) and named Bioglass® 45S5, exhibits a high bioactivity and can join readily even to soft tissues. This is the most widely studied bioactive glass, which consists of 45 wt% SiO₂, 24.4 wt% CaO, 24.5 wt% Na₂O and 6 wt% P₂O₅.

Bioglass® 45S5 was based on the SiO₂-CaO-Na₂O-P₂O₅ system. As can be seen in Figure 1, the projection of its composition on the SiO₂-CaO-Na₂O system falls near a eutectic point, but far from the typical compositions of soda-lime glasses, which contain much more silica.

The composition of Bioglass® 45S5 in three different microstructural forms (viz. amorphous, partially crystalline and fully crystalline) was studied both in vitro and in vivo. All implants examined bonded to a rat femur model within 6 weeks, with no differences in this respect between the vitreous and crystalline implants (4, 8, 9).

From Bioglass® 45S5, Hench et al. developed and characterized a large series of glasses based on the SiO₂-CaO-Na₂O-P₂O₅ quaternary system, all containing 6 wt% P₂O₅. Table I shows the compositions of some of them. All were characterized in terms of a bioactivity index, which was defined as the time needed for 50% of an implant surface to attach to bone (t_{0.5}) (1), i.e.

$$I_b = [100/t_{0.5}] \text{ (days}^{-1}\text{)}$$

TABLE I. COMPOSITIONS IN WT% OF SOME GLASSES.

Bioglass	SiO ₂	CaO	Na ₂ O	P ₂ O ₅	B ₂ O ₃	F ₂ Ca	K ₂ O
45S5	45	24.5	24.5	6.0			
45S5F	43	12	23	6.0		16	
45B15S5	30	24.5	24.5	6.0	15		
45B5S5	40	24.5	24.5	6.0	5		
KCP1	45	24.5		6.0			24.5
45S5-N	50	24.5	19.5	6.0			
45S5-C	50	19.5	24.5	6.0			

This allowed to establish a series of isobioactivity lines as a function of the glass composition that are shown in the 6 wt% P₂O₅ section of the SiO₂-CaO-Na₂O-P₂O₅ system (Fig. 2). All glasses lying in region A, in the centre of the figure, were bioactive and bonded to bone. All them containing less than 60 mol% of SiO₂ and diminishing their bioactivity dramatically with a slight increase of this silica proportion. Region A includes a central composition zone of I_b > 8, bound by a dotted line in Fig. 2, where the glasses bond to both bone and soft tissues. On the other hand, the glasses in region B behaved as inert materials and were encapsulated by fibrous tissue upon implantation. The glasses in region C were reabsorbed within a few days of implantation. Finally, in the region D glasses cannot be obtained.

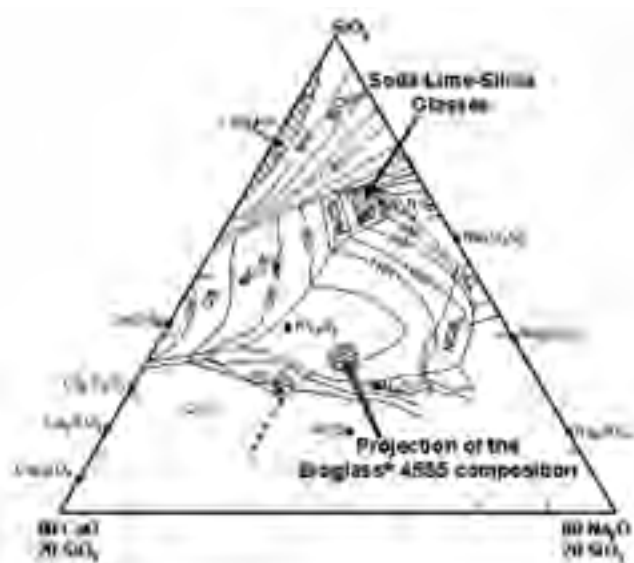


Fig. 1- SiO₂-CaO-Na₂O system (7) showing the position of traditional sodalime- glasses and the projection of the composition of the Bioglass® 45S5.

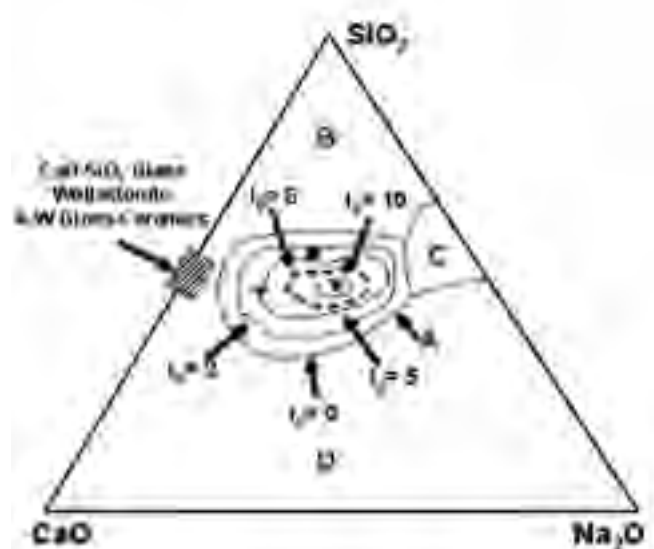


Fig. 2- Section corresponding to 6 wt% P₂O₅ in the system SiO₂-CaO-Na₂O-P₂O₅ and isobioactivity lines as a function of the wt% composition (10). (□Bioglass® 45S5, ▼Ceravital®, ●Bioglass®).

