Excess entropy and thermal behavior of Cu- and Ti-doped bioactive glasses

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Abstract Bioactive glasses belong to the ceramic family. They are good materials for implantation due to their excellent capacities to create an intimate bond with bones. Copper is known for its anti-inflammatory, antibacterial, and antifungal properties. Titanium is biocompatible and resistant to corrosion. These chemical elements can be introduced in bioactive glasses to provide a wide variety of uses and to enhance the physiological properties of implanted biomaterials. In this work, bioactive glasses doped with different contents of copper and titanium were synthesized by the melting method. The purpose is to study the effect of doping metal element on the thermal characteristics (T_g, T_c and T_f). The results revealed that the increase of the content of copper and titanium in the glass matrix decreases the melting temperature and induces an increase of the thermal stability. The excess entropies of pure and doped glasses were calculated. Obtained results highlighted the decrease of the excess entropy with the increase of metal elements contents.

Keywords Copper, Titanium, Glasses, Entropy, Thermal behavior

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Introduction

Biomaterials are considered like an interesting option to replace bone grafts. Even if the bone is the best biomaterial for filling bone, biomaterials can avoid the risks as the transmission of viruses and are available in unlimited quantity [1-2]. The use of biomaterials was significantly developed for the bone repair. However, the introduction of a new material in the medical field requires a precise study to evaluate the biocompatibility and the physico-chemical properties.

The studied bioactive glasses are used as filling bone biomaterial in orthopedic and maxillofacial surgery. They are composed of several oxides: SiO_2, Na_2O, CaO, and P_2O_5. Their bioactive character results of their ability to form a hydroxyapatite layer $Ca_{10}(PO_4)_6(OH)_2$ on their surface when they are immersed in a simulated body fluid [3-5]. Moreover, the mineral part of human bones is composed of hydroxyapatite. This formation induces a bone bonding improving the bone growth.

Some kind of glasses, in the silicate-phosphate glass compositions, has been studied [6-11]. Indeed, Hill et al. [12] proved that the adding of strontium in the glass matrix has an impact on the glass transition and crystallization temperatures. Lusvardi et al. [13-14] have evaluated the effect of fluoride- and zinc-doped phosphosilicate glasses. Handke, Sitarz, and coauthors [15-18] have studied the structures of multiples glasses having different chemical compositions.

However, there is possible appearance of complications during bone repair such as bacterial infections. The originality of this study is based on the introduction of Cu and Ti in bioactive glass 46S6 by adding CuO and TiO_2. Indeed, these chemical elements present interesting physiological properties.

Titanium is mainly used in bio-inert materials such as hip implants made of titanium alloy, screws, and plates to repair bone fractures. It is a chemically biocompatible element which allows having mechanically interesting materials [19].

It is recognized that the use of copper materials in hospitals and in public areas reduces the risk of infections. Copper is a chemical element known for its anti-inflammatory and anti-infectious properties. It is necessary for a lot of biological processes in the human body. Copper is an essential component of the angiogenic response [20]. Angiogenesis is a process in the repair of new biological tissues [21]. *In vivo* copper release has been shown to decrease the risk of ischemia, to induce a vascularised capsule around a cross-linked hyaluronic acid hydrogel [22-23] and to stimulate endothelial cell proliferation [24].

The glass is an amorphous system with an unordered structure composed of network forming, modifying, and intermediate oxides. The introduction of metal elements in the glass involves specific changes of thermal characteristics. In a previous work, the effect of zinc has been proven on the melting temperature and the excess entropy. The increase of zinc oxides in the glassy matrix decreases these characteristics [25]. Copper and titanium oxides are intermediate elements generally used in the industry to give a colored glass. In the glassy matrix, if there are no enough alkaline ions, then the intermediate element will be a network modifier by creating two oxygen bridges. Conversely, if there are enough alkaline ions, then the intermediate element will be a network former [25-26].

