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A R T I C U L O

Main Contributions to Bioceramics by Salvador De Aza

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A full compilation of Salvador De Aza works on biomedical materials is a huge task beyond the aim of this paper; instead it is intended to stand out De Aza's thoughts and leadership in the field of Bioceramics and to pay tribute to his memory. The most outstanding works of Professor Salvador De Aza related to Bioceramics, from the point of view of the authors, are commented and discussed.
Topics the authors chose among many other De Aza's works on biomedical materials are: The prediction and demonstration of bioactivity in pseudo-wollastonite ceramics; the use of phase diagrams to design bulk-bioactive ceramics with eutectic microstructures; the relationship between bioactivity and microstructure in ceramic biomaterials; and the studies on the polymorphic phase transitions in tricalcium phosphate.

Keywords: Bioceramics, Bioeutectic, Wollastonite, Pseudowollastonite, Tricalcium Phosphate, Microstructure, Polymorphic Transformation

Las principales contribuciones de Salvador de Aza a las Biocerámicas

Una recopilación completa de la obra de Salvador De Aza sobre materiales biomédicos es una tarea enorme más allá del objetivo de este trabajo, que está destinado a destacar sus enfoques y liderazgo en el campo de las Biocerámicas y rendir merecido tributo a su memoria. Para ello se discuten y comentan aquellos trabajos del Profesor Salvador De Aza sobre Biocerámicas que a juicio de los autores resultan más sobresalientes. Entre muchos otros trabajos de De Aza sobre materiales biomédicos, los autores han elegido los siguientes tópicos: la predicción y demostración de la bioactividad de las cerámicas de pseudo-wollastonita; el uso de diagramas de fase para el diseño de materiales bioactivos en masa con microestructura eutéctica; y sus estudios sobre la transición polimorfica de fases en el fosfato tricálcico.

Palabras Clave: Biocerámicas, Bioeutectic, Wollastonita, Pseudowollastonita, Fosfato tricálcico, Microestructura, Transformación polimórfica

1. INTRODUCTION

Half a year has passed since the sudden and unexpected decease of Professor Salvador De Aza, time enough to digest pain and sadness and to recover the serenity needed to recall his thoughts and works related to the field of Bioceramics and attempt to review and resume it.

Salvador De Aza is well known among ceramists from Europe, North America and even Asia for his scientific and technical works on theoretical and experimental studies of phase equilibrium diagrams and their application to the development of materials exhibiting specific properties, and the application of the scientific methods to ceramic industry. In fact, it has been recognised that the S. De Aza decisively contributed to the blooming that Spanish ceramic industry experienced since the 1970s till the first years of the present century (1).

However, themes related to conventional ceramics do not predominate evidently when S. De Aza's scientific production is analysed. Forty three per cent of his papers referenced by the Web of Knowledge deals on Biomaterials and the percentage increases to 53 when the last 20 years are considered. Moreover, the most popular of his papers (more than a hundred citations) reports the *in vitro* evaluation of the bioactivity of pseudowollastonite bioceramic (2), and more than a half of those with 20 or more citations are related to Bioceramics too, which indicates the professional interest he devoted to the subject.

The first encounter of Prof. De Aza with biomedical materials happened during the Course on "Biomaterials and Biocompatibility: Materials, Techniques and Applications" held at Pazo de Mariñan, A Coruña, Galicia, in June 1990. The course was organised by De Aza's closest friend J. Espinosa with the support of CSIC and the UE-Comett I Programme. Spanish scientists from Materials Science, Medicine and Dentistry fields were gathered up for almost a week and attended a series of lectures on hot topics on Biomaterials and Biocompatibility. After the lectures, discussion was promoted between Materials Science and Medicine scientists. From these discussions and exchange several collaboration actions arose, some of them lasting till present day. Most of attendants to that course agree in considering it a milestone in research and development of biomedical materials in Spain (3). Soon afterward Salvador De Aza started his works on wollastonite bioceramics and its eutectic composition with tricalcium phosphate jointly with her daughter P. N. De Aza and F. Guitian from the Instituto de Cerámica de Galicia, University of Santiago de Compostela. Besides, he brought the staff of his

team of Phase Equilibrium Diagrams and Refractories at the Instituto de Cerámica y Vidrio, CSIC, in Bioceramics research. All of his works on the subject are characterized by the good use of his sound knowledge on physical chemistry of silicates to design materials with the desired structure and properties.

An attempt to summarize Prof. De Aza's main contributions related to Bioceramics is provided below.

2. PSEUDOWOLLASTONITE: THE FIRST POLYCRYSTALLINE CERAMIC REPORTED AS BIOACTIVE

At the beginning of 1990 glasses and glass-ceramics mainly constituted of CaO, P_2O_5 and SiO_2 were the only known materials exhibiting *in vitro* type A bioactivity (4-7). In 1991 Ohura et al. showed that a P_2O_5-free CaO-SiO_2 glass was also able to develop an apatite (Ap) layer on its surface after soaking in simulated body fluid (SBF) (8).

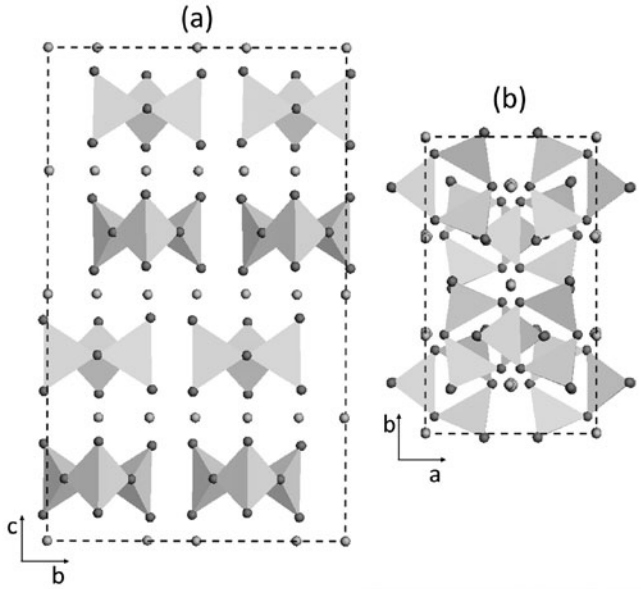

Fig. 1. (a) The psW unit cell showing the layering feature of Ca atoms and Si_3O_9 ternary rings along the c axis. (b) Projection along c-axis of the unit cell of psW displaying Ca atoms stacking in columns parallel to c-axis.