Partially replacing CaO with MgO or CaF₂ or Na₂O with K₂O, causes little change in bioactivity. By contrast, adding fluoride decreases the dissolution rate and alters the position of the boundary between regions A and C. Also, B₂O₃ and Al₂O₃ have been used to alter the production process of glasses or their surface dissolution rate. The amount of alumina added must be carefully controlled in order to avoid inhibiting the bioactivity of the glass completely. The maximum amount that can be used depends on the particular composition of the glass, but rarely exceeds 1.0 or 1.5 wt%. The addition of other multivalent cations usually shrinks region A in Figure 2 and can even suppress bioactivity altogether, as found by Gross and Strunz (11, 12) with Zr⁴⁺, Ta⁵⁺ and Ti⁴⁺ in addition to Al³⁺.

On the other hand, Anderson et al. (13), by applying a statistical method to the results of an in vivo study involving 16 types of SiO₂-CaO-Na₂O-P₂O₅ glasses, they developed the following empirical relation between the response of a glass (RN) implanted in rabbit tibia and its composition:

$$RN = 88.3875 - 0.0116272 [SiO_2]^2 - 0.980188 [Na_2O] - 1.12306 [CaO] - 1.20556 [P_2O_5] - 0.560527 [B_2O_3] - 2.08689 [Al_2O_3] \quad [1]$$

where the quantities in brackets represent the percentages by weight of the different oxides in the glass. Both the regression coefficient ($r^2 = 0.9725$) and the standard deviation (± 0.42 RN units) were reasonably good. The model is applicable over the composition ranges listed in Table II.

TABLE II. APPLICABILITY RANGES, IN WT%, OF THE EQUATION [1].

Compound	Minimum	Maximum
SiO ₂	38	65
Na ₂ O	15	30
CaO	10	24
P ₂ O ₅	0	8
B ₂ O ₃	0	3
Al ₂ O ₃	0	3

The model not only measures implant biocompatibility, but also discriminates between acceptably (RN = 4) and tightly bonded implants (RN > 5). It should be noted that Bioglass® 45S5 exhibited a value of RN = 6.

The presence of P₂O₅ was initially thought to be essential for glasses to be bioactive. However, Li et al. (14) showed that glasses of the SiO₂-CaO-Na₂O system containing no phosphate ions, which had been prepared via a sol-gel procedure, were bioactive even with as much as 85 mol% SiO₂. In addition, Ohura et al. (15) showed that a calcium silicate binary glass, called CS and containing 48.3 wt% CaO and 51.7 wt% SiO₂, it joins firmly to bone tissue. Subsequently, De Aza et al. (16-19) showed, for the first time, that a crystalline compound other than hydroxyapatite and containing no phosphate (viz. wollastonite, CaSiO₃) not only exhibits a high bioactivity in both simulated body fluid (SBF) and parotid saliva, but also bonds strongly to bone tissue (20, 21).

In summary, most glasses capable of bonding to living tissues contain phosphates and all contain silicates; the latter provide a scarcely soluble matrix that offsets the excess solubility of phosphate glasses. Also, bioactive glasses can be classified into two large groups according to whether they are: (a) rich in alkalis (viz. those developed by Hench et al.), which contain more than 20 wt% alkali oxides, or (b) poor in

alkalis, with less than 5 wt% of such oxides (22)

From the foregoing it follows that a wide range of bioactive vitreous compositions exists, which can be used, in theory, to adapt their reactivity to various clinical uses. Such a high flexibility is an outstanding feature that sets them apart from other biomaterials.

2.1. Preparation of bioactive glasses

Bioactive glasses are typically prepared from high-purity raw materials as their quality strongly influences that of the end-product. Such materials include highly pure quartz or silica sand, sodium and/or potassium carbonates of reactive grade, calcium phosphates containing no constitution water, less often, high-purity wollastonite (CaSiO₃), etc. Accurately weighed amounts of the ingredients are melted (usually in Pt or Pt/Rh crucibles), the melt being homogenized as required and care being exercised to avoid the loss of especially volatile components such as Na₂O and P₂O₅. The sol-gel process is frequently used starting from appropriate organic or inorganic soluble salts as raw materials (23) The melting temperature can range from 1200 to 1450 °C, depending on the particular composition. The melt is cast in graphite moulds, which do not contaminate or adhere to the glass, or in steel moulds. Annealing of the glass is essential with a view to suppressing the thermal stress generated during its casting and cooling, the optimum annealing temperature ranging from 400 to 550 °C depending on the glass composition.