Numerous studies have proved the effect of copper and titanium on the thermal behavior and characteristics.

The addition of TiO_2, into oxides glass-forming system, usually contributes to the stabilization of their structure and to the improvement of their properties: chemical durability, mechanical properties, electrical conductivity [27].

In the borophosphate glasses, the addition of TiO_2 results in a non-linear increase of glass transition temperature [28]. In glasses in the ternary system Na_2O-TiO_2-P_2O_5, the addition of TiO_2 (from 0 to 5 mol% TiO_2) resulted in a non-linear increase of glass transition temperature and dilatation softening temperature. The increase of TiO_2 content involves the increase of the contribution of the surface crystallization mechanism. With increasing TiO_2 content, the temperature of maximum nucleation rate is also gradually shifted from a value close to the glass transition temperature toward the crystallization temperature. The chemical durability of the glasses without titanium oxide is very poor, but with the replacement of Na_2O or P_2O_5 by TiO_2, it increases sharply [29].

In silicate–phosphate glasses, the introduction of copper has an impact on the thermal characteristics. Indeed, the relationship between the parameters characterizing glass transformation effect and an amount of phosphorous and copper forming the glassy structure showed that an increasing content of phosphorous increases solubility of copper in the structure. Changes of T_g were higher in glasses with higher content of P_2O_5 and CuO [30]. Moreover, in this kind of glass, the crystallization temperature was found to decrease with the increasing copper content [31]. Various studies were undertaken to investigate the thermal properties of glasses containing copper. For example, in metallic glasses $Cu_{50}Zr_{43}Al_7$, the glass-forming ability and thermal stability may improve with the adding of Be [32].

Generally, the study of the vitreous state is a approach to the description of the structural disorder. It is the general definition of the entropy. In recent literature on thermal behavior of glasses, several authors believe that the glass formation from a liquid lust be obtained by a loss of entropy at the glass transition temperature [33, 34]. The applicability of thermodynamics to the vitreous state was recognized in the first papers considered now as classic ones [35]. It was shown that the entropy of a glass is higher than that a crystal of the same composition at T = 0 K [36]. Moreover, the temperature during the synthesis of glasses could be an impact on the entropy. Indeed, Tropin et al. [37] have proved that the entropy production in glass transition becomes of increasing importance with an increase of the rates of change of temperature. Moreover, both thermodynamic and statistical–mechanical approaches are shown to confirm the conventional point of view that non-zero residual entropy is frozen-in in the system in the course of the glass transition [37]. The respective value of the residual entropy increases with increasing absolute values of the rate of change of temperature [37]. In a previous work [25], the entropy calculation was carried out on Zn-doped bioactive glasses. The results have showed that the increase of the amount of Zn in the glass matrix involves a decrease of the excess entropy and an increase of the thermal stability.

Thereby, the purpose of this study is to investigate the effect of the introduction of copper and titanium ions on the thermal characteristics of bioactive glasses used in bone filling. For each chemical composition, the excess entropy was calculated according to the changes of thermal characteristics [25]. This entropy corresponds to the difference between the melting entropy of crystal and the entropy of glass [25]. Contrary to crystals, synthesized glasses have entropy different to zero at $T = 0$ K and versus T_f [38].

Materials and methods

Preparation of bioactive glasses

Eight bioactive glasses had been synthesized from the composition of 46S6 (46 mass% SiO_2, 24 mass% CaO, 24 mass%, Na_2O, and 6 mass% P_2O_5). Moreover, this bioactive glass composition 46S6 was studied doped by introduction of different concentrations of copper and titanium: 46S6-*x*Cu and 46S6-*x*Ti *(*where x = 0, 0.1, 1, 5, and 10 in mass%). TiO_2 and CuO were introduced at the expense of Na_2O and CaO [25].