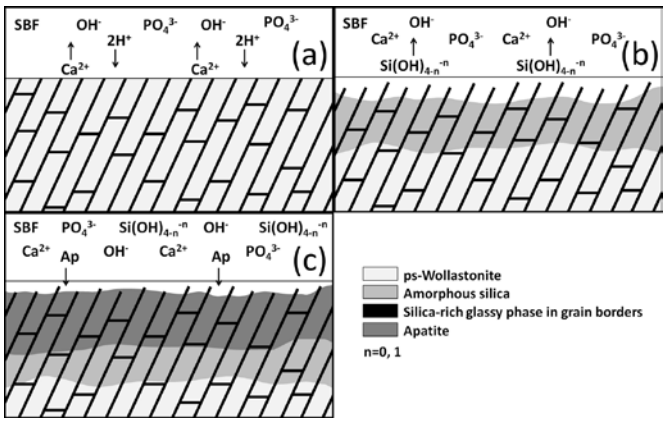

Fig. 2. Schematic representation of the mechanism for Ap formation on polycrystalline pseudowollastonite bodies (Redrawn from (12)).

S. De Aza et al. were the first to demonstrate that polycrystalline silicate-based ceramics may also be bioactive. The silicate chosen was pseudowollastonite (psW; ps$CaSiO_3$), a polymorph of $CaSiO_3$ stable above 1030 ºC to the melting point, which may exist in metastable state at room temperature.

The selection of psW was not arbitrary. S. De Aza used to point out that empiricism was the main shortcoming in the works of Hench (4) and Kokubo (5) conducting to Bioglass® and Cerabone A/W® glass-ceramic, respectively. In contrast, De Aza et al. chose psW because of its crystalline structure, keeping in mind that type A bioactive materials bond directly to bone through a surface apatite (Ap) layer formed by a complex process which starts with the exchange of H_3O^+ ions from the environment for labile Na^+, K^+, Ca^{2+}, Mg^{2+}, etc., ions existing in the glass or glass ceramic matrix. The monoclinic (C2/c) unit cell of psW is constituted of four layers, each of which is composed of alternate layers of Si_3O_9 tetrahedral rings and Ca atoms, parallel to ab-plane (see Fig. 1a). Besides, Ca atoms are disposed in columns oriented along c-axis and contained in the channels left between SiO_4 tetrahedra (Fig 1b) (9).

The rational was that such structure should permit a fast diffusion of H_3O^+ ions from physiological fluid inside the crystal and its exchange with Ca ions as required for starting the Ap layer formation on the surface of bioactive materials. The idea was supported by existing reports on the dissolution of natural wollastonite-2M (W-2M, $CaSiO_3$-2M), which proceeds in a similar way (10, 11).

In 1994 appeared the first report by De Aza et al. on the *in vitro* bioactivity exhibited by psW (2,12). They observed the formation of a surface Ap layer of psW polycrystalline ceramic when soaked in a solution of SBF. They stated that at the beginning of the reaction of psW with physiological fluid an ionic exchange of Ca^{2+} for $2H^+$ takes place in the psW network, which is supported by the results of Weissbart and Rimstidt, and Bailey and Ressman (10, 11) (Fig. 2a). This step is controlled by diffusion of the ionic species through the solution film in contact with the surface of the ceramic: the release of Ca^{2+} decreases as interfacial pH increases. As a result of the above ionic exchange the crystalline psW network in the surface layer transforms into an amorphous silica phase and the Ca^{2+} and OH^- concentrations in the solution increase (Fig. 2b). These conditions induce partial dissolution of amorphous silica (probably as H_4SiO_4 and $H_3SiO_4^-$ species (14)) and subsequent precipitation of Ap (Fig. 2c). Reaction goes on until the formed Ap layer hinders the ionic exchange (2, 12, 13).

Subsequent works showed that psW manifests *in vitro* bioactivity also in human saliva (15) and it was soon confirmed that it is also a type A bioactive material *in vivo*. Implantation studies conducted in rat tibiae showed that new bone was growing in direct contact with the implants. Osteoblastic cells migrated towards the implant-tissue interface and colonized the surface at the contact areas with the cortical and bone marrow. The new bone formed was fully mineralized and after 12 weeks the bone-implant interface active remained biologically and chemically active (16).

S. De Aza always recognized the relevance of the early works of E. M. Carlisle (17-19) on the role of silicon in bone metabolism and mineralization, which laid the foundations for the more recent findings on ostegenesis and angiogenesis produced by the dissolution products of Bioglass® (20, 21).

De Aza et al. supposed that the dissolution products of psW act in a similar way and they performed a series of studies employing acellular and cellular *in vitro* models to proof their thesis. They found that neither significant alteration of membrane integrity nor signs of cell suffering were detected when human osteosarcoma cells were cultured in presence of extracts of psW in culture medium. However, increased cell metabolism did was observed for cultures made with extracts corresponding to the longest extraction time (22).

Furthermore, when rat calvarial osteoblasts were cultured in the presence of psW ceramic they adhered rapidly to the psW surface and this process seemed to be aided by the binding of serum proteins to the surface Ap layer. Additionally, a novel phenomenon was observed whereby osteoblasts far away from the material changed its phenotype, which reinforced the suggestion that the release of soluble factors as well as direct interaction of osteoblasts with the surface of the material may mediate the osteogenic effects of bioactive psW ceramic (23).

De Aza et al. developed effective solid state synthetic and analytical methods to prepare and characterize psW ceramic (24) and the products of its surface reaction with SBF (25-27). They also evaluated the feasibility to employ natural W-2M as a cheaper precursor for obtaining psW ceramics (28, 29).