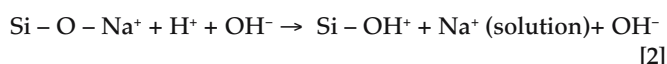
As a rule, bioactive glasses are fairly soft, so they can be shaped and sized as required by using appropriate diamond disks or wheels under heavy refrigeration. Powdered bioactive glasses can be obtained by grinding or by pouring the melted glass into water. The latter provides a frit that is easy to grind but must be rapidly dried in order to avoid hydrolytic corrosion.

2.2. Reactivity in physiological media

As noted earlier, for bioactive glasses to bond to bone tissue, a biologically active layer of carbohydroxyapatite (CHA) must be formed on the surface of the implanted material; this is probably the sole common feature of all bioactive materials known to date (24).

The ability of bioactive glasses to bond to bone tissue is a result of their chemical reactivity in physiological media. The underlying bonding mechanism was first reported by Hench (10) and involves the following steps:

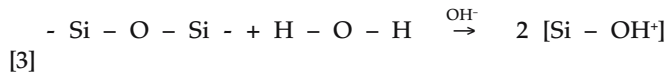
(1) Leaching through the exchange of protons from the physiological medium with labile network-modifying ions such as Na⁺, K⁺, Ca²⁺, Mg²⁺, etc.:



The reaction rate and the formation of silanol groups (Si-OH) at the bioactive glass/solution interface are diffusion-controlled and exhibits a $t^{-1/2}$ dependence. The cation-exchange process increases the concentration of hydroxyl ions at the bioactive glass/solution interface, thereby raising the pH to levels around 10.5 as shown by De Aza et al. (25) from interfacial pH measurements made with a microsensor (ISFET) on various bioactive materials.

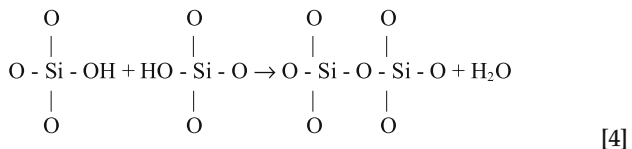
(2) The previous pH rise facilitates dissolution of the

network and formation of additional silanol groups according to the reaction:



as well as the loss of soluble silica as Si(OH)₄ that passes into the solution .

(3) Polymerization of the SiO₂-rich layer through condensation of neighbouring Si-OH groups, which produces a layer rich in amorphous silica:

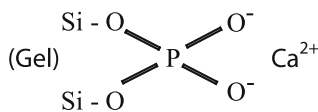


(4) Migration of Ca²⁺ and PO₄³⁻ ions to the surface of the silica-rich layer to form an amorphous film rich in CaO-P₂O₅, followed by thickening of the film by incorporation of soluble Ca²⁺ and PO₄³⁻ ions from the solution.

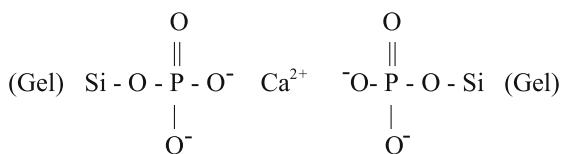
(5) Crystallization of the amorphous CaO-P₂O₅ film by incorporation of OH⁻, CO₃²⁻ or F⁻ ions from the solution, to form a carbohydroxyapatite or fluorocarbohydroxyapatite.

Step (4), which involves the migration of calcium and phosphate ions across the amorphous silica layer, in order to facilitate the nucleation of calcium and phosphate ions from the physiological medium, has been deemed unnecessary. Especially after Ohura et al. (15) and De Aza et al. (16-19) demonstrated the formation of a CHA layer on Ca-SiO₂ glasses and wollastonite (CaSiO₃) respectively, both of which contain no phosphate ions and bond to bone tissue (20, 21, 26 - 27).

Therefore, Karlsson et al. (28) concluded that, for glass to be bioactive, it must form a surface layer of amorphous silica. Silica gel provides a large number of sites with distances between -O-O- ions favoring chelation. Consequently, the chelation of phosphate ions by silica gel may thus be the initial step, calcium ions remaining bonded to phosphate ions through charge compensation as follows:



Later on, Anderson and Karlsson (29) modified the chelation hypothesis and suggested that an active site might hold two phosphate ions bonded to two separate silicon atoms, the former being bonded to a calcium ion as follows:



Based on the predominantly ionic character of the bond, the resulting complex cannot be considered a chelate. The effect inhibitor of the aluminium could be explained in this way, because when replacing this to the calcium it would give place to a more covalent bond and hence a true chelate.

One other, simpler hypothesis by De Aza et al. (25) is that the interfacial pH may result in precipitation of Ca²⁺

and PO₄³⁻ ions from the solution. This is consistent with the fact that no amorphous silica layer was detected between the CHA layer and the bioactive material in the A/W glass-ceramics developed by Kokubo et al. (30-32) or the pSW/α-TCP Bioeutectics® obtained by De Aza et al. (33-38).

2.3. Mechanism of bonding to living tissues

The surface of an implanted bioactive glass seemingly undergoes the five above-described steps irrespective of whether some tissue is present. However, for a bioactive glass to bond to a tissue a series of additional interfacial reactions, that are more ill-defined as a result of the poor knowledge about the biological processes involved, are required. According to Hench and Andersson (39), such interfacial reactions occur in the following sequence:

- (a) Adsorption of biological components on the CHA layer;
- (b) Action of macrophages;
- (c) Bonding of stem cells;
- (d) Differentiation of stem cells;
- (e) Generation of the matrix; and
- (f) Mineralization of the matrix.