For elaboration of the bioactive glass, sodium metasilicate (Na_2SiO_3), silicon oxide (SiO_2), calcium metasilicate ($CaSiO_3$), sodium metaphosphate ($Na_3P_3O_9$), copper oxide (CuO), and titanium oxide (TiO_2) were weighed and mixed in a polyethylene bottle, for 2 h using a planetary mixer.

The premixed mixtures were melted in platinum crucibles that were placed in an electric furnace. The first rise of temperature rate was 10 °C min^{-1} and it was hold at 900 °C for 1 h to achieve the decarbonation of all products. The second rise of temperature rate was 20 °C min^{-1} and it was hold to 1,350 °C for 3 h. The samples were casted in preheated brass molds, in order to form cylinders of 13 mm in diameter, and annealed at 565 °C for 4 h near the glass transition temperature of each glass [25].

Thermal analysis

Differential thermal analysis (DTA) was used to determine the characteristic temperatures of different bioactive glasses. The DTA principle is based on the detection of whether the phenomenon was exothermic or endothermic phenomenon. The glass transition temperature T_g, the crystallization temperature T_c and the melting temperature T_f have been recorded using a Setaram Labsys 1600TG-DTA/DSC thermal analyzer under N_2 gas atmosphere. Therefore, the onset temperature of crystallization $T_{onset}c$ represented the beginning of the crystallization has been recorded. The bioactive glasses were studied under heating rate of 5 °C min^{-1} raised from room temperature to 1,400 °C. Moreover, 40 mg of the glass powder was heated in platinum crucible and, at the same time, another empty platinum crucible for use as control. It is necessary to regularly carry out temperature calibration and sensitivity calibration. Thereby, before the thermal analysis, the melting temperature of copper sulfate was checked for calibration. The thermal stability (TS) of bioactive glass has been expressed by the temperature difference between T_g and $T_{onset}c$ introduced by Dietzel [39]:

$$TS = T_{onset}c - T_g$$

Results and discussion

Characterizations of bioactive glasses doped with Cu and Ti

The X-ray diffraction patterns were recorded between 5 and 80 (2θ/°) using a Bruker D8 advance diffractometer with Cu Kα radiation. Diffractograms of pure and doped glasses, presented in Fig. 1, revealed a halo of diffraction from 24 to 38 (2θ/°) that was characteristic of an amorphous system. A high content of Cu or Ti introduced in the glass matrix does not affect the amorphous character of these glasses.