3. BIOEUTECTIC®: THE FIRST BULK-BIOACTIVE MATERIAL

Bioactive ceramics, bioglasses, and glass-ceramics have succeeded for several decades for bone repairing applications. They are capable to bond tightly to bone; however they are not fully replaced by new bone. The dissolution-precipitation processes responsible for the formation of the Ap layer proceed only in a relatively thin surface layer, the bulk of the material remaining unchanged. The golden standard for bone repairing is a material such as it gradually reabsorbs at the same rate that new bone grows, so that it is completely replaced by new bone after an appropriate period of time.

Macroporous scaffolds are recommended to achieve complete colonization and integration of the implant to bone, however, the low strength of macroporous materials during the initial implantation period, when the new formed tissue has not colonized the porous implant yet, limits their applications to low stress bearing situations (30).

De Aza et al. proposed a new approach to overcome this problem which consists in a dense and strong bioactive ceramic capable to degrade and to develop a porous structure *in situ* after implantation. Such a material should be composed of at least two phases, one bioactive and the other resorbable (30-34). S. De Aza knew very well the thermodynamic and kinetic rules of binary systems with and eutectic invariant point. In a binary system a solid crystalline microstructure consisting of discrete and distinguishable domains of both phases is obtained when solidifies a melt with the eutectic composition (35). The connectivity of the resulting structure is generally 1-3 or 2-2 (36), being the last the most common (35).

After reviewing several systems and on thermodynamic basis, they selected the binary system wollastonite-tricalcium phosphate ($CaSiO_3$-$Ca_3(PO_4)_2$) where an invariant eutectic point exists. This way a eutectic microstructure consisting of psW and α-$Ca_3(PO_4)_2$ (α-tricalcium phosphate; α-TCP) may be obtained that fulfills the requirement mentioned above: to be composed of a resorbable phase (α-TCP) and a bioactive one (psW). De Aza et al. studied the system and found the exact eutectic composition and temperature are $CaSiO_3$ 60 wt.-%, $Ca_3(PO_4)_2$ 40 wt.-%, and 1402 ± 3 ºC, respectively (37). Then they prepared a ceramic material with a microstructure formed by rounded colonies (rosettes) by slow solidification of a melt with the eutectic composition, under a radial gradient of heat extraction (31-34, 38).

Figure 3 shows a Scanning Electron Microscopy (SEM) photograph of the microstructure of the eutectic material comprising *quasi*-spherical colonies formed by alternating lamellae of psW and α-TCP. The colonies or rosettes are always embedded in psW because of the greater volume fraction of this phase. The new material was called Bioeutectic and the mark was registered at the Oficina Española de Patentes y Marcas under file M 1780697.

De Aza et al. observed fast increase of the concentration dissolved Si when Bioutectic® was soaked in SBF corresponding to dissolution of psW lamellae. On the other hand Ca and P concentrations slowly increased and decreased, respectively. At the same time they observed the formation of a typical Ap layer on the surface of the material (Fig. 4). The study

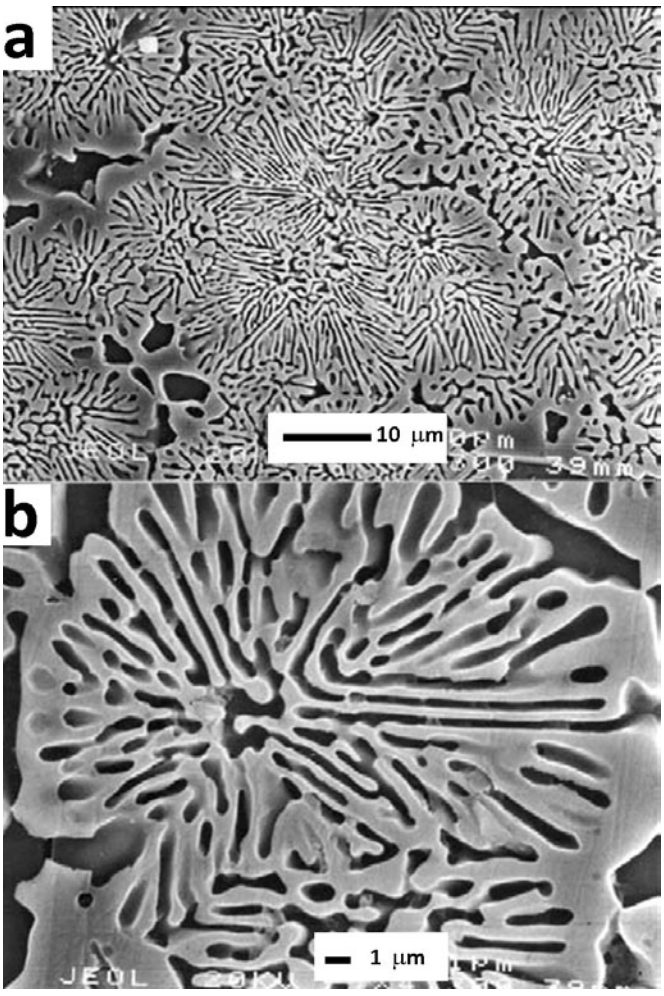

Fig. 3. SEM micrograph of Bioeutectic® after etching in diluted acetic acid. (a) General view; (b) Detailed view of a colony. Dark areas correspond to empty spaces left by α-TCP which dissolves during acid etching (from S. De Aza personal files).