Based on the analysis of the interface between Bioglass® and tissue (Fig. 3) conducted by Wilson et al. (40, 41), it was concluded that the bond was due to a combination of chemical and mechanical factors.

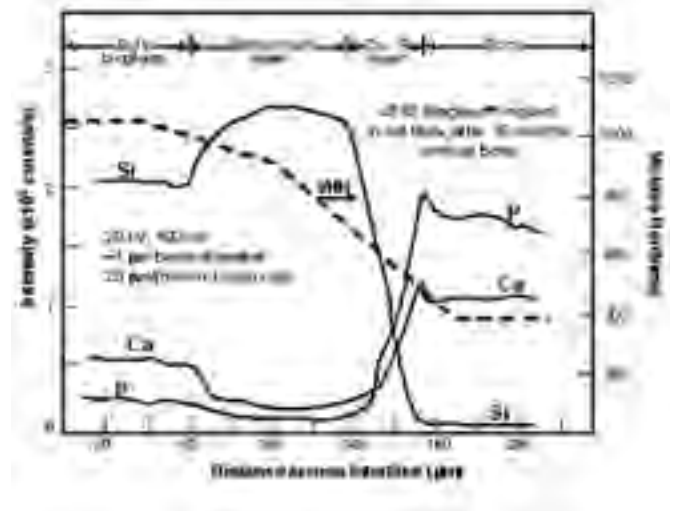


Fig. 3- EMP analysis of the Bioglass®45S5/bone interface (40).

Seemingly, collagen fibres provide scaffolding with the sites required for the micro-nucleation of apatite crystals (42), taking place an interdigitation of the collagen with the surface of the material (5). Apatite crystals grow epitaxially across the bone-implant interface; this means, in bone biology terms, that CHA crystals grow oriented along the collage fibres (43-46);. However, according to Davies (47), no unambiguous bonding mechanism has yet been proposed.

3. MECHANICAL STRENGTH OF THE BONE-IMPLANT INTERFACE

The mechanical strength of the interface between a bioactive glass and living tissue decreases with increasing thickness of the interface. Such a thickness is proportional to the bioactivity index (I_b) of the particular biomaterial (48). Thus, Bioglass® 45S5, which possesses a high I_b value, forms a 200 μm thick interface with a relatively low torsional strength. By contrast, the glass-ceramic Cerabone A/W®, with a medium I_b value, produces an interface 20-25 μm thick that possesses a high strength. The interfacial strength, S_f , can be calculated from the expression

$$S_f = c_1 d^{-1t^x} = c_2 I_b^{-1t^x}$$

where d is the interface thickness, I_b is the bioactivity index of the material, and c_1 , c_2 and t^x are three time-dependent variables. According to Hench (10), the optimum interfacial bond strength corresponds to an I_b value of ca. 4.

The interfacial strength is time-dependent and a function of morphological factors such as the variation of the interfacial area with time and the extent of mineralization of interfacial tissues, which increases the elastic modulus with time. Quantifying all these variables is quite a difficult task.

In many cases, the interfacial adhesion strength is comparable to, or even greater than, the strength of the biological material or the bone itself, so fracture occurs in the implant or bone, but hardly ever at the interface (49).

Hench et al. (50, 51) found that, if a Bioglass® implant, immobilized for a critical length of time, bonds to adjacent tissue, the strength of the bond is identical with that of healthy cortical bone.

Biomechanical measurements on femoral implants in primates (52, 53) have revealed that the bond between a ceramic implant coated with Bioglass® 45S5 and bone is so strong that fracture under a torsional force migrates across the implant or surrounding bone without breaking the implant-bone interface.

4. BIOACTIVE GLASS-CERAMICS

A glass-ceramic material is one that has been obtained by using an appropriate thermal treatment of glass that results in the nucleation and growth of specific crystal phases within the residual vitreous matrix.

The high interest of bioactive glass-ceramic materials, in the biomedical field, has been aroused by two interesting advantages. One is that such materials can be obtained in highly complex shapes; in fact, the first step of the process involves producing a glass that can be obtained by using a variety of well-known, inexpensive techniques, including casting, blowing, pressing or rolling. The other advantage is that, by effect of the subsequent crystallization of the glass, glass-ceramic materials usually possess a very fine microstructure, containing few or no residual pores, these features resulting in improved mechanical properties in the end-product.

However, the crystallization process requires a well-founded knowledge of the nucleation and growth mechanisms of the crystal phases. Figure 4 shows a sketch of the rates of crystal nucleation and growth as a function of

temperature. The rate of formation of the crystalline nuclei (i.e. the number of nuclei forming per unit volume and time) presents a maximum to a temperature that is strongly dependent on the particular mechanism but is usually close to the glass transition temperature (T_g), which corresponds to a viscosity of ca. $10^{13.3}$ Pa·s.