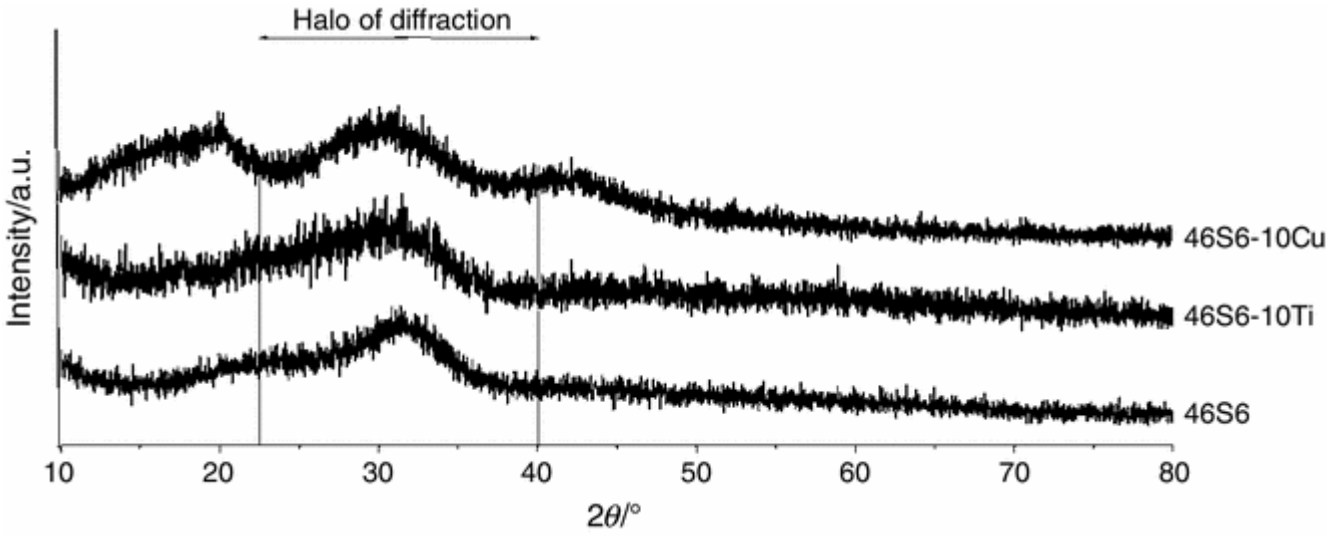

Fig. 1
Diffractograms of pure and doped glasses

The infrared spectra were recorded by using Fourier transformer infrared (FTIR) spectrometer Bruker Equinox 55 between 4,000 and 400 cm^{-1} with a resolution of 2 cm^{-1}. The infrared spectra of bioactive glasses revealed several characteristic bands (Fig. 2).