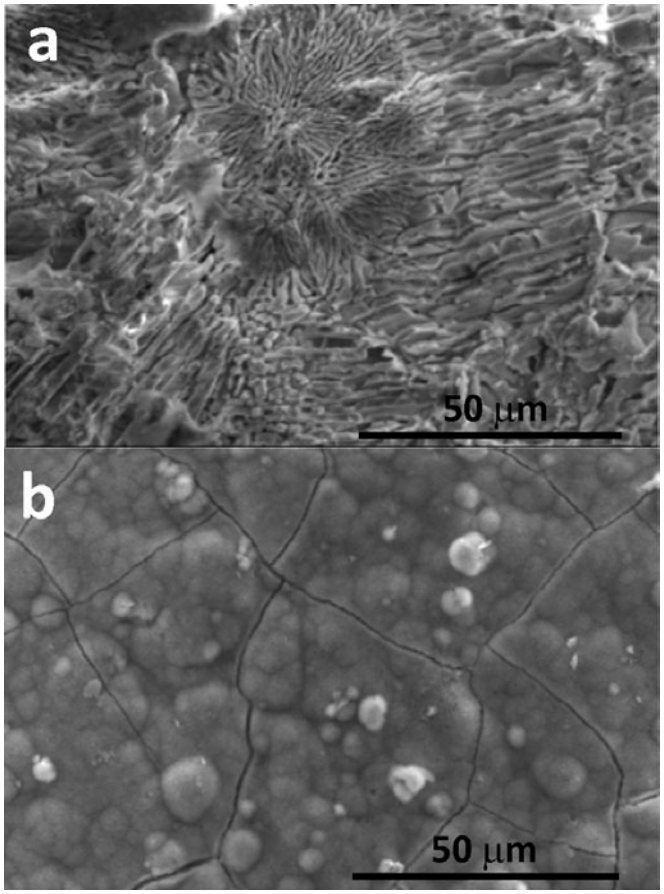

Fig. 4. SEM images of the surface of Bioeutectic® after immersion in SBF for (a) 1 week; and (b) 2 week (Reproduced from (40).

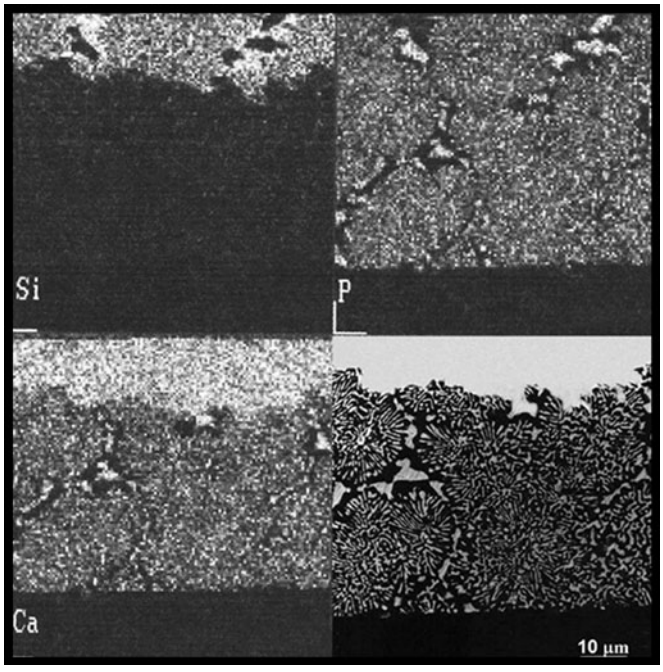

Fig. 5. SEM micrograph of a cross section of Bioeutectic® material after soaking in SBF for 1 week and the corresponding Si, P. and Ca X-ray maps (from S. De Aza personal files).

of polished cross sections of Bioutectic® after 1 week in SBF by SEM and Energy Dispersive X-Ray Spectroscopy (EDS) confirmed that psW dissolves rapidly and remains a porous calcium phosphate phase as shown in Fig. 5. (31-34). To identify the nature of the remaining calcium phosphate phase they made good use of their studies on Raman spectra of calcium phosphates (25-27) and found that poorly crystallized Ap was the remaining phase after Bioeutectic® reacted with SBF for 1 week.

Thus, the experimental findings contradicted the hypothesis they employed during the initial design of the material, i. e. psW was the resorbable phase instead of α-TCP, which *in turn* was the one that transformed into Ap. They explained the experimental facts with the mechanism schematized in Fig. 6. Ion exchange of Ca^{2+} for H_3O^+ takes place at the psW lamellae with the consequent formation of a layer of amorphous silica and increase in pH at the interface SBF-Bioeutectic®. As a result of the increase in pH amorphous silica dissolves leaving channels where fresh SBF penetrates to continue the process of dissolution of psW. As psW dissolves the channels left between α-TCP lamellae become deeper and pH increase because of diffusion is restrained.

These conditions favor the pseudomorphic transformation of α-TCP to Ap according to the reaction of Eq. 1.

$$3\alpha - Ca_3(PO_4)_2 + (1-x)Ca^{2+} + (2-2x)OH^- + xH_2O \rightarrow Ca_{10-x}(HPO_4)_x(PO_4)_{6-x}(OH)_{2-x}$$

Eq. 1

At the same time Ap layer is formed on the surface of Bioeutectic® as result of the reaction of Eq. 2.

$$6HPO_4^{-2} + (10-x)Ca^{2+} + (8-2x)OH^- \rightarrow Ca_{10-x}(HPO_4)_x(PO_4)_{6-x}(OH)_{2-x} + (6-x)H_2O$$

Eq. 2

As the surface Ap layer becomes thicker the inner reaction is slowed down until it finally stops (31-34).

Bioeutectic® reacted in a similar way when SBF was substituted by human parotid saliva but in lesser extension

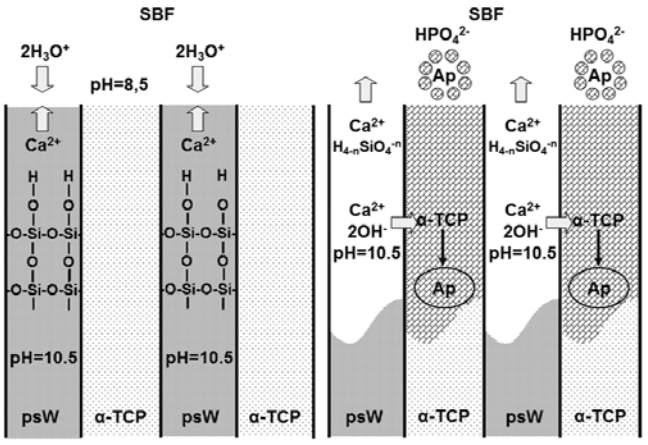

Fig. 6. Schematic representation of the mechanism of Ap formation in Bioeutectic during immersion in SBF. n=0, 1 (Redrawn from (31)).

and the resulting Ap phase presented partial substitution of CO_3^{2-} for PO_4^{3-} as evidenced the μ-Raman spectra (39).