The growth rate of crystal nuclei, as a length per unit time, usually exhibits a maximum, around 100 °C below the liquidus temperature (T_L) and, as the temperature diminished, it drops to very low values by effect of the viscosity increasing as the glass transition temperature, T_g , is approached. As can be seen from Fig. 4, a broad temperature range usually exists below T_L where no nucleation occurs even if crystals grow at a substantial rate.



Fig. 4- Sketch of the rate of crystal nucleation (V_n) and growth (V_g) as a function of temperature. T_L denotes the liquidus temperature and T_g the glass transition temperature.



Fig. 5- Simplified scheme of the two-step thermal treatment used to obtain a glass-ceramic material.

Figure 5 depicts the typical scheme of a two-step process leading to the formation of a glass-ceramic material.

Once the vitreous material is at room temperature, it is heated at its optimum nucleation temperature. The heating rate used is not critical, but due care must be exercised to avoid large temperature gradients. A rate of 2 to 5 °C/min is typically employed, the specific choice depending on the size of the starting product. It is convenient a high nucleation rate, preferably near the maximum, whose temperature stays constant for a certain time. Alternatively, the glass can be directly cooled to the nucleation temperature once shaped (dotted line in Figure 4).

The next step is critical. The temperature must be raised slowly usually at no more than 5 °C/min in order to avoid any stress due to volume change during crystallization, which could result in cracking or even fracture of the material. Slow heating facilitates suppression of such stress via viscous flow in the residual glass, the material becoming increasingly rigid as the crystal fraction increases. Once the "growth" temperature is reached, it is held for the time required to achieve the desired degree of crystallinity. Finally, the glass-ceramic product is cooled to room temperature.

Depending on the particular glass composition, crystallization can start at the surface and occur unevenly in the material, leading to products of low strength. Volume nucleation can be ensured and an appropriate microstructure obtained by using additives: nucleating agents. The additive usually consists of metal particles (Cu, Ag, Au, Pt) or a metal oxide (SnO₂, Ce₂O₃, TiO₂), which act favoring the heterogeneous nucleation of the crystal phases.

In the field of the glass-ceramics for biomedical applications, P₂O₅, which is an ingredient of all of them, has the same nucleation properties as TiO₂.

4.1. Bioactive glass-ceramic compositions

Most biomedical glass-ceramics are based on compositions similar to those of Hench's bioactive glasses (Bioglass®)(54), however, all of them have very low contents in alkali oxides. Table III summarizes the properties of bioactive glass-ceramics used in the clinical field as compared to those of Bioglass® 45S5.

Ceravital®

The earliest glass-ceramic material of clinical use was developed by Brömer and Pfeil in 1973 (55, 56) and named Ceravital®. This designation, however, includes a wide range of glass-ceramic compositions. Originally, Ceravital® was believed to possess extraordinary properties as a replacement material even for bone in loaded zones and teeth. However, as can be seen from Table III, their mechanical properties, even for the optimum compositions, they are below the 160 MPa of the human cortical bone and are similar to those of sintered dense hydroxyapatite (115 MPa).

Also, long-term in vivo tests questioned the stability of these materials. However, subsequently Gross et al. (57, 58) developed improved compositions, the solubility of which was reduced by using various metals as nucleating agents.

The bioactivity of Ceravital® is roughly one-half that of Bioglass® 45S5 (5.6 versus 12.5). At present, Ceravital® implants are exclusively used to replace the ossicular chain in the middle ear, where loads are minimal and the mechanical properties of this material are thus more than adequate.

Cerabone® A/W

One of the glass-ceramics of more clinical success, be probably the denominated A/W, which is constituted by two crystalline phases: oxyfluorapatite Ca₁₀(PO₄)₆(O,F₂) and wollastonite (β- CaSiO₃) and a residual vitreous phase. This was originally developed by Kokubo et al. (30-32, 59, 60) and is commercially available under the trade name Cerabone® A/W. Its composition is shown in the Table III.

After some failed attempts of producing a glass-ceramic

of the Ca₃(PO₄)₂-CaSiO₃-MgCa(SiO₃)₂ system, starting from a monolithic glass or even powdered glass, the glass-ceramic A/W was obtained by adding a small amount of CaF₂ to the original composition. Glass ground to an average particle size of 5 μm was isostatically pressed at 200 MPa in the desired shapes and thoroughly densified at ca. 830 °C, which resulted in the precipitation of oxyfluorapatite and β-wollastonite at 870 and 900 °C, respectively. The end-product was thus a glass-ceramic with a very fine microstructure free of cracks and pores.

