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Bioactive ceramics and glasses

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Zásady pro vypracování:

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3. Popište postupy stanovení bioaktivity keramiky a skla.
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ANNOTATION

This bachelor's thesis is focused on bioactive glasses, ceramics and glass-ceramics. This work begins with a brief description of biomaterials and the following parts summarize the compositions, preparations and uses described in several studies of bioactive glasses, ceramics and glass-ceramics.

KEYWORDS

Biomaterials, Bioglass, Bioceramics, Glass-ceramic

NÁZEV

Bioaktivní keramika a sklo

ANOTACE

Tato bakalářská práce je zaměřena na bioaktivní skla, keramiku a sklokeramiku. Práce začíná krátkým obecným popisem biomateriálů a v dalších částech pak shrnuje složení, postupy přípravy a použití bioaktivních skel, keramiky a sklokeramiky popsané v literatuře.

KLÍČOVÁ SLOVA

Biomateriál, biosklo, biokeramika, sklokeramika

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LIST OF ABBREVIATIONS

BBG – borate-based bioactive glass

FDPs – fixed dental prostheses

FITR – Fourier-transform infrared spectroscopy

GCs – glass-ceramics

HA – hydroxyapatite

HCA – hydroxycarbonate apatite

NC – network connectivity

TEOS – tetraethylorthosilicate

TMOS – tetramethoxysilane

SBF – simulated body fluid

1P – one phase

2P – two phases

INTRODUCTION

For several years, several types of biomaterials classified under different categories have been studied in order to improve or expand their uses in stomatology, in the orthopaedic field and many more. Among these materials we can mention bioactive glass, bioceramics and glass-ceramics.

Biomaterials are defined as materials capable of being implanted into the human body for therapeutic purposes, but this definition is only one of several others. Biomedical materials are divided into four groups as follows: [1]

Bioinert biomaterials are materials that tend to have minimal reaction with surrounding tissues when placed in the human body. This particular type of biomaterials can be made of titanium, alumina, partially stabilized zirconia and ultra-high molecular weight polyethylene.

Biotolerant biomaterials are materials capable of causing non-toxic reactions, for example nickel-containing stainless steels.

Bioactive materials are materials that can interact with surrounding bone when placed in the human body. This reaction is defined by an ion exchange between the bioactive implant and the surrounding bodily fluids, which later causes the formation of a layer of biologically active apatite carbonate on the implant. This layer has chemical and crystallographic properties equivalent to the mineral phase in the bone. Among these materials are for example bioactive glasses and glass-ceramics.

Bioresorbable biomaterials, such as tricalcium phosphate [$Ca_3(PO4)_2$] and polylactic-polyglycolic acid copolymers, are materials that, when placed in the human body, begin to dissolve and are slowly and gradually replaced by tissue regeneration (such as bone).

When synthesizing biomaterials, it is very important to consider the physical and chemical properties of the material such as permeability, elasticity and strength. For example, a tendon material should be strong and flexible. Biocompatibility is also important, especially in determining how the structure of the surface of the material to be implanted is transformed in connection with the response of proteins, cells and the whole organism as such. And for that, it is important to assess the roughness of the material, its wettability, surface mobility, chemical composition, crystallinity and heterogeneity. [1]

1 BIOACTIVE GLASSES

Glass is defined as a material with a network of atoms (most commonly silicon) bonded to each other through covalent bonds with oxygen atoms. [2] The structure of glass is irregular compared to crystals with a regularly arranged structure.

The study of bioactivity of glasses began many years ago, one of the first bioactive glasses was developed by professor Larry Hench [3] in 1969 and it is known as 45S5 Bioglass® with a composition of $Na_2O–CaO–P_2O_5·SiO_2$ a soda–lime–phosphosilicate and properties to regenerate bone tissue. The molecular and weight percentages of each compound of 45S5 Bioglass® [3,4] are shown in Table 1 below.

Table 1: Molecular and weight percentages of each compound of 45S5 Bioglass®. [3]

Composition	**SiO_2**	**Na_2O**	**CaO**	**P_2O_5**
Molecular %	46.13	24.35	26.91	2.60
Weight %	45.00	24.50	24.50	6.00

What makes glasses bioactive according to Larry Hench [5] studies is their ability to dissolve in contact with body fluids and then release ions such as calcium and phosphate ions and the result is the formation of a surface layer of hydroxyapatite (HA), the inorganic component of bone. The processes of the implantation of bioactive glasses in the human body can be seen in Table 2.

It is possible to predict the structure of bioactive glasses and network connectivity (NC) from their composition in the case that the forming oxides are P_2O_5, B_2O_3, V_2O_5 and SiO_2. Network connectivity is the average number of bridge-oxygen links for each atom forming a network. This number can also be used to deduce whether glasses are bioactive or not, since for glass to be bioactive its network connectivity number must be between 1.8 and 2.6. The value of network connectivity can be calculated using the following formula:

$$NC = 2 + \frac{BO - NBO}{G}$$

where BO refers to the total number of bridging oxygens per network-forming ion, NBO is the total number of non-bridging oxygens per network and G represents the total number of glass-forming units. [3,4]

Table 2: Processes of the implantation of bioactive glasses in the human body [5]

Time scale (h)	No.	In vitro/in vivo	In vivo only
0	1	Simple cation exchange and silanol formation	
1	2	Release of complex ions	
	3	Silica polycondensation	
	4	Ca^{2+}, $(PO_4)^{3-}$ absorption, formation of the amorphous layer	
2	5	HA crystallization	Protein absorption and cell attachment
10	6		Macrophage adhesion
20	7		Osteoblast precursor cell arrival
100 +	8		Stem cell differentiation Extracellular matrix generation Onset of ECM mineralization

1.1 Synthesis of bioactive glasses

Bioactive glasses are prepared via two methods: the melt quenching process and the sol-gel method.

The most popular method for the synthesis of bioactive glasses is the melt quenching process where the components used are mixed at temperatures ranging from 1200 ° C and 1240 ° C. [6]

Based on the synthesis of the first bioactive glass, a study used the melt quenching process to create Bioglass and the preparation was as follows: [7]

The prepared glass composition was 45% SiO_2, 24.5% Na_2O, 24.5% CaO, and 6% P_2O_5 (wt%). In addition to the base Bioglass®, the Bioglass was synthesized with various percentages by weight of $AgNO_3$ (BG0.5, BG1 and BG2%wt), substituting the amount of Na_2CO_3. During the first stage, the high−purity starting chemicals (SiO_2, P_2O5, $CaCO_3$, Na_2CO_3 and $AgNO_3$) were mixed and homogenized, using a planetary ball milling process for 1 hour at 300 rpm. An agate vessel and balls were used. The powder was then calcined for 8 hours at 800°C. Subsequently, the melt ‑ quenching process was deployed, using a platinum crucible. The melt temperature was 1350°C, and the melt time was 1 hour. The glass was melted twice to improve the homogeneity of the samples. When quenched, all samples were annealed at 400°C for 15 hours and then slowly cooled inside the annealing furnace, to minimize the internal mechanical stresses resulting from quenching.

The sol-gel process is one of the methods used for the synthesis of many materials such as ceramics and bioactive glasses for the regeneration of soft and hard tissues. In comparison with the previous method, the sol-gel process has manifested that it is possible to get a chemically pure product even without using higher processing temperatures. During the sol-gel synthesis, the gel is formed at a room temperature due to the polymerization reaction of a solution containing appropriate precursors chosen to adapt the composition of the system to the final aim.

The sol-gel process has been mainly used to produce ceramic materials, but as science keeps evolving, further research has been done in the field of biomedicine to demonstrate that the sol-gel process can be used for the synthesis of bioactive glasses as nano-porous materials which are able to improve bioactive behaviour and cellular response.