On the other hand, De Aza et al. realized that the *in vitro* bioactivity test based in soaking the material in static fluids does not reproduce the actual *in vivo* conditions, where physiological fluids circulate continuously and its composition is kept invariable through homeostasis. They designed a dynamic test consisting in immersing the material in a slow stream of SFB (50 cm3/h) instead of using a static solution. In these conditions ions dissolved from the psW surface can easily leave the sample surface and diffuse into the SBF solution. The concentration of ionic Ca at the sample surface concentration is approximately the same than in the bulk of SBF and supersaturation is not reached, thus preventing nucleation and precipitation of Ap on the outer surface of the material through the reaction of the Eq. 2. However, high concentrations of Ca^{2+} and OH^- can be reached in the channels formed after dissolution of psW, and α-TCP reacts pseudomophically into Ap according to the reaction of Eq. 1 rendering an apatitic porous structure similar to that of cancellous bone as shown in Fig. 7 (40).

The above results supported the statement S. De Aza use to issue: "Bioeutectic® is the only bioactive material, at present, which is totally colonized in SBF".

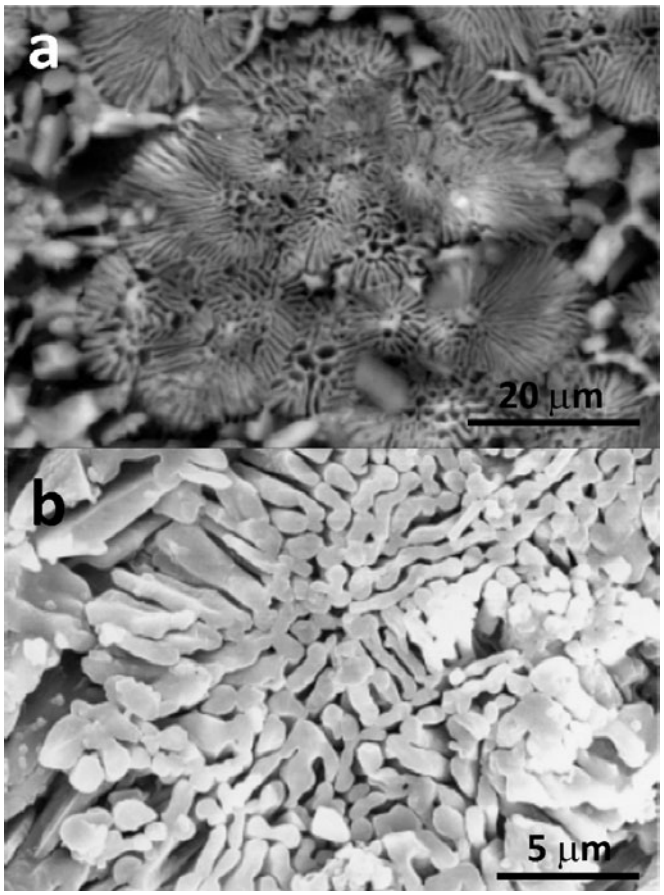

Fig. 7. SEM images of the surface of Bioutectic® after immersion in dynamic SBF (50 cm^3/h) for 2 weeks. (a) Surface; and (b) fracture surface (Reproduced from (40).

4. MICROSTRUCTURE DETERMINES BIOACTIVITY

As a good ceramist, S. De Aza knew that the properties and performance of ceramics depend on neither their intrinsic properties nor its chemical composition, but the microstructure which in turn is determined by the processing method employed during manufacturing. Keeping in mind that *in vitro* bioactivity is a property that determines the performance of a material in a given environment he realized the importance of studying its dependence on microstructure. The first case he studied was the above mentioned eutectic composition of the system $CaSiO_3$-$Ca_3(PO_4)_2$. (37). De Aza et al. prepared two materials from the eutectic composition ($CaSiO_3$ 60 wt.-% - $Ca_3(PO_4)_2$ 40 wt.-%). The first one was Bioeutectic®, a polycrystalline biphasic ceramic with the typical irregular eutectic microstructure shown in Fig. 3. It was obtained as described elsewhere by slow heat extraction from the melt under a radial heat gradient (32-35, 41, 42). The second one, with the same eutectic composition was a glass, obtained by quenching the melt to room temperature and annealing at 775 ºC for 15 min.

Both materials were crushed and the resulting powder was placed in direct contact with a specially designed ISFET electrode and the set immersed in SBF and the interfacial pH monitored. The detailed experimental set is described elsewhere (35, 43). The interfacial pH at the samples of Bioeutectics and eutectic glass grew rapidly from the initial value of 7.25 to 8.6-8.7 in the first 10 min of soaking, whereas in the bulk of the SBF solution pH remained practically unchanged.

In other experiment they prepared thin plates of both materials and immersed them in SBF for several periods of time. After 1 week both materials had reacted in different ways (Fig. 8). Bioeutectic® reacted as described above. A porous apatite structure resulted of the dissolution of psW phase and the pseudomorphic reaction of the remaining α-TCP into apatite as shows the micrograph of a cross section displayed in Fig. 8a.

On the other hand, the eutectic glass reacted forming a thin and dense surface layer of Ap on an intermediate layer of amorphous silica. They suggested that the eutectic glass reacted through a different mechanism, schematized in Fig. 9. First the eutectic glass exchanges Ca^{2+} ions for H_3O^+ from

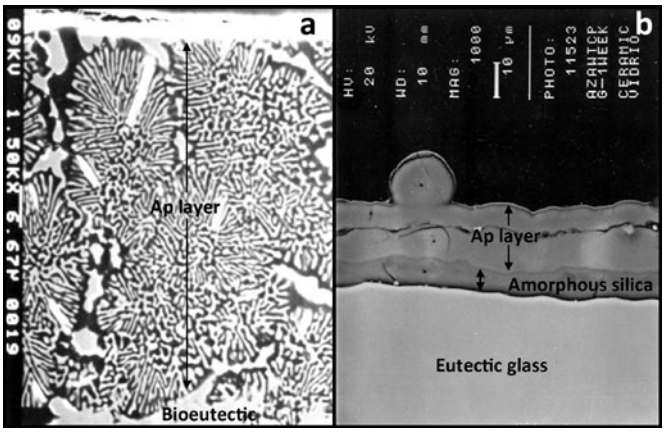

Fig. 8. SEM micrographs of cross sections of materials showing the Ap layer formed after soaking in SBF for 1 week. (a) Bioeutectic®; (b) Eutectic glass (Reproduced from (45)).