TABLE III. COMPOSITION AND SELECTED PROPERTIES OF GLASS-CERAMICS WITH CLINICAL APPLICATIONS AS COMPARED TO THOSE OF BIOGLASS 45S5*

Compound (wt%)	Bioglass® 45S5.	Ceravital®	Cerabone® A/W	Ilmaplant®	Bioverit®
Na ₂ O	24.5	5-10	0	4.6	3-8
K ₂ O	0	0.5-3.0	0	0.2	0
MgO	0	2.5-5	4.6	2.8	2-21
CaO	24.5	30-35	44.7	31.9	10-34
Al ₂ O ₃	0	0	0	0	8-15
SiO ₂	45.0	40-50	34.0	44.3	19-54
P ₂ O ₅	6.0	10-50	6.2	11.2	2-10
CaF ₂	0	0	0.5	5.0	3-23
Phases	Glass	Apatite + Glass	Apatite + β-wollast. + Glass	Apatite + β-wollast. + Glass	Apatite + Flogopite + Glass
Flexural Strength σ _f (MPa)	42	100 – 150	220	170	100 – 160
Compressive Strength (Mpa)	n.d	500	1060	n.d	500
Young's Modulus (GPa)	35	n.d	117	n.d	70 - 88

n.d = not determined

The special microstructure of this glass-ceramic endows it with the best mechanical properties among all the materials shown on Table III; thus, its σ_f (220 MPa) is nearly twice that of dense hydroxyapatite (115 MPa) and exceeds that of human cortical bone (160 MPa). In addition, its tenacity is ca. 2.0 MPaAm^{-1/2} and its Vickers hardness about 680 HV (61,62).

Equally that in the bioactive glasses, an apatite layer is formed on the surface of the glass-ceramic A/W in simulated body fluid and it is also attributed to this layer the capacity of joint to bony tissue. Due to the chemical and structural characteristics of this CHA, similar to the bony tissue, it is of expecting that, in the interface with the bone, proliferate the osteoblasts preferably to the fibroblasts.

However, unlike bioactive glasses, no amorphous silica layer between the carbohydroxyapatite (CHA) and the A/W glass-ceramics has been observed not even by high-resolution electron microscopy. In any case, Kokubo and coworkers believe that silanol groups formed at the glass-ceramic surface are those responsible for the formation of the CHA layer as they provide the favourable sites required for its nucleation and growth. Their hypothesis relies on the following mechanism for the formation of the CHA layer on A/W glass-ceramics: dissolution of calcium ions from the

glass-ceramic surface increases the ionic activity product of apatite in the simulated body fluid, while hydrated silica at the glass-ceramic surface provides favourable sites for CHA nucleation (see Fig. 6).

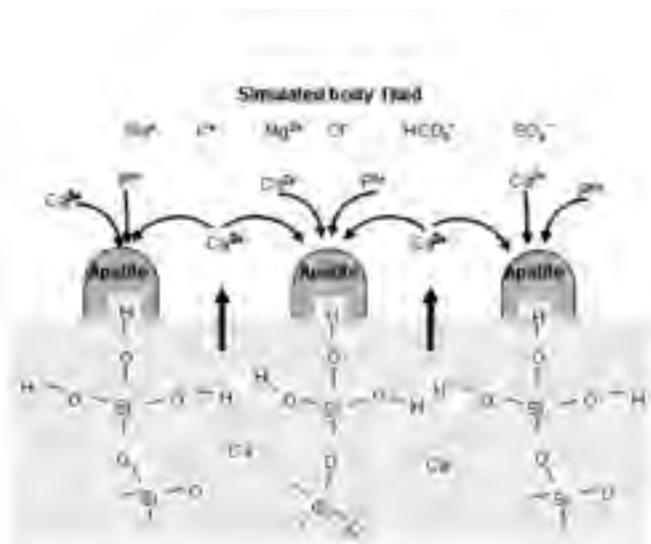


Fig. 6- Mechanism for the formation of the apatite layer on A/W glass-ceramic according to Kokubo et al.(32).

As a result, CHA nuclei rapidly form on the glass-ceramic surface. Once the first few nuclei have formed, they grow consuming calcium and phosphate ions from the simulated body fluid spontaneously. Although no amorphous silica layer has been found on the surface of A/W glass-ceramics, the fact that a substantial amount of silicate ions are dissolved in the SFA suggests that a large number of silanol groups are formed at the A/W glass-ceramic surface (30).

Like Hench et al., Kokubo et al. believe that silanol groups constitute favourable sites for CHA to nucleate in both glass-ceramics and bioactive glasses. However, these authors do not consider the effect of the interfacial pH on the formation of the CHA layer, as has been suggested by De Aza et al. (25). The interfacial pH is a result of the interchange of protons from the simulated body fluid with labile ions from the vitreous network.

Although its bioactivity index, $I_B = 3.2$, is roughly one-fourth that of Bioglass® 45S5 ($I_B = 12.5$), it is slightly higher than that of dense sintered hydroxyapatite ($I_B = 3.0$). Upon implantation in a bone defect, A/W glass-ceramic forms a Ca- and P-rich layer through which it bonds to bone. Bonding is so strong that tensile fracture never occurs at the A/W-bone interface, but rather in the bone. The Ca- and P-rich layer has been identified by X-ray microdiffraction to consist of apatite (Fig. 7).

The good biocompatibility, bioactivity and mechanical properties of this glass-ceramic which facilitate its machining with diamonds discs and drills have fostered its use in reconstructing iliac crests, vertebrae and intervertebral discs and, in granules form, in filling in bone defects, since the 1980s.