Seven reactions steps are used for the synthesis of bioactive sol-gel glasses: these steps are shown in Figure 1 and are as follows: [5]

The first step is a mixing step where the reagents are mixed at room temperatures to form a strong covalent bond between the elements. During the mixing step, hydrolysis and poly-condensation reactions occur simultaneously until the homogenization of the solution is complete. Silica gels can be obtained by hydrolysing alkoxide precursors under the action of catalysts that could be either an acid or a base. Tetra-functional monomeric alkoxides with a general chemical formula Si(OR)n,where R is the alkyl group are usually used as network forming agents. The most common precursors used are tetraethylorthosilicate (TEOS, $Si(OC_2H_5)_4$) and tetramethoxysilane (TMOS, $Si(OCH_3)_4$) and since TEOS are insoluble in water, a co-solvent (alcohol) is used in this first step (mixing) to avoid a possible creation of a phase separation.

After the first step a step named as casting of the sol follows, in order to obtain the geometry of the final product. This is not so important in those cases where the container used for mixing is made of a material that will not adhere to the gel (e.g. polytetrafluoroethylene, PTFE) and has the required form.

The afore-mentioned reactions lead to the gelation characterized by the formation of a 3D network and the formation of an O - Si - O bonding network, and a gradual increase in viscosity is also observed. Gelation continues until all the precursors are used.

The reaction that results in gelation does not end after the formation of the gel and continues until the so-called aging process, where the gel is aged for hours and days in its aqueous by-products. This step involves strengthening of the gel and prevents the gel from cracking during the drying process.

Once gelled, the material is dried to have the liquid phase (water or alcohol) removed from the pores. This drying step can cause shrinkage of volume.

The next step is to stabilize the solid by removing silanol bonds from the pore network. This step is called chemical stabilization.

The final step is densification that is achieved by heating the glass to high temperatures in order to remove the pores. However, the temperature must not be higher than crystallization temperature so that the formation of glass-ceramic is avoided.

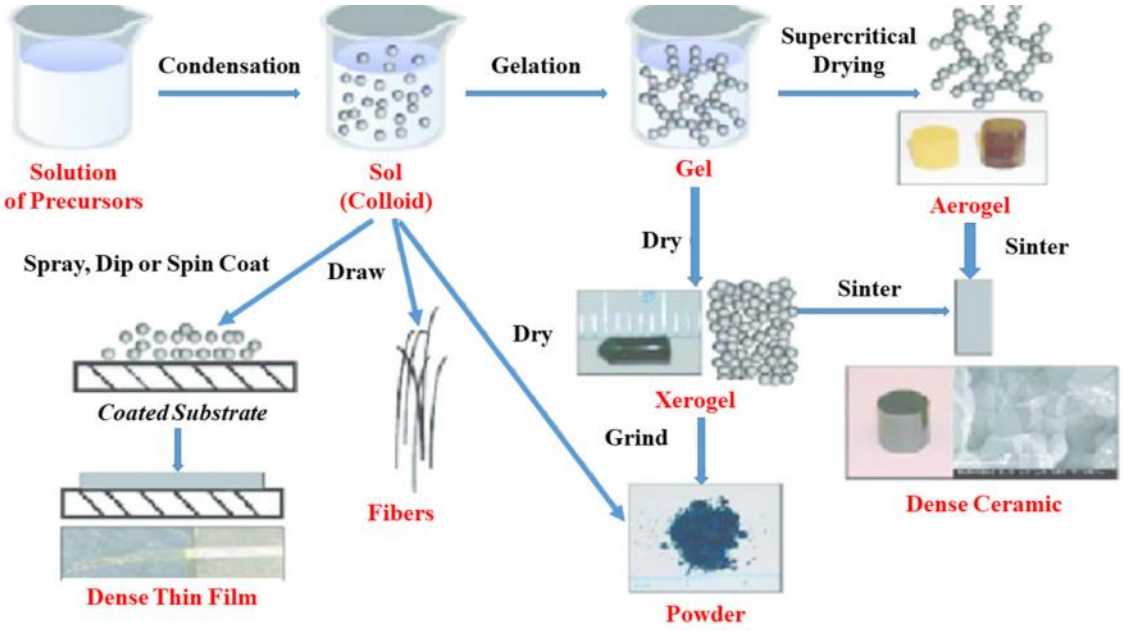


Figure 1: Steps of the sol-gel process [8]

1.2 Types of bioactive glasses and their properties

Over the years until today, several studies have been made in the field of medicine based on the first bioactive glass not only to introduce new substances with more promising positive effects, but also to expand their use in biomedical application such as dental filling, drug delivery, coating to load-bearing metal implants, and tissue engineering. From these bioactive glasses, borate/borosilicate glasses or phosphate-based glasses are particularly worth mentioning. [9]

Bioactive glasses based on boron

The incorporation of metal ions into glass preparation is very important for the purpose of developing biological activity. Metallic ions regulate several biochemical processes in the human body and are part of human tissue elements. Boron is a bioactive element that is beneficial to animals and humans, as it is known to influence the performance of several metabolic enzymes and boron deficiency; in rats, to take one example, it can decrease bone volume fraction. The amount of boron in the human body is around 3 to 20 mg with the highest concentrations found in bone tissue. In recent years, different amounts of boron, borate and borosilicate have been added to bioactive glasses so that their biological effect on regeneration of bones can be studied. [6]

The first research began with scientist Richard,[10] who replaced SiO_2 with B_2O_3 in the composition of 45S5 glass. In vitro research, immersing borate-based 45S5 in a simulated body fluid (SBF) has shown a rapid formation of a hydroxyapatite layer due to their low chemical durability. As a result, the research was further investigated in vivo by placing borate-based 45S5 in a rat tibial defect and the results were rather positive, as not only was there a more rapid bone formation than in the case of 45S5 glass silicate base, but also a total conversion of borate glass to hydroxyapatite by dissolving B_2O_3 and Na_2O in the solution and the reaction of CaO with PO_4^{-3} phosphate solution.[7]

In the search for bioactivity of glasses containing boron, several glasses were synthesized using the melt quenching process. Nevertheless, it is also important to know whether borate glasses derived from the sol-gel process are also bioactive or not. Sol-gel derived bioactive glasses offer more advantages than melt-quench derived glasses. Studies have shown that due to the low treatment temperatures used during the synthesis of glasses using the sol-gel method, it is possible to achieve greater homogeneity. Furthermore, studies have also revealed specific surfaces with higher porosities of at least two orders of magnitude greater than melt-quench derived glasses which allow faster ion release rates and thus higher conversion rates in hydroxycarbonate apatite (HCA). Research based on the study of sol-gel derived bioactive borate glasses with decreasing sodium (see Table 3 for the composition of the glasses studied) has shown that even the synthesis of glasses using the sol-gel method with the sodium content had no negative effect on bioactivity of glasses, because in less than 2 hours there was a rapid conversion of hydroxycarbonate apatite in simulated body fluid. The test results are shown in Figure 2. [8]

Table 3: Compositions (mol%) and Codes of sol-gel derived bioactive glasses. [12]

ID	B_2O_3	CaO	P_2O_5	Na_2O	% CaO + Na_2O
Na24	46.1	26.9	2.6	24.4	51.3
Na16	51.1	29.8	2.9	16.3	46.1
Na8	56.0	32.7	3.2	8.1	40.8
Na0	61.0	35.6	3.4	0	35.6