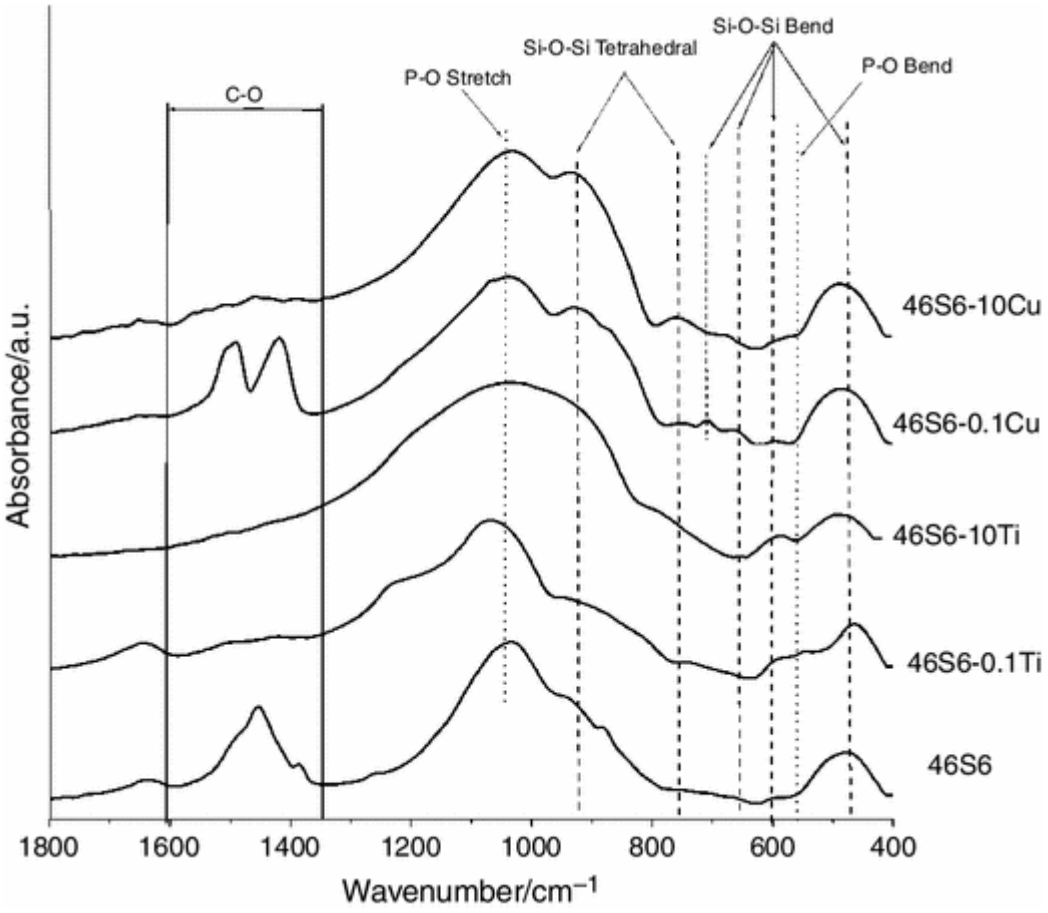

Fig. 2
FTIR spectra of pure and doped glasses

Numerous infrared spectroscopy studies have been carried out about phosphate materials. Jastrzebski et al. [40] have shown that non-tetrahedral cations have an influence on the shape of the FTIR spectra and the positions of P–O chemical bonds bands. In silicate glasses, Sitarz [41] has proven that the presence of alkaline ions in silicate glass structure leads to elimination of Si=O structural defects, which means that the ions are located between the ordered domains.

Concerning all chemical compositions, bands characteristic of bend vibrations of Si–O–Si bonds are visible at 479 cm^{-1} [41]. Between 1,350 and 1,600 cm^{-1}, vibrations of C–O bonds are due to the carbon dioxide present during the analysis. At 757 and 924 cm^{-1}, bands characteristics of tetrahedral vibrations of Si–O–Si bonds are present except for pure glass 46S6 where the band at 757 cm^{-1} is not present. And a stretch vibration of P=O bonds is visible at 1,050 cm^{-1} for pure and doped glasses. Thereby, the introduction of doping elements allows creating other chemical bonds.

Changes appear according to the doping element introduced in the glass. At 567 cm^{-1}, there is a vibration characteristic of bend vibrations of P–O bond for Ti-doped glasses. This bond, in the Ti-doped glasses, could be due to a breaking of P=O bond. Silva et al. [42] explain that in the glass, with a low content of TiO_2, the metaphosphate units are dominant and increasing the content; metaphosphate units are replaced by pyrophosphate units. This could also explain the formations P–O bonds for Ti-doped glasses. Indeed, RMN study in calcium phosphate glasses containing titanium has proved that the introduction of TiO_2 in the matrix involves the formation of Ti–O–P bonds [42]. The increase of TiO_2 could allow the replacement of a P–O–P bond by a Ti–O–P bond and thus increase the intensities of P–O bands at 557 and 1,050 cm^{-1}.

At 667 and 706 cm^{-1}, bend vibrations of Si–O–Si bonds are just present on the Cu-doped glasses FTIR spectra. The presence of copper ions in SiO_2 amorphous structure leads to network depolymerization, i.e., breaking of Si–O–Si bridges, leading to an increase in the number of Si–O− non-bridging terminal bonds [41]. Also, the presence of copper element, whose electronegativity is almost identical to that of silicon, results in additional bands in the FTIR spectra characteristic of Si–O bonds.

Thereby, either copper or titanium, new chemical bonds are formed in the vitreous matrix. Si–O–Si bonds are formed in the Cu-doped glasses while P–O bonds appear in those doped with titanium. The electronegativity of these elements (Table 1) may explain these differences. Copper, with its high electronegativity, will form more new chemical bond than titanium. These data are important to the extent that these formations of chemical bonds may have an influence on the thermal behavior of glasses.

Table 1
Atomic radius, electronegativity, and fusion point of copper and titanium

Chemical element	Atomic radius/pm	Electronegativity	Fusion point/ °C
Cu	145	1.90	1,083
Ti	176	1.54	1,660

The DTA analysis was undertaken in order to measure the characteristic temperatures and calculate the excess entropy.