SBF which causes an increase of pH at the interface and the formation of a layer of amorphous silica containing silanol end groups. Under the alkaline conditions existing at the interface, part of the amorphous silica dissolves and apatite nucleates on the remaining amorphous matrix. The nuclei grow to confluence at expenses of the Ca^{2+}, HPO_4^{2-}, and OH^- ions in SBF. As the Ap layer becomes thicker the reaction slows down until it stops, the bulk of the glass remaining unchanged.

With this work De Aza et al. pointed out that the mechanism of Ap-like phase formation depends on the microstucture in the case of bioactive ceramic materials with identical chemical composition and even more, how this could affect the osseointegration of the ceramic implant.

Other typical case of how microstructure determines bioactivity was found in the system $CaSiO_3$-ZrO_2, which was studied by De Aza et al. who found that it is a pseudo-binary system with a peritectic invariant point at 1467 ºC ± 2ºC (44). They chose the composition which totally melts at a minimum temperature, corresponding to 13 wt.-% ZrO_2 (35). Then, glass-ceramics with the same composition but differing in microstructure were prepared from the glass with that composition. The glass was prepared by quenching the melt to room temperature and annealing at 700 ºC to remove stresses (35, 45, 46). Then two different processing routes were employed, the first consisting in bulk devitrification of the glass by thermal treatment in two steps (nucleation: 850 ºC/6h; growth: 950 ºC/2h). The resulting material, called WZ1, presented the phase composition of Table 1, and the microstructure displayed in Fig. 10. To prepare the second material (WZ2), the glass was milled to an average particle size of 5 μm, the powder was isostatically pressed at 200 MPa, and submitted to the same thermal treatment than WZ1.

Fig. 10a shows a SEM micrograph of a polished section of WZ1 glass-ceramic. W-2M nucleates as radial fibres from the periphery of the sample, whereas zirconia does with the shape of arborescent dendrites in the bulk of the sample as is shown in the micrograph of Fig. 10b. The gray phase surrounding zirconia in Fig.10 is non-devitrified amorphous glassy phase. In contrast the microstructure of the WZ2 glass-ceramic is homogeneous as displayed in Fig. 11. White areas in Fig. 11 are constituted of zirconia and the light grey ones to W-2M. The small dark grey zones correspond to residual glassy phase.

The interfacial pH of both materials was measured as described above and the results are shown in Fig. 12. pH increased rapidly at the SBF-WZ2 interface during the first minutes of soaking in SBF and remained practically constant at the interface SBF-WZ2. Micrographs of cross sections of plates of both after immersion in SBF for 1 month are displayed in Fig. 13. No visible reaction was observed for sample WZ1 in agreement with the results for the interfacial pH. On the other hand, WZ2 do react with SBF as other bioactive materials and an Ap layer is formed on its surface.

De Aza et al. explained the absence of bioactivity in WZ1 glass-ceramic as a consequence of the low interfacial pH which in turn is caused by the Zr-rich residual glassy phase, more abundant than in WZ2. The residual glassy phase in contact with SBF releases Zr that precipitates at physiological pH on the surface of the material as oxide, hydroxide and/or carbonate forming very thin multilayers that hinder the ionic exchange of H_3O^+, the first step in the typical bioactive reaction (35, 45, 46). Thus, they showed that materials with the same global chemical composition and containing the same crystalline phases can react differently in dependance of their microstructure and present distinct in vitro bioactivity.

5. THE POLYMORPHIC TRANSFORMATION OF TRI-CALCIUM PHOSPHATE

A review of the synthesis of pure α-TCP in the literature reveals several contradictory results. Most of reports fail in obtaining pure phase instead a mixture of α- and β-phases is obtained. The presence of β-TCP has sometimes been attributed to partial reversion of the high temperature α-phase already formed during cooling. That is why many authors recommend quenching to avoid the polymorphic transformation α→β (47, 48).

S. De Aza was convinced that the reverse α→β transformation was impossible unless unusually slow cooling rate is employed or too large volume of reaction mass is involved which makes heat conduction and removal difficult (48). He supported this view on the fact that the polymorphic transformation α→β is reconstructive, according to the Buerger classification, i.e. ''involves a major reorganization of the crystal structure, in which many bonds have to be broken and new bonds formed'', so considerable energy has to be provided to the system to transform from one polymorph to another (49, 50). Thus, reverting from α- to β-phase should be

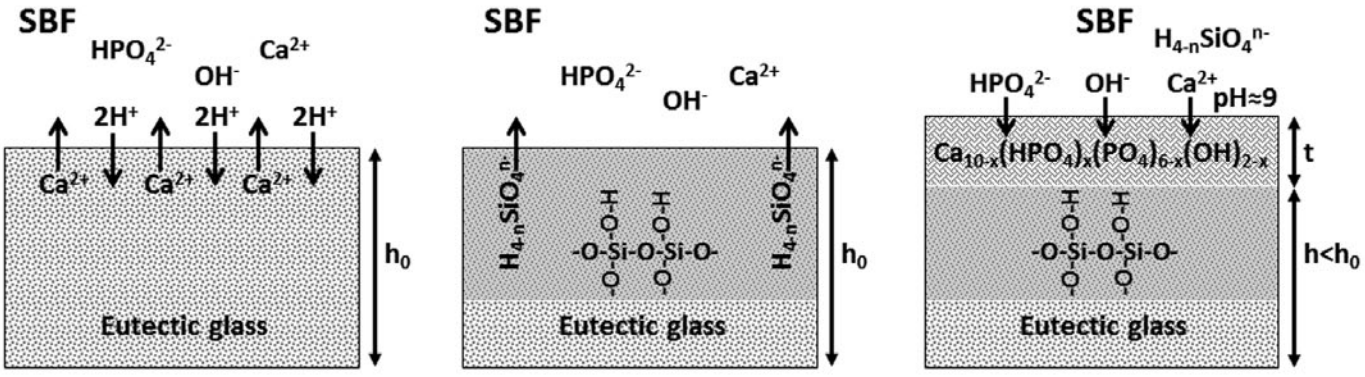

Fig. 9. Scheme representing the mechanism of reaction in SBF of the eutectic glass (Redrawn from (45).