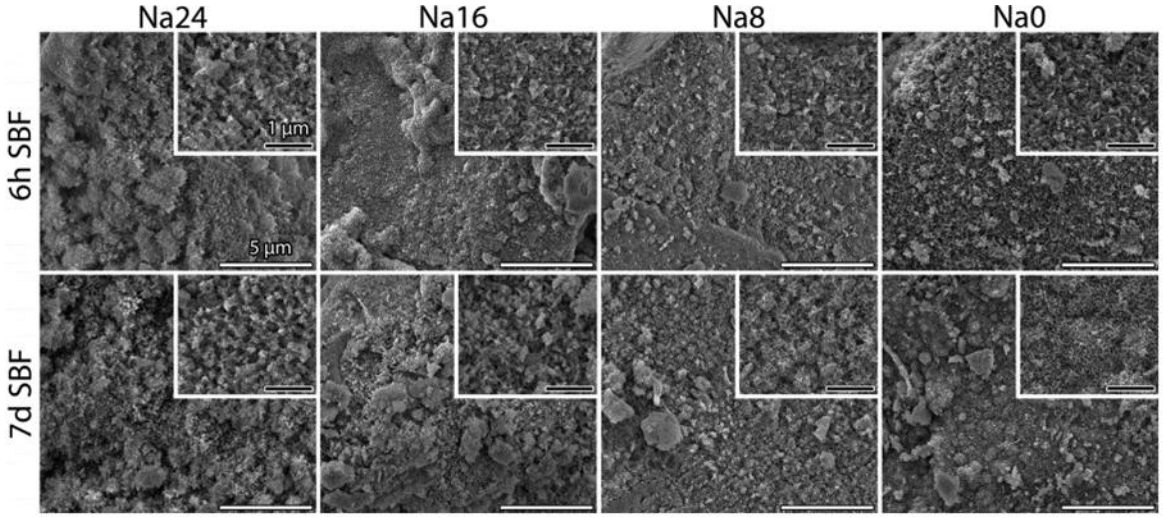


Figure 2:SEM micrographs of the glasses after immersion in SBF for 6 h and 7d. Typical HCA crystals begin to form at 6 h and become more defined at 7d for all glasses (white scale bars = 5 µm and black scale bars = 1 µm). [12]

Another study has also shown that highly bioactive borate-based glasses (BBG) synthetized using the sol-gel method, contribute to the formation of nanoporosity on high specific surface areas and large pore volumes. Tests in SBF have shown an increase of at least 25-times the rate of bioactivity compared to melt-derived borate-glasses, which is important when repairing and augmenting mineralized tissue. [9]

Several studies have manifested that the use of boron in glasses (borate glasses, borosilicate glasses) in moderate amounts can improve angiogenesis, healing and osteogenesis, because in vivo it promotes the proliferation and differentiation of stem cells, and in vitro it helps the regeneration of bones without toxicity. In addition, borate glasses are used as substrates for wound treatment and for axon growth. [14-16]

2 BIOCERAMICS

Ceramics can be defined as a class of inorganic, non-metallic solids that are subjected to high temperatures in manufacture or use. [17] Bioceramics are inorganic materials used in the replacement of a part or function of the human body while being biocompatible and chemically stable in a biological environment. Bioceramics are classified as bioinert ceramics, for example alumina (Al_2O_3) and zirconia (ZrO_2), resorbable bioceramics (tricalcium phosphate) and bioactive ceramics (bioactive glass, hydroxyapatite). [18]

2.1 Zirconia for dental implants

The tooth is one of the vital organs with many functions. One of the roles of the tooth is to bite and chew food, which can then be easily swallowed. Teeth in humans also play a crucial role in terms of appearance and beauty. The tooth consists of two types of tissue: hard tissue composed of enamel, dentin and cementum, and soft tissue known as the pulp. [19]

Dental enamel with a thickness of up to 2.5 mm^3, is the hard-outer layer that covers the surface of the crown. The colour of the enamel is milky white or light yellow, depending on its thickness and degree of mineralization. Dentin is the essential base of the tooth. Dentinogenesis is the formation of dentin and it begins with odontoblasts, which develop from the contact of the dental papilla with the enamel organ. Dentin improves the attachment of ligaments to the surrounding bone and does not stop forming throughout life, which is not the case in enamel. The pulp is the inner part of the tooth and its role is to form dentin with odontoblasts thanks to its prevalence in blood vessels. It also keeps the organic components of the mineralized tissue surrounding nutrients, keeps teeth healthy, and neutralizes pain. Figure 3 shows the tooth anatomy. [19]

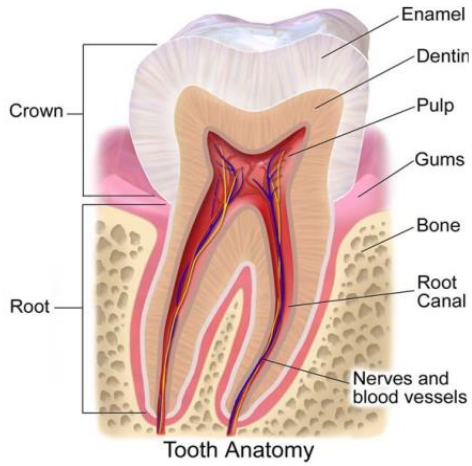


Figure 3: Cross-section of a tooth. [19]

Due to its rather positive chemical properties, toughness, mechanical strength and several other properties, zirconium dioxide (ZrO_2) is used in the manufacture of prostheses. [20]

Zirconia is characterized by dense and monocrystalline homogeneity, good radiopacity and its thermal conductivity, as well as its corrosion potential. Polycrystalline yttrium oxide (Y-TZP) partially stabilized in tetragonal zirconia contains high values of flexural strength (900-1200 MPa) and tensile strength (9-10 MPa m0.5) thanks to a phase transformation enhancement mechanism. Y-TZP has several purposes in root canal channels, all-ceramic posterior teeth and implant-supported crowns, and also fixed dental prostheses (FDPs). [21]

Treatment options for fixed implant restorations include simple crowns or fixed dental prostheses. The treatment alternatives are, for example, primary splints (screwed restorations) or secondary splints (simple abutments with sealed restoration) of the implants that can be seen in Figure 4. [21]

Due to the evolution of the technology, fixed dental prostheses can be made entirely of zirconia-based ceramics and screwed on. For the ease of recovery, FDPs are designed and manufactured in a zirconia monobloc substructure on the implant attachment surface. The structure supported by the implant is milled out of a single block of zirconia to the level of the implant or the abutment. That being so, the porcelain is directly fired on the abutment / zirconia framework, and the crown / FDP pillar complex can be screwed onto the implant as we can see in Figure 5. There may arise some complications during restoration processes such as peeling of the coating ceramic due to the discontinuity of the porcelain at the access opening to the central screw. [21]