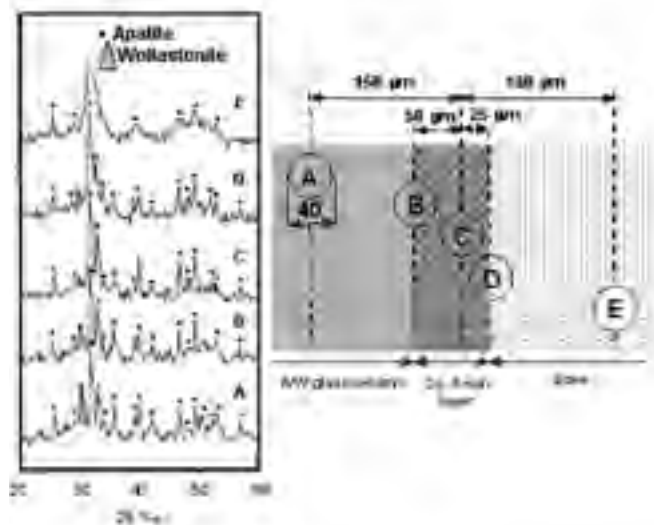


Fig. 7- X-ray microdiffraction pattern for the A/W-bone interface (32).

Ilmaplant-L1®

Berger et al. (63) developed this implant, which consists of apatite/wollastonite glass-ceramic. As can be seen from Table III, it differs from A/W glass-ceramics in its alkali contents; increased proportions of CaF_2 , SiO_2 and P_2O_5 ; and decreased content in CaO . Because of its low mechanical bending strength (see Table III), its use is restricted to maxillofacial implants.

Bioverit®

In 1983, Holand et al. (64), of the University of Jena, developed a new series of bioactive glass-ceramics, which they called Bioverit® I (Table III). Bioverit® glass-ceramics can be readily machined with standard tools and even retouched in the operating theatre. These materials are obtained from a silicate-phosphate glass of complex composition in the SiO_2 - Al_2O_3 - MgO - Na_2O - K_2O - F - CaO - P_2O_5 system. The procedure involves generating phase separation in the glass, through controlled nucleation and subsequent growth of the crystalline phases, by thermal treatment at 610 y 1050 °C. The resulting product consists of residual glass plus a mixture of apatite crystals (1-2 μm in size) and a fluoroflogopite-like mica ($\text{Na/KMg}_3[\text{AlSi}_3\text{O}_{10}\text{F}_2]$) which facilitates machining of the material.

Subsequently, the same authors developed another family of also readily machined glass-ceramics, which they called Bioverit® II. As can be seen from Table IV, the new materials contained very little P_2O_5 relative to Bioverit® I. Like its predecessor, Bioverit® II contains fluoroflogopite-like mica, (whose crystals present a curved morphology that are not encountered in nature), in addition to other crystalline compounds, specially prominent among of cordierite ($\text{Mg}_2[\text{Si}_5\text{Al}_4\text{O}_{14}]$).

Finally, Vogel and Hölland (65, 66) developed a further family of glass-ceramics named Bioverit® III (see Table IV) from a phosphate glass containing no silica. To this end, they used a inverted phosphate glass in the P_2O_5 - Al_2O_3 - CaO - Na_2O system, consisting of mono- and diphosphate

structural units and doped it with Fe_2O_3 or ZrO_2 . The end product consisted of residual glass in addition to apatite, berlinite (AlPO_4) and complex structures of phosphates of the varulite-like type (Na-Ca-Fe phosphate).

TABLE IV. COMPOSITION AND SELECTED PROPERTIES OF THE BIOVERIT® TYPES II AND III

Compound	Bioverit® II (wt%)	Bioverit® III (wt%)
SiO_2	43 – 50	---
Al_2O_3	26 – 30	6 – 18
MgO	11 – 15	---
$\text{Na}_2\text{O}/\text{K}_2\text{O}$	7 – 10.5	11 – 18
F	3.3 – 4.8	---
Cl	0.01 – 0.6	---
CaO	0.1 – 3	13 – 19
P_2O_5	0.1 – 5	45 – 55
$(\text{MeO}/\text{Me}_2\text{O}_5/\text{MeO}_2)^*$	---	1.5 – 10
Density (gr/cm^3)	2,5	2.7 – 2.9
Coefficient of Expansion (K^{-1})	$7.5 - 12 \cdot 10^{-6}$	$14 - 18 \cdot 10^{-6}$
Flexural strength (MPa)	90 – 140	60 – 90
Toughness (K_{IC}) ($\text{MPa}\cdot\text{m}^{1/2}$)	1.2 – 1.8	0.6
Young's Modulus (GPa)	70	45
Compressive strength (MPa)	450	---
Vickers hardness (HV 10)	up to 8000	---
Hydrolytic Class (DIN 12111)	1 - 2	2 – 3
Roughness (after polishing) (μm)	0.1	---

* (MnO , CoO , NiO , FeO , Fe_2O_3 , Cr_2O_3 , ZrO_2)

The contents in crystalline phases and vitreous matrix in Bioverit® glass-ceramics can be modified with a view to modulating their physical properties and bioactivity by changing the ingredient contents within the composition ranges shown in Tables III and IV. Thus, translucence in these materials is a function of the proportion of crystal phases, whereas machinability depends on their mica content (e.g. Bioverit® II is easier to machine than is Bioverit® I). In addition, the material colour can be modified by addition of small amounts of oxides such as NiO , Cr_2O_3 , MnO_2 , FeO , Fe_2O_3 , etc.