TABLE 1. PHASE COMPOSITION OF THE GLASS-CERAMICS DETERMINED BY X-RAY QUANTITATIVE ANALYSIS WITH THE RIETVELD METHOD (46).

Glass-ceramic	Wollastonite-2M	Tetragonal Zirconia	Amorphous phase
WZ1	65.6 ± 1.5	6.5 ±0.6	27.9 ± 0.3
WZ2	83.5 ± 1.8	12.4 ± 0.5	4.1 ± 0.1

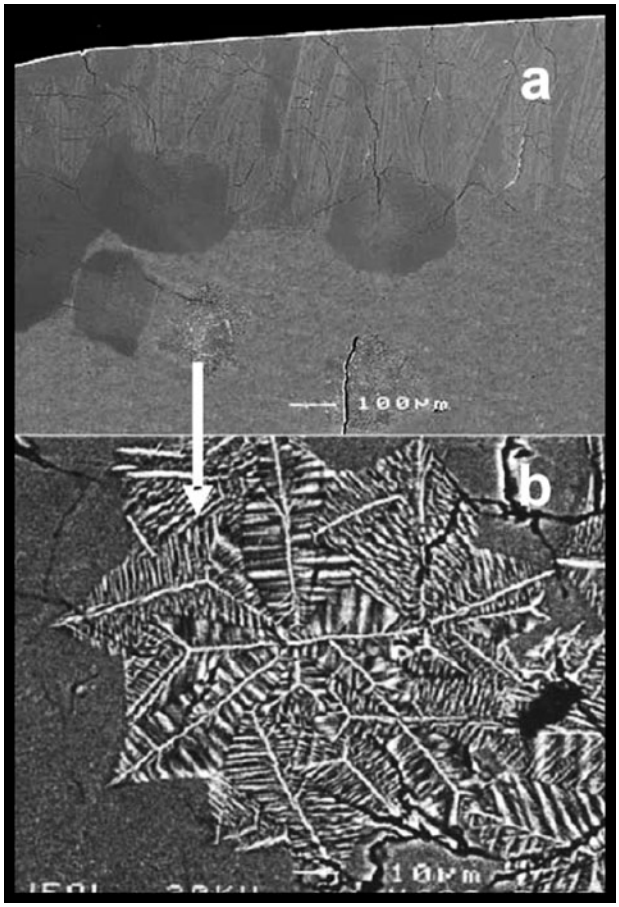

Fig. 10. (a) SEM micrograph of a polished section of WZ1 glass-ceramic. (b) A detail of a zone of devitrification of zirconia. (Reproduced from 45).

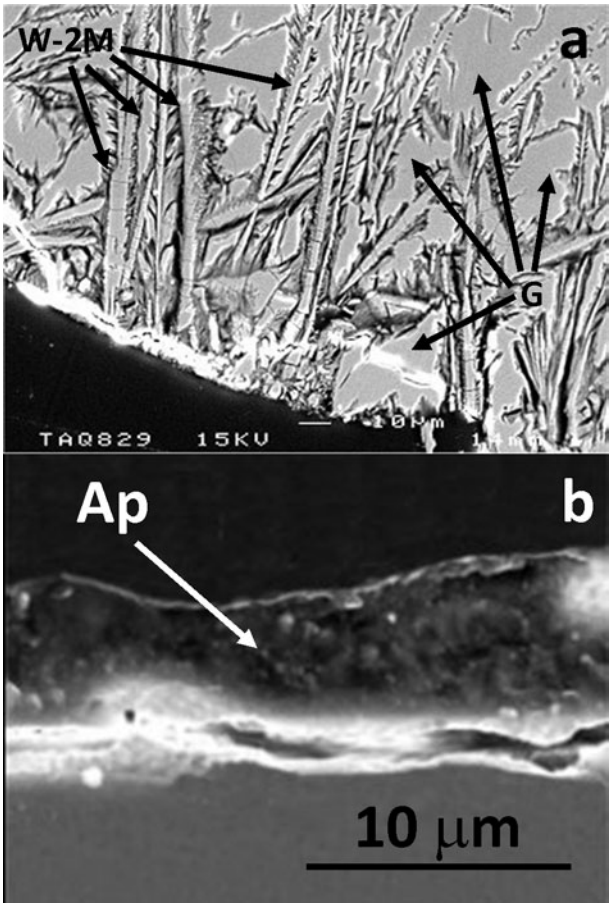

Fig. 13. SEM micrographs of cross sections of WZ1 and WZ2 glass-ceramics after immersion in SBF for 1 month. (a) WZ1; (b) WZ2. (Reproduced from 45).

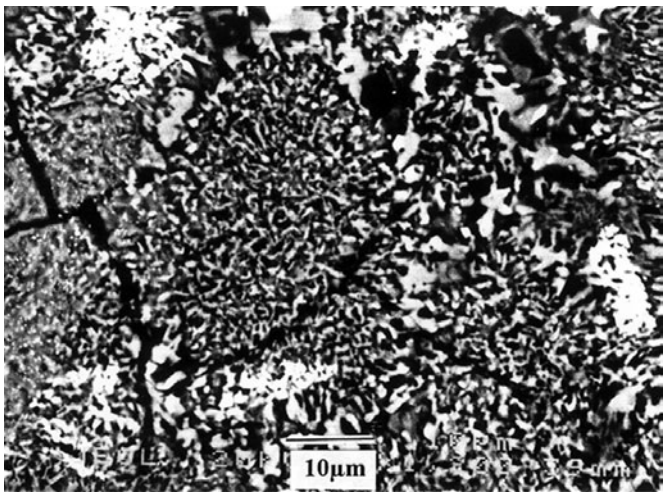

Fig. 11. SEM micrograph of a polished section of WZ2 glass-ceramic. (Reproduced from 45).