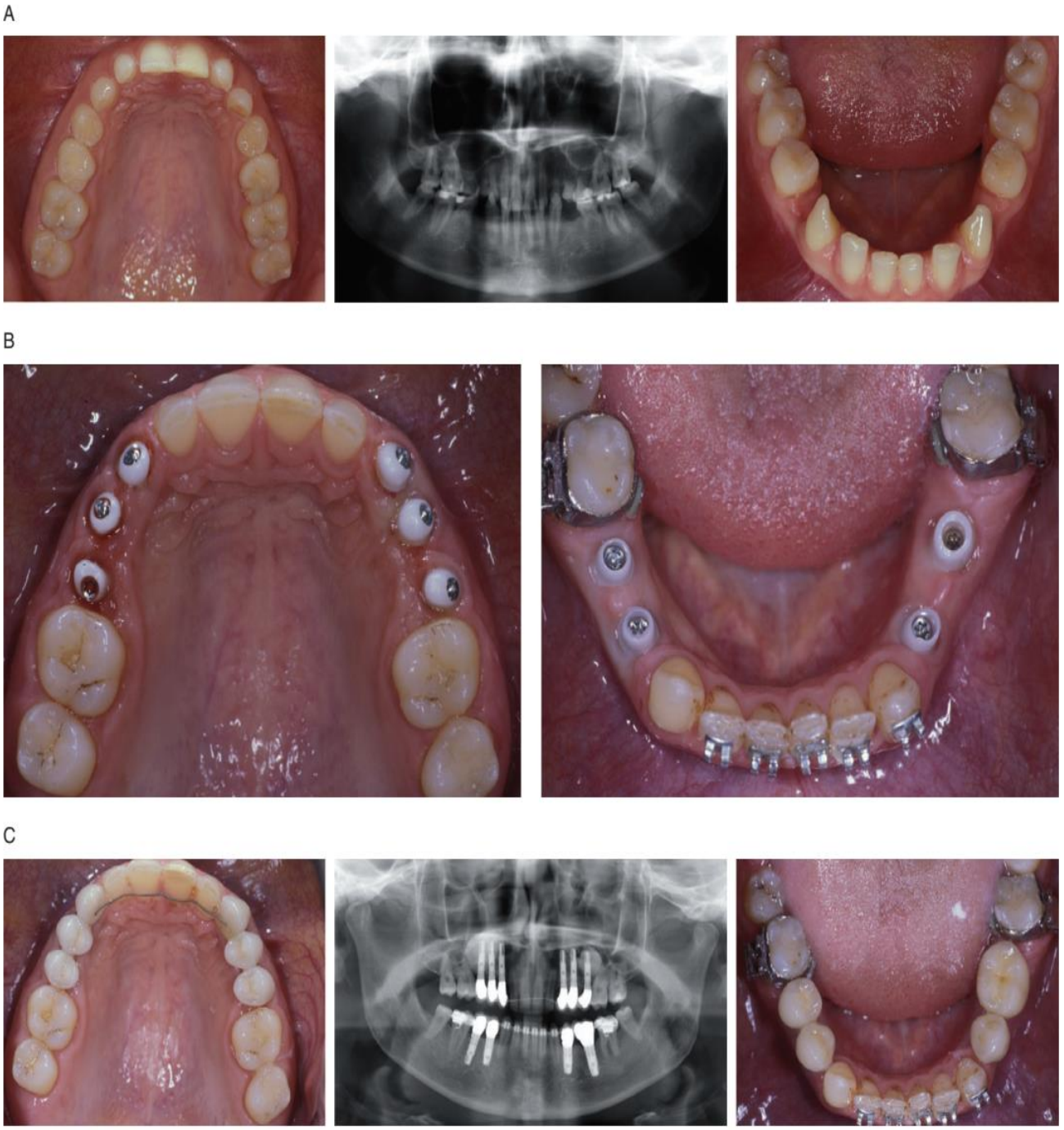


Figure 4: Clinical example of cemented zirconia-based implant-supported single restorations. A, Occlusal view and radiograph of the clinical situation. The patient presented with congenitally missing premolars and canines in the maxilla (left) and premolars in the mandible (right). B, the deciduous teeth were extracted, and implants were placed. Zirconia abutments were screwed onto the implants in the upper (left) and lower jaws (right). C, the patient received zirconia-based single crowns that were cemented on the zirconia abutments in the upper (left) and lower jaws (right). Control radiograph after delivery of final restorations (middle). [21]

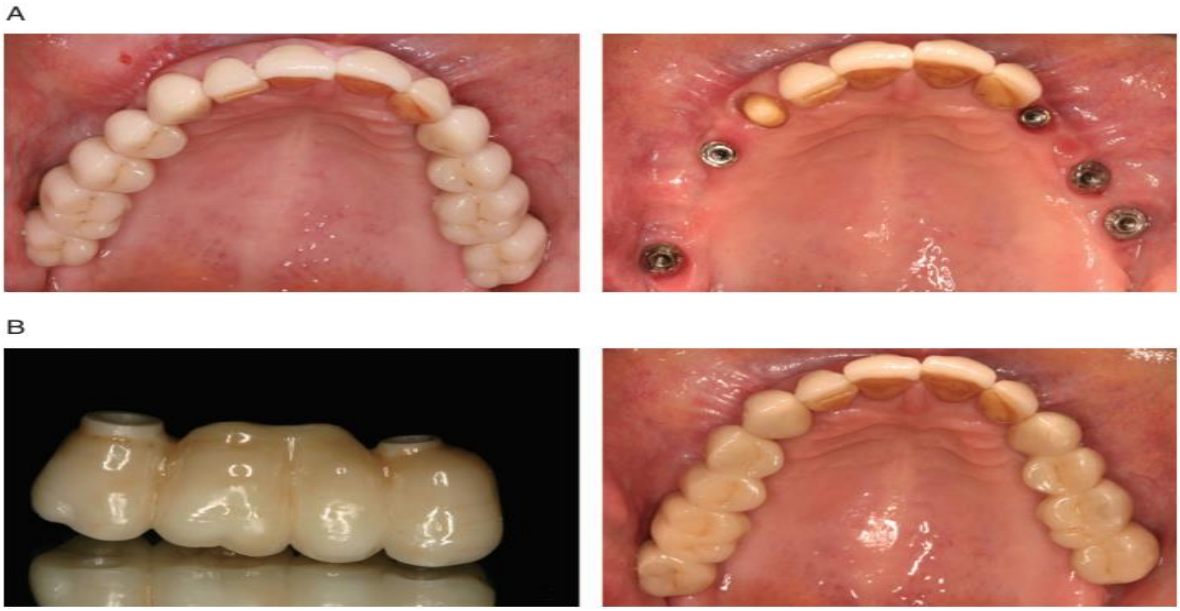


Figure 5: Clinical example of one-piece zirconia fixed dental prostheses (FDPs) fitted directly onto the implant platform. A, Occlusal view of the clinical situation. The patient presented with palladium allergy (left), which indicated the removal of the current metal-ceramic implant-supported restorations (right). B, Zirconia-based implant-supported FDP (left). The framework was milled out of a zirconia block and veneered with a press-on ceramic. Occlusal view of the screw-retained zirconia restorations. Occlusal screw access holes were closed with a composite resin (right). [21]

There was a study based on a clinical evaluation (radiographic) of dental implants in zircon with a follow-up period of 1 to 5 years in 12 patients (5 men, 7 women). The medical records of the patients were studied namely: systemic conditions, history of periodontal disease and smoking. Information on implants placed in native bones, bone graft sites or immediately placed after extraction was also recorded. Clinical and radiographic measurements of the relevant implant region were done, too. [22]

The measurements deployed two specific indices describing the state of the implant regions of the above-mentioned patients. The first one being called ‘gingival index’ was ranked in the following manner: 0 for normal gingiva, 1 for mild inflammation, slight change in colour, slight oedema, as well as for no bleeding on probing. 2 represented moderate inflammation, redness, oedema, glazing and bleeding on probing; 3 was used for severe inflammation, marked redness and oedema, and ulcerations with obvious tendency towards spontaneous bleeding.

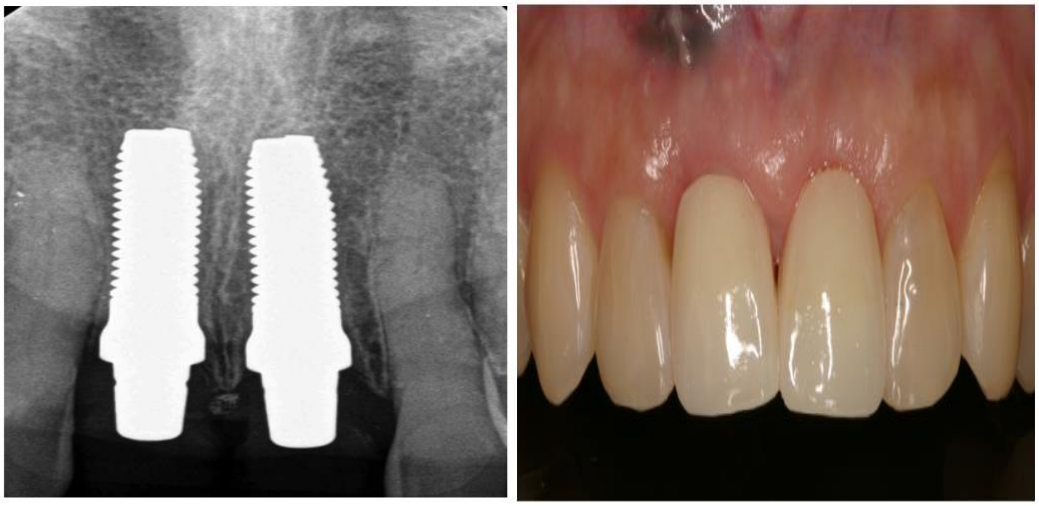
The other, ‘plaque index’, had the following criteria: 0 for no plaque in gingival area, 1 for no plaque visible to the naked eye, but visible on the point of the probe after removal of the probe across the surface at the entrance of the gingival crevice; 2 for marginal area with a thin to moderately thick layer of plaque, and deposit visible without magnification, 3 for heavy accumulation of soft matter the thickness of which would fill a niche produced by the gingival margin and tooth surface, and interdental area filled with soft debris. The results of both indices are shown in Table 4.