By the mid-1990s, more than one thousand bone replacement implants had been successfully fitted in various biomedical fields including orthopaedic surgery (e.g. acetabular reconstruction, vertebral replacement, tibial head osteoplastic, joint plastic surgery) and head and neck surgery (middle ear implants, orbital base repair, cranial base reconstruction, rhinoplasty, etc.).

5. BIOACTIVE GLASS COATINGS AND COMPOSITES

As noted earlier, the greatest constraint on a wider use of bioactive glasses and glass-ceramics is derived from their relatively poor mechanical properties, especially in zones under mechanical loads. This shortcoming has been circumvented by using various methods to increase the strength of these glass materials and facilitate their use as implants.

One solution to the problem is using bioactive glasses as a coating for materials with a high mechanical strength. This method has been used with a number of substrates, including dense alumina (67, 68), various types of stainless steel (69, 70), cobalt-chromium alloys (71) and titanium

alloys (72-77). This last alloy is especially attractive on account of its high strength, low elasticity modulus and good biocompatibility. The methods used to prepare the coatings range from immersion in the molten glass or in a solution, suspension or gel (dip coating); electrophoresis from a solution or suspension (the metal to be coated acting as an electrode), biomimetic coating growth or flame or plasma spraying. The last choice is the most widely used at present to deposit a bioactive glass onto a metal substrate.

One other application of bioactive glasses is in the production of composites, being reinforced the bioactive glass with a second phase. The materials thus obtained include "biofibre glass" and alumina, organic polymers or metal fibres. The former has fallen short of the original expectations as it seemingly releases large amounts of alumina powder that are detrimental to tissues. The materials reinforced with metal fibres are those with the strongest potential. In fact, metal fibres strengthen bioactive glasses and improve their deformability. The most widely used procedure for producing these materials is hot pressing (78, 79).

Ducheyne and Hench (80) reported a composite material consisting of Bioglass® 45S5 and metal fibres of AISI 316L stainless steel. The material, which was prepared by immersing the metal fibres in molten glass, exhibited improved mechanical strength and ductility, in addition to a Young modulus comparable to that of human cortical bond.

Other glass-based composite materials include Ceravital® reinforced with titanium particles (81) and A/W glass-ceramic reinforced with partially stabilized zirconia (82) or polyethylene (83).

The essential requirements for these composite materials to be useful as dental implants or in orthopaedic applications are a low elasticity modulus, good deformability, good tensile strength and good impact resistance and ready machining.

6. CLINICAL USES OF BIOACTIVE GLASSES AND GLASS-CERAMICS

Some uses of bioactive glasses and glass-ceramics have been described above in dealing with various aspects of these materials. Interested readers are referred to the comprehensive reviews by Gross et al. (57), Hench and Wilson (5), and Yamamuro (84, 85), for a wider description.

Bioglass® is typically used in implants intended to preserve the alveolar chain or partly or completely replace the ossicular chain of the middle ear in patients with chronic otitis. Merwin et al. (86) have demonstrated the long-term stability of these implants resulting from their bonding to the tympanic membrane.

After eight years of clinical use of Ceravital®, Reck et al. (87) concluded that this material provides the most effective prostheses for complete reconstruction of the ossicular chain.

The use of A/W glass-ceramic prostheses for iliac crest reconstruction has so far provided clinically and radiologically acceptable results (84).

Animal testing has shown that Bioglass® coatings are useful to obtain durable hip prostheses by effect of combining high bioactivity and mechanical strength, which avoids of using bony cement to attach implants to bone.

Table V summarizes the most common uses of the different types of bioactive glasses and glass-ceramics in various presentation forms.

TABLE V. BIOACTIVE GLASSES AND GLASS-CERAMICS AND THEIR CLINICAL APPLICATIONS

PRESENTATION	MATERIAL	CLINICAL APLICATION
Dense materials	Bioglasses	Maxillofacial reconstruction Middle ear reconstruction Junction of spinal vertebrae Dental implants Percutaneous access devices
	Glass-ceramics	Dental implants Maxillofacial reconstruction Vertebral prosthesis devices Iliac crest prostheses
Porous materials	Bioglasses (porous surfaces)	It doesn't have any application until today
Coating	Bioglasses on Al ₂ O ₃ (high density)	Maxillofacial reconstruction Middle ear reconstruction Junction of spinal vertebrae
	Bioglasses on stainless steel	Hip articulation prostheses Attachment of artificial members to the bone Isolation of neuronal electrodes
	Bioglasses on Ti or Ti-alloys	Bone prostheses
Composites	Al ₂ O ₃ + Bioglasses	It doesn't have any application until today
	Polymers + Bioglasses	Joints of soft tissues/bone. Cements.

ACKNOWLEDGEMENTS

The authors wish to acknowledge funding from Spain's CICYT within the framework of Projects MAT2003-08331-C02-01-02 and MAT2006-12749-C02-01-02 and Generalitat Valenciana (GVA) ACOMP06/044.

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Recibido: 20.11.06

Aceptado: 23.01.07