Influence of Cu and Ti on the thermal characteristics of bioactive glasses

In bioactive glasses, the ratio CaO/Na_2O was kept constant and equal to 1. The content of Na_2O and CaO decreases in favor of the content of CuO or TiO_2. In a previous work concerning the study of Zn-doped glasses, the variation of the CaO/Na_2O ratio was involved in the decrease of characteristic temperatures [25]. Indeed, the introduction of Na_2O creates two bridge-oxygen in the amorphous system. The two negative charges of oxygen are balanced by the charge of Na^+ pair forming a neutral electrostatic matrix. Thereby, the network structure is modified and changes the glass thermal properties [25]. The introduction of CaO does not involve any modifications because the two positive charges of Ca^{2+} are balanced and create two tetrahedrons linked by ionic bonds [25]. Also it is proved that the increase of $NaCaPO_4$ amount in studied glasses causes a significant increase of their resistance to crystallization [43].

The impact of Cu and Ti was described.

DTA curves are showed in Fig. 3a for Cu-doped glasses and in Fig. 3b for Ti-doped glasses. Each thermal curve presents 3 peaks characteristics of glass transition, crystallization, and melting temperatures. To determine the start of fusion phenomenon ($T_{onset}f$) and the start of crystallization phenomenon ($T_{onset}c$), the tangent method was used, and the thermal characteristics of doped glasses are summarized in Tables 2 and 3. $T_{onset}c$ is an important data to calculate the thermal stability of each glass according to the Dietzel relation.