With a result of 92%, the zirconia implantation was a success with excellent clinical and aesthetic results. There was a failure in the implants of 2 patients and the important values for the intermediate and final restorations were weak gingival and plaque indices. Pictures of the dental implant process are shown in Figure 6 below. [22]

Table 4: Patients gingival and plaque indices, including the follow-up months for each patient. The table indicates the predominant low scores for each patient at baseline and latest follow-up. [22]

	Gingival index		Plaque index		
Patient	Baseline	Latest follow-up	Baseline	Latest follow-up	Follow-up (months)
2	0	1	1	0	65
3	0	0	1	0	44
4	0	0	0	0	21
5	0	0	0	1	12
6	0	0	0	0	16
7	0	0	0	0	12
8	0	0	0	0	27
9	1	0	0	1	36
10	0	0	0	0	16
11	0	0	0	1	14
12	0	0	0	0	16

A B



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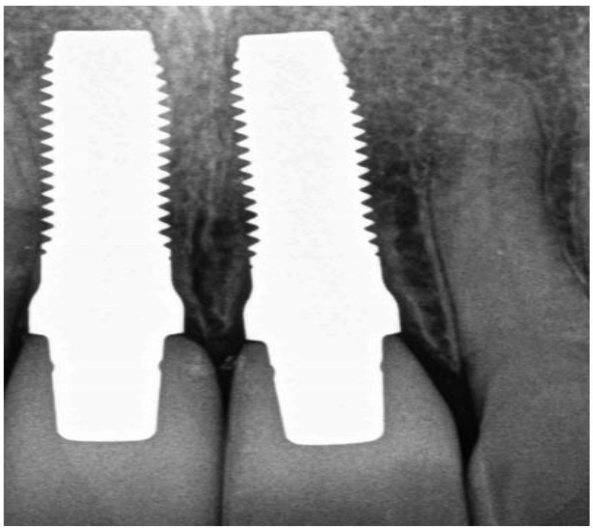

Figure 6: A: peri-apical radiograph following implant placement, B: clinical photographs at 39 months post implant placement and C: peri-apical radiograph at 39 months post implant placement. [22]

3 BIOACTIVE GLASS-CERAMICS DERIVATES

Glass-ceramics (GCs) are defined as polycrystalline materials that contain one or more crystal phases embedded into residual glass and are produced by the controlled heat treatment of certain glasses. The crystallinity of glass-ceramics is most often between 30 to 70%, the composition of several bioactive glass-ceramics is like that of Bioglass®, but with a very low content of alkaline oxides. [6,23]

Even if glass-ceramics are prepared by the melt quenching process or the sol-gel method, the heat treatment is used in both methods and is carried out in two stages. The first step is conducted at a low temperature near glass transition for inducing nucleation, and the second stage occurs at elevated temperatures to promote crystal growth. The steps of the synthesis of glass-ceramics are shown in Figure 7**.** The nucleation in glass-ceramics is either homogeneous (which means that it occurs at the very moment when crystals are formed in supersaturated fluid due to local variations in density and kinetic energy, and there is no need of adding foreign particles or undergoing amorphous phase separation) or heterogeneous, which is the opposite of homogeneous nucleation as it involves foreign particles, and is most often used in the development of many glass-ceramics. [23]

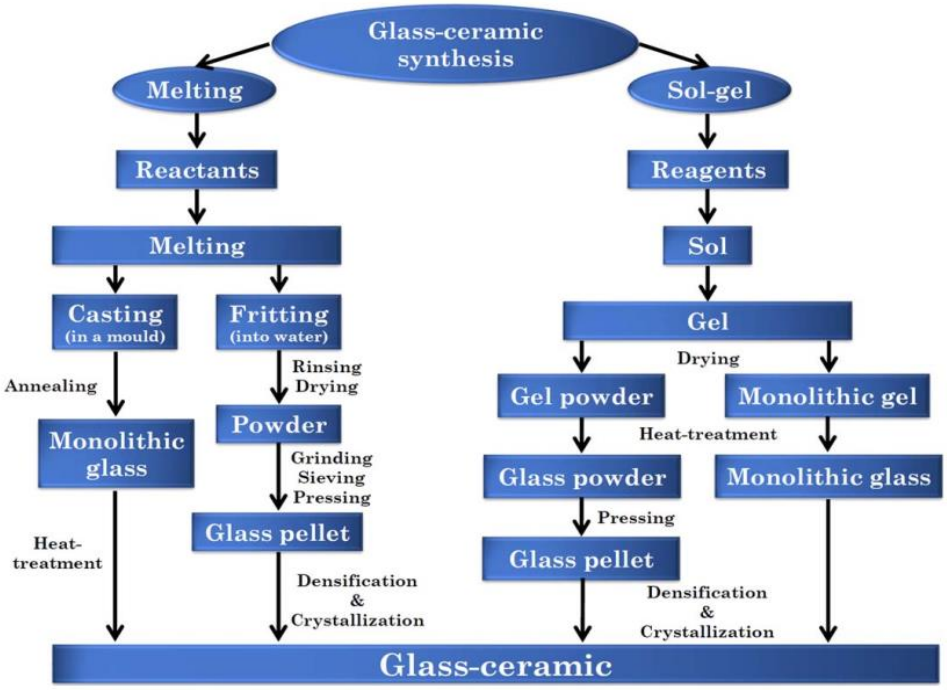

Figure 7: Main stages in the synthesis of glass-ceramics. [23]

Similarly, bioactive glass and glass-ceramics are materials that can induce a precise biological reaction on the surface of the material, stimulating cell proliferation, gene response and the formation of a link between living tissue and the material itself. [23]

A common and in fact rather essential denominator of bioactive glasses and glass-ceramics is the development of a biologically active layer of hydroxycarbonate apatite (HCA) on their surface that binds to bone and is chemically and structurally equivalent to the mineral phase of bone tissue. We can see the growth of the apatite hydroxycarbonate layer on a glass-ceramic surface in Figure 8. Unlike bioactive glasses, bioactive glass-ceramics do not have a weak mechanical resistance and a low toughness, because their resistance efficiency has been improved by developing several types of crystals. [23]

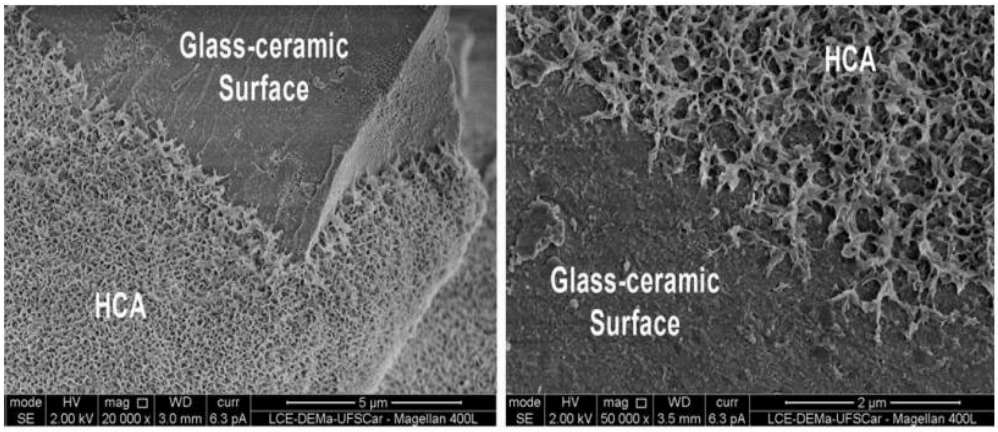

Figure 8 **:**Growth of the apatite hydroxycarbonate layer on a glass-ceramic surface. [23]

Among the most popular bioactive GCs, we could certainly mention for example Cerabone® (where apatite and wollastonite crystallize in a $MgO\text{-}CaO\text{-}SiO_2\text{-}P_2O_5$ glass), Biosilicate® and Bioverit® (with apatite and mica dispersed in $Na_2O\text{-}MgO\text{-}CaO\text{-}Al_2O_3\text{-}SiO_2\text{-}P_2O_5\text{-}F$ glass). The different uses of bioactive GCs are stated in the following chapter. [23]

3.1 Biosilicate®

Biosilicate® is a biomaterial with many different uses. Not only does it have antibacterial properties, but it is also very bioactive, osteoconductive, osteoinductive, not to mention that it is nontoxic and non-genotoxic. It is possible to use Biosilicate® in several forms, such as in powder or in a monolithic form, which is strong and solid. [24]

Biosilicate® has a composition of 23.75Na_2O - 23.75CaO - 48.5SiO_2-4P_2O_5 (% by wt). One or two crystalline phases can be obtained based on Biosilicate® under the effect of controlled double dosing thermal treatments. One of the phases is the sodium-calcium silicate phase ($Na_2CaSi_2O_6$), or both $Na_2CaSi_2O_6$ and the other sodium-calcium phosphate phase (NaCa-PO4). In order to evaluate the efficacy of Biosilicate® in clinical trials, several in vitro and fin vivo tests have been performed. Among the in vivo studies performed are tests using simulated body fluid and cell culture.