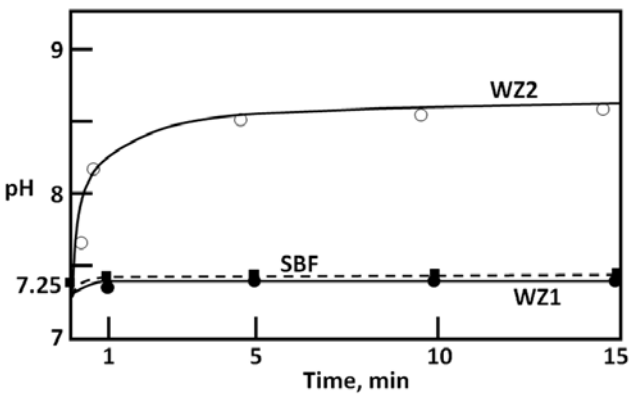

Fig. 12. Variation of the interfacial pH for WZ1 and WZ2 glass-ceramics in comparison to pH at the bulk of solution during soaking in SBF. (Reproduced from 45).

unfeasible, unless either a very slow cooling rate or a large dwell at temperature slightly below that of transformation is used.

He believed that contradictory reports in literature were due to the influence of small amounts of impurities, such as Mg, commonly present in the materials used in the preparation of TCP and frequently disregarded by the investigators (47, 48).

On the other hand, S. De Aza realized that something had been missed out in previous studies of the system $Ca_3(PO_4)_2$-$Mg_3(PO_4)_2$ (51, 52). In these reports the boundary between the field of the low temperature β-TCPss and the high temperature α-TCPss is a line (one-dimension), which contradicts Palatnik–Landau's Contact Rule of Phase Regions (CRPR), lately reformulated as the Boundary Theory (BT) (53-57). As stated by the CRPR and the BT a phase boundary line (one-dimension) cannot separate two mono-phase fields in a binary phase equilibrium diagram at constant pressure (47).

Then De Aza et al. carried out several experiments to prove the above hypothesis. The α↔β polymorphic transformation was studied in real time by neutron diffraction, X-ray diffraction and SEM microscopy on samples of Mg-free and Mg-doped TCP. Their results demonstrated the existence of a two new biphasic fields: β+α-TCPss and α+α'-TCPss, and confirmed the validity of the Palatnik–Landau's CRPR. The micrograph of Fig. 14 corresponds to a polished surface of Mg-doped TCP treated at 1300 ºC for 2 h and acid etched. Due to the differences in solubility of β-TCPss and α-TCPss the coexistence of both phases in equilibrium becomes evident. Besides, neutron and X-ray diffraction experiments confirmed the reconstructive character of the α↔β transition, which requires to surpass a large activation energy barrier to proceed and indicates that quenching is not required to retain the pure α-TCP phase, but it is only needed to reach a temperature inside the primary field of α-TCP_{ss} and to keep it for a period of time enough to complete the β→α transformation (47).

The results listed above permitted to redraw the phase equilibrium diagram of the system $Mg_3(PO_4)_2$–$Ca_3(PO_4)_2$ as shown in Fig. 15.

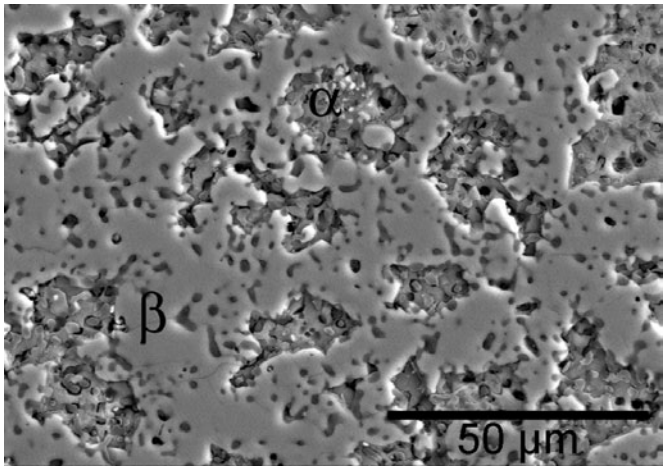

Fig. 14. SEM micrograph of a polished and etched sample of Mg-doped TCP treated at 1300 ºC (Reproduced from (47)).

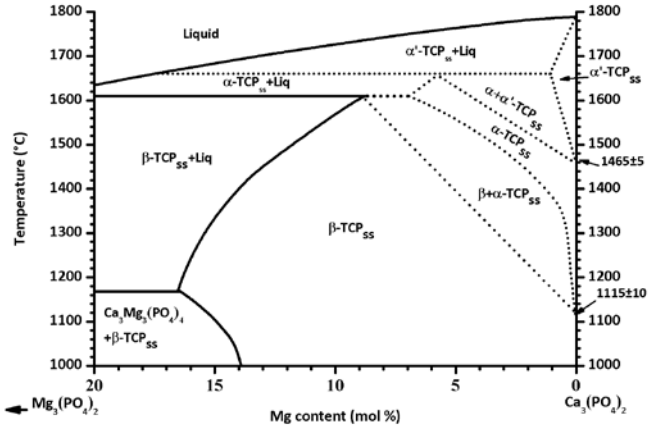

Fig. 15. Tentative phase equilibrium diagram of the tricalcium phosphate-rich region of the system $Mg_3(PO_4)_2$–$Ca_3(PO_4)_2$, after S. De Aza results (47).

6. CONCLUDING REMARKS

The four examples exposed above pretend to illustrate the way Salvador De Aza used to face scientific challenges. His method was based in a solid knowledge of Physical Chemistry, especially Thermodynamics and Phase Equilibrium, and Materials Science jointly with a careful design of experiments. The cases discussed constitute important contributions of S. De Aza to Materials Science, specifically to the field of Bioceramic materials.

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