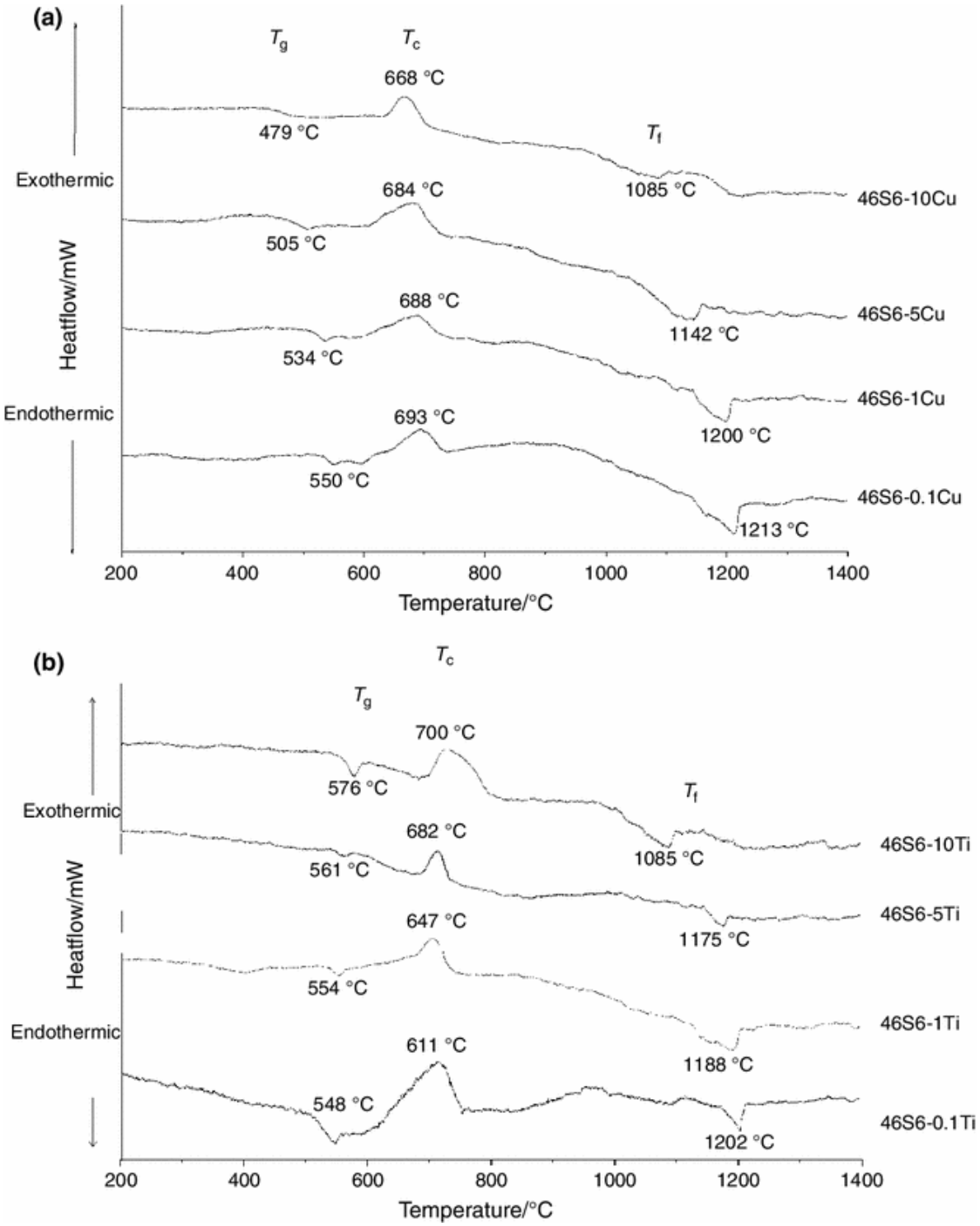

Fig. 3
a Thermal curves of Cu-doped glasses, b thermal curves of Ti-doped glasses

Table 2

Thermal characteristics of Cu-doped glasses

	46S6-0.1Cu	**46S6-1Cu**	**46S6-5Cu**	**46S6-10Cu**
L_f	57	40	34	22
T_{onset}c/K	906	893	882	911
T_g/K	823	807	778	752
TS/K	83	86	104	129
T_f/K	1,486	1,473	1,415	1,358
ΔS/J K^{-1}	37	28	23	14

Table 3

Thermal characteristics of Ti-doped glasses

	46S6-0.1Ti	**46S6-1Ti**	**46S6-5Ti**	**46S6-10Ti**
L_f	110	51	23	9
T_{onset}c/K	898	915	948	964
T_g/K	821	827	834	849
TS/K	77	88	114	115
T_f/K	1,475	1,461	1,448	1,358
ΔS/J K^{-1}	73	36	15	5

Characteristic temperatures versus the content of Cu or Ti are presented in Figs. 4 and 5. It shows that for Cu-doped glasses, a decrease of T_g, T_c and T_f is observed when the content of Cu increases. These results are in accordance with the results obtained by Sulowska et al. [30]. Indeed, the increasing amount of copper introduced to the amorphous matrix of glasses at the cost of decreasing amount of CaO was the reason of the increasing degree of internal strains relaxation in the glass structure which was accompanied by the decrease of transformation temperature (T_g) [30]. The same phenomenon is observed for our glasses.