Simulated body fluid is an acellular solution that includes ions that have similar concentrations to those found in human blood plasma. By exposing inorganic materials, such as Biosilicate®, in this fluid, information is obtained on the kinetics of the formation of hydroxycarbonate apatite (HCA) on the later surface. There was a study where FITR was used to analyse the surface of Biosilicate® after exposure in the SBF. Biosilicate® containing a crystalline phase, 2 crystalline phases and Bioglass were used during the tests, and after a few hours of exposure of these materials, there was a formation of HCA in Bioglass (after 6h), in Biosilicate® with one crystalline phase (after 10h) and one containing 2 phases (after 4h). The conclusion of this study was that the formation of HCA was faster in Biosilicate® than in Bioglass; see Figure 9. [24]

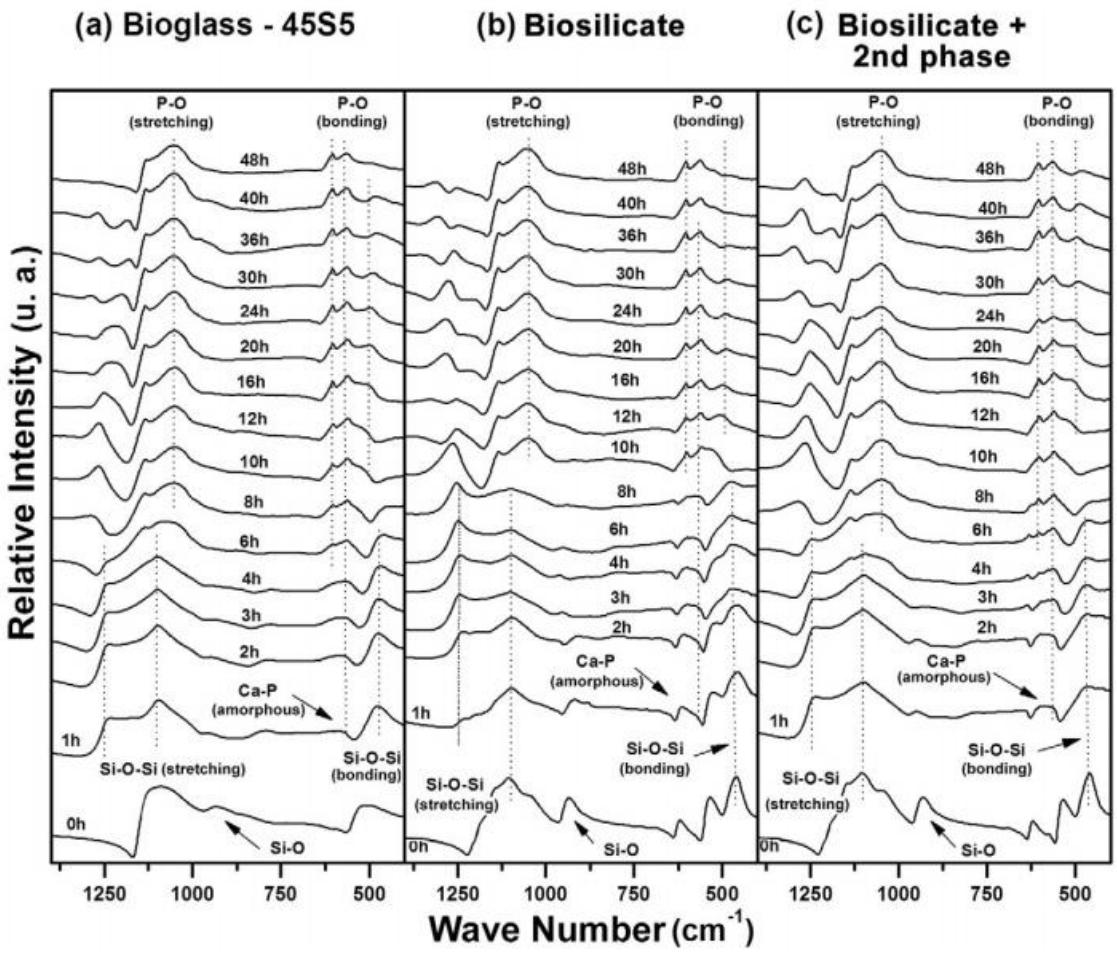

Figure 9: FTIR spectra for Bioglass 45S5 (a), Biosilicate® (1P) (b) and Biosilicate® containing two crystal phases (2P) exposed to SBF-K9 solution from 1 h to 48 h. [24]

Some other studies have shown that after a few hours of immersion of Biosilicate® in the simulated fluid, the crystallization of Biosilicate® parent glass, in solid form or on scaffolding, does not significantly affect the formation of HCA, but it actually improves it.

In vitro testing does not end only with exposing the biomaterial studied in the SBF. It is also important to do cytotoxicity tests which depend on evaluating whether the dissolution products of a given biomaterial and the pH resulting from the solution are toxic to the cells or not. A study analysing the effect of Biosilicate® (2P) scaffold dissolution products with concentrations ranging from 12.5% to 100% in osteoblast and fibroblast cell cultures has shown that the proliferation of osteoblasts and fibroblasts was reduced in cells exposed to a high concentration (100%) of the biomaterial, which may be due to the elevated pH (see Figure 10). [24]

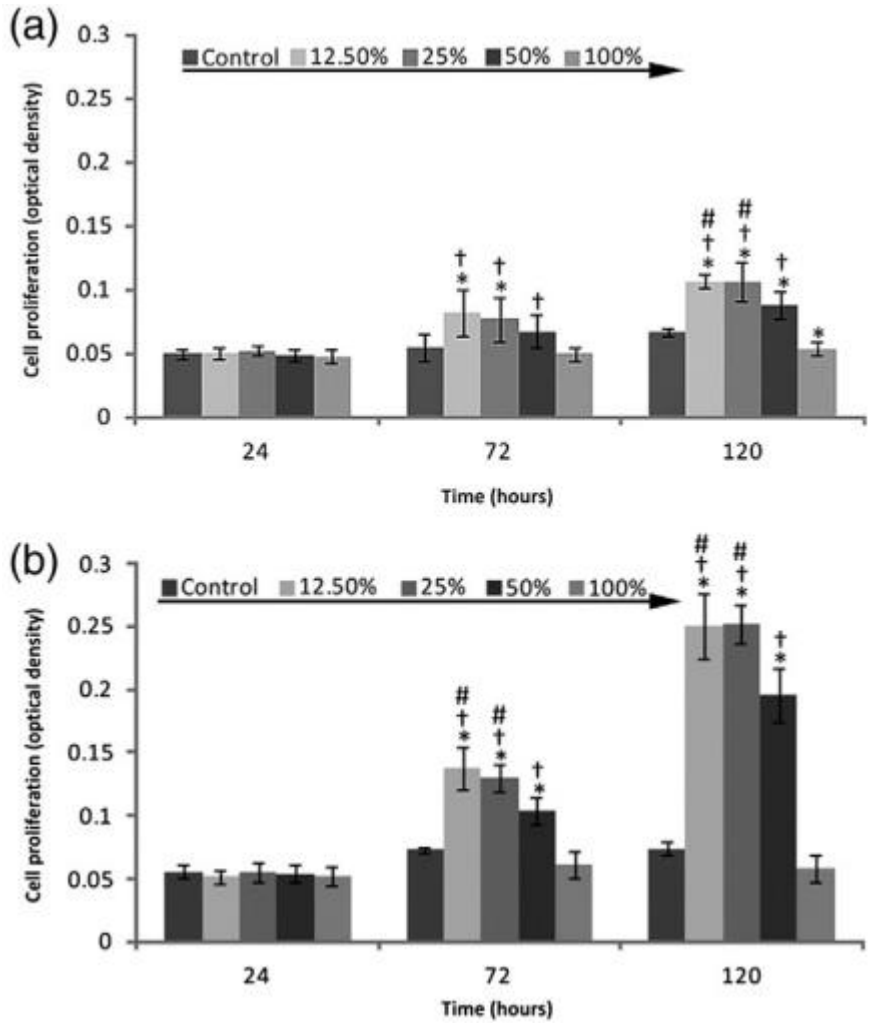

Figure 10: (a) Proliferation of the osteoblastic cell line grown in solutions containing different concentrations of the Biosilicate® scaffold extract (12.5%, 25%, 50%, and 100%) at different times of cultivation (24, 72, and 120 h). *p ≤ 0.05 versus control, †p ≤ 0.05 versus 100 %, and *p ≤ 0.05 versus 50%. (b) Proliferation of the fibroblastic cell line grown in solutions containing different concentrations of Biosilicate® scaffold extract (12.5%, 25%, 50%, and 100%) at different times of cultivation (24, 72, and 120 h). *p ≤ 0.05 versus control, †p ≤ 0.05 versus 100%, and *p ≤ 0.05 versus 50%. [24]

There have also been several studies of Biosilicate® in vivo. One of the investigations was based on the histological and histomorphometric bone response of Biosilicate® in rabbits and at the end, the effect of Biosilicate®, Biosilicate® (1P) and Biosilicate® (2P) parent glass as stem implants in bone defects of the rabbit femur was analysed. During this study, sixteen

animals underwent surgery and biomaterial rods with a size of 2.2 × 4.0 mm were implanted bilaterally and Bioglass 45S5 was used as a control material. From 8 to 12 weeks later, histological analyses showed no evidence of persistent inflammation or a foreign body reaction at the implantation sites during all experimental periods and that 1F = Biosilicate® 1P and 2F = Biosilicate® 2P had a higher cortical bone formation than Bioglass 45S5 and Biosilicate® ($p = 0.02$), see Figure 11. This study concluded that all the materials studied were biocompatible. Biosilicate® has also proven to be a potential biomaterial capable of providing an immediate, effective and long-lasting treatment alternative for patients who suffer from cervical dentin hypersensitivity. [24]

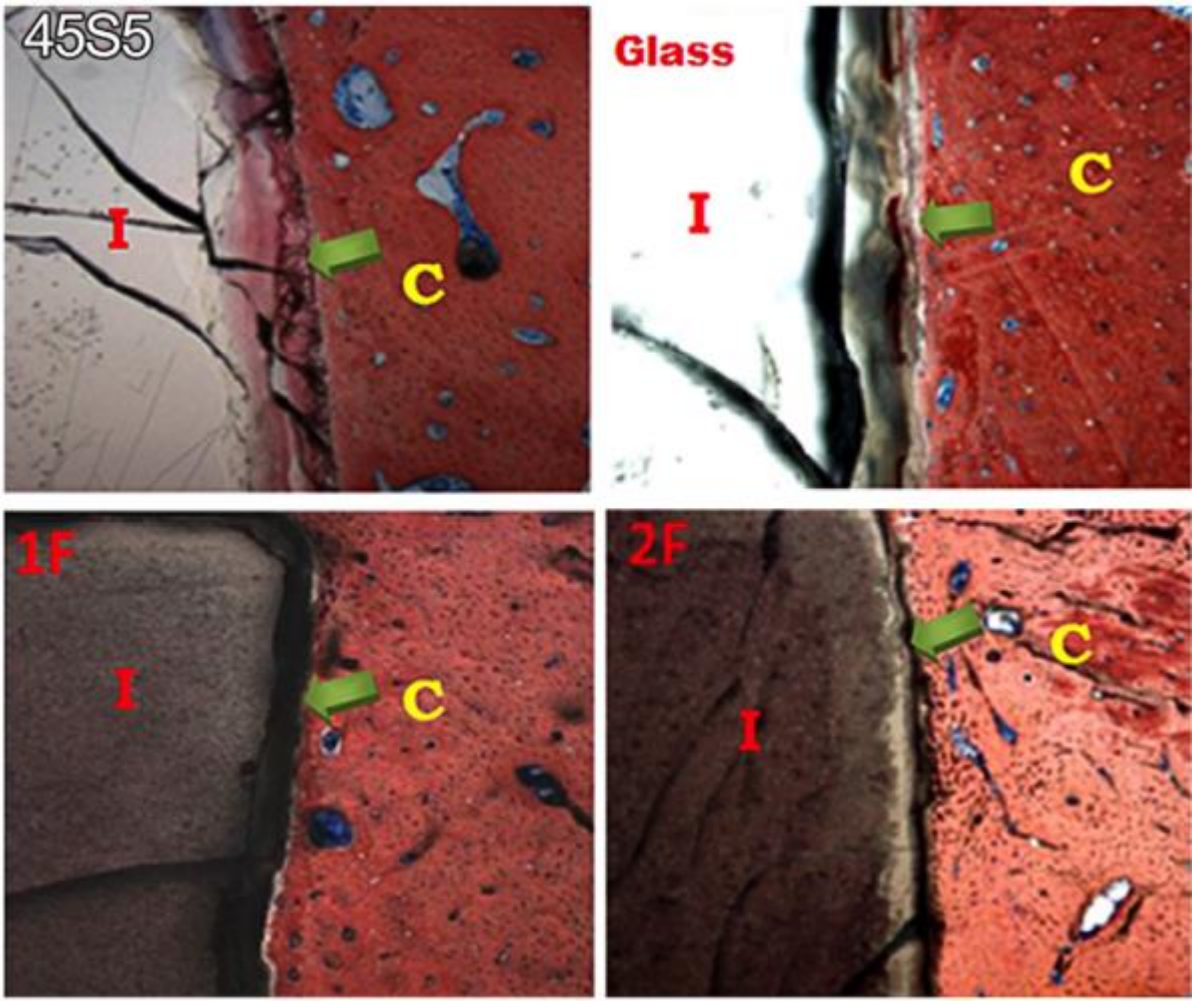

Figure 11: Histological analysis showing the direct contact between the implants (I) and the cortical bone (C) after 12 weeks. 1F = Biosilicate® 1P and 2F = Biosilicate® 2P. [24]

4 CONCLUSION

The aim of this thesis was to discuss bioactivity of glass, ceramics and glass-ceramics as biomaterials.

As far as bioactivate glasses are concerned, glasses containing boron have been analysed and in the field of glass-ceramics, Biosilicate® was focused on. These two biomaterials have demonstrated positive applications in the orthopaedic field, as they have a common property – they improve the formation of new bone tissue due to their ability to create a layer of hydroxycarbonate apatite on their surface similar to that of bone. On the other hand, bioactive glasses have poor mechanical resistance when compared to bioactive glass-ceramics. Bioceramics are used in dentistry and orthopaedics. This thesis focused on ceramics in dentistry. Zirconium dioxide ceramics have proved very useful because of their chemical, physical and aesthetic properties in the fabrication of prostheses, canal ducts, implant crowns and others.

Naturally, the amount of research on biomaterials in the field of biomedicine has been on the increase. The main reason for this is humanity's eternal effort to increase the lifespan of the human body. And to do this, it is very important to continue improving the properties of biomaterials used in implants, particularly their resistance and their biocompatibility.

REFERENCES

[1] *Kirk-Othmer Encyclopedia of Chemical Technology* [online]. Hoboken, NJ, USA: John Wiley & Sons, 2011 [cit. 2019-06-04]. ISBN 0471238961.

[2] RATNER, B. D. *Biomaterials Science* [online]. Boston: Elsevier, 2013 [cit. 2019-06-13]. DOI: 10.1016/C2009-0-02433-7. ISBN 9780123746269.

[3] JONES, Julian R. and Alexis CLARE. *Bio-glasses: an introduction*. Chichester, West Sussex: Wiley, 2012. ISBN 9780470711613.

[4] EL-RASHIDY, Aiah A., Judith A. ROETHER, Leila HARHAUS, Ulrich KNESER and Aldo R. BOCCACCINI. Regenerating bone with bioactive glass scaffolds: A review of in vivo studies in bone defect models. *Acta Biomaterialia* [online]. 2017, **62**, 1-28 [cit. 2019-06-04]. DOI: 10.1016/j.actbio.2017.08.030. ISSN 17427061.

[5] BAINO, Francesco. Bioactive glasses – When glass science and technology meet regenerative medicine. *Ceramics International* [online]. 2018, **44**(13), 14953-14966 [cit. 2019-03-17]. DOI: 10.1016/j.ceramint.2018.05.180. ISSN 02728842.

[6] JUHASZ, Judith A. and Serena M. BEST. Bioactive ceramics: processing, structures and properties. *Journal of Materials Science* [online]. 2012, **47**(2), 610-624 [cit. 2019-04-11]. DOI: 10.1007/s10853-011-6063-x. ISSN 0022-2461.

[7] GAVINHO, Sílvia R., Pedro R. PREZAS, Diogo J. RAMOS, et al. Nontoxic glasses: Preparation, structural, electrical and biological properties. *International Journal of Applied Ceramic Technology* [online]. 2019 [cit. 2019-06-07]. DOI: 10.1111/ijac.13243. ISSN 1546-542X.

[8] BAINO, Francesco, Elisa FIUME, Marta MIOLA and Enrica VERNÉ. Bioactive sol-gel glasses: Processing, properties, and applications. *International Journal of Applied Ceramic Technology* [online]. 2018, **15**(4), 841-860 [cit. 2019-05-12]. DOI: 10.1111/ijac.12873. ISSN 1546542X.

[9] KAUR, Gurbinder, O.P. PANDEY, K. SINGH, Dan HOMA, Brian SCOTT and Gary PICKRELL. A review of bioactive glasses: Their structure, properties, fabrication and apatite formation. *Journal of Biomedical Materials Research Part A* [online]. 2014, **102**(1), 254-274 [cit. 2019-06-06]. DOI: 10.1002/jbm.a.34690. ISSN 15493296.

[10] BALASUBRAMANIAN, Preethi, Teresa BÜTTNER, Valentina MIGUEZ PACHECO and Aldo R. BOCCACCINI. Boron-containing bioactive glasses in bone and soft tissue engineering. *Journal of the European Ceramic Society* [online]. 2018, **38**(3), 855-869 [cit. 2019-04-17]. DOI: 10.1016/j.jeurceramsoc.2017.11.001. ISSN 09552219.

[11] ABDELGHANY, A.M. Novel method for early investigation of bioactivity in different borate bio-glasses. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy [online]. 2013, 100, 120-126 [cit. 2019-04-19]. DOI: 10.1016/j.saa.2012.02.051. ISSN 13861425.

[12] LEPRY, William C., Sophia SMITH and Showan N. NAZHAT. Effect of sodium on bioactive sol-gel-derived borate glasses. Journal of Non-Crystalline Solids [online]. 2018, 500, 141-148 [cit. 2019-04-20]. DOI: 10.1016/j.jnoncrysol.2018.07.042. ISSN 00223093.

[13] LEPRY, William C. and Showan N. NAZHAT. Highly Bioactive Sol-Gel-Derived Borate Glasses. *Chemistry of Materials* [online]. 2015, **27**(13), 4821-4831 [cit. 2019-05-27]. DOI: 10.1021/acs.chemmater.5b01697. ISSN 0897-4756.

[14] BALASUBRAMANIAN, Preethi, Teresa BÜTTNER, Valentina MIGUEZ PACHECO and Aldo R. BOCCACCINI. Boron-containing bioactive glasses in bone and soft tissue engineering. *Journal of the European Ceramic Society* [online]. 2018, **38**(3), 855-869 [cit. 2019-05-27]. DOI: 10.1016/j.jeurceramsoc.2017.11.001. ISSN 09552219.

[15] GU, Yifei, Wenhai HUANG, Mohamed N. RAHAMAN and Delbert E. DAY. Bone regeneration in rat calvarial defects implanted with fibrous scaffolds composed of a mixture of silicate and borate bioactive glasses. *Acta Biomaterialia* [online]. 2013, **9**(11), 9126-9136 [cit. 2019-05-27]. DOI: 10.1016/j.actbio.2013.06.039. ISSN 17427061.

[16] FERNANDES, João S., Piergiorgio GENTILE, Robert MOOREHEAD, Aileen CRAWFORD, Cheryl A. MILLER, Ricardo A. PIRES, Paul V. HATTON and Rui L. REIS. Design and Properties of Novel Substituted Borosilicate Bioactive Glasses and Their Glass-Ceramic Derivatives. *Crystal Growth & Design* [online]. 2016, **16**(7), 3731-3740 [cit. 2019-05-27]. DOI: 10.1021/acs.cgd.6b00231. ISSN 1528-7483.

[17] *Kirk-Othmer Encyclopedia of Chemical Technology: Ceramics, Overview* [online]. Hoboken, NJ, USA: John Wiley & Sons, 2000 [cit. 2019-06-07]. ISBN 0471238961.

[18] HEIMANN, Robert B. Ullmann's Encyclopedia of Industrial Chemistry: Ceramics, Bioceramics [online]. Weinheim, Germany: Wiley-VCH Verlag GmbH & Co., 2011 [cit. 2019-05-19]. ISBN 3527306730.

[19] SHEN, James Zhijian and Tomaž KOSMAČ. Advanced ceramics for dentistry. Waltham, MA: Elsevier/BH, 2014. ISBN 978-0-12-394619-5.

[20] OZKURT, Zeynep and Ender KAZAZOGLU. Clinical Success of Zirconia in Dental Applications. *Journal of Prosthodontics* [online]. 2010, **19**(1), 64-68 [cit. 2019-04-26]. DOI: 10.1111/j.1532-849X.2009.00513.x. ISSN 1059941X.

[21] GUESS, Petra Christine, Wael ATT and Joerg Rudolf STRUB. Zirconia in Fixed Implant Prosthodontics. *Clinical Implant Dentistry and Related Research* [online]. 2012, **14**(5), 633-645 [cit. 2019-05-18]. DOI: 10.1111/j.1708-8208.2010.00317.x. ISSN 15230899.

[22] RODRIGUEZ, Angel E., Mona MONZAVI, Chester L. YOKOYAMA a Hessam NOWZARI. Zirconia dental implants: A clinical and radiographic evaluation. *Journal of Esthetic and Restorative Dentistry* [online]. 2018, **30**(6), 538-544 [cit. 2019-06-20]. DOI: 10.1111/jerd.12414. ISSN 14964155.

[23] MONTAZERIAN, Maziar and Edgar DUTRA ZANOTTO. History and trends of bioactive glass-ceramics. Journal of Biomedical Materials Research Part A [online]. 2016, 104(5), 1231-1249 [cit. 2019-05-10]. DOI: 10.1002/jbm.a.35639. ISSN 15493296.

[24] CROVACE, Murilo C., Marina T. SOUZA, Clever R. CHINAGLIA, Oscar PEITL and Edgar D. ZANOTTO. Biosilicate® — A multipurpose, highly bioactive glass-ceramic. In vitro, in vivo and clinical trials. *Journal of Non-Crystalline Solids* [online]. 2016, **432**, 90-110 [cit. 2019-06-01]. DOI: 10.1016/j.jnoncrysol.2015.03.022. ISSN 00223093.