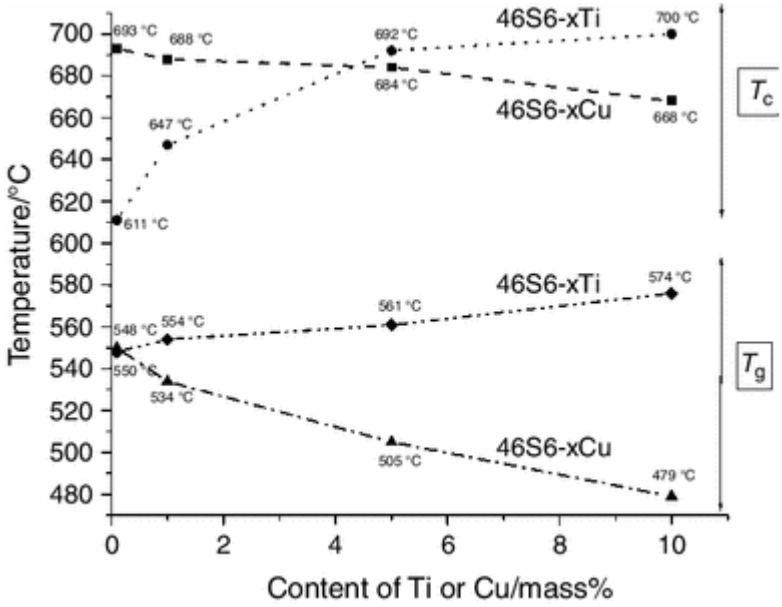

Fig. 4
T_c and T_g function of the content of doping metal element

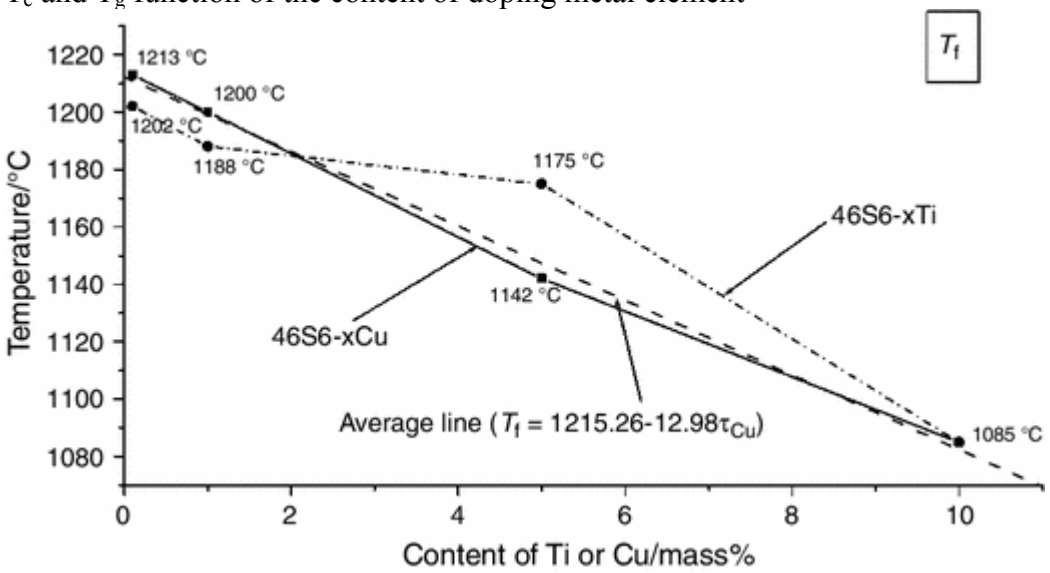

Fig. 5
T_f function of the content of doping metal element

The introduction of copper ions involves a linear decrease of the melting temperature. A mathematic relationship is determined in Fig. 5 giving the melting temperature versus the content of Cu introduced in the glassy matrix. Concerning to Ti-doped glasses, variations are observed for the three characteristic temperatures. Indeed, T_g and T_c increase (up to 574 and 700 °C respectively), T_f decreases (up to 1,085 °C) when the content of Ti increases in the glassy matrix. For T_g and T_c, these results are found in phosphate glasses [44]. Important differences are observed between the low content and the high content of doping element introduced in glasses. Indeed, between 46S6-0.1Ti and 46S6-10Ti, ΔT_g = +26 °C and ΔT_c = +89 °C while between 46S6-0.1Cu and 46S6-10Cu, ΔT_g = –25 °C and ΔT_c = –69 °C. Thereby, the significant result is that Ti involves opposite variations on T_g and T_c compared to Ag.

And for all glasses, when the amount of metal element increases, the thermal stabilities are higher (up to 129 for 46S6-10Cu and 115 for 46S6-10Ti) as shown in Fig. 6. An important thermal stability reveals a low

tendency to crystallization [25]. Here, Cu-doped glasses present ΔTS = 46 K between 46S6-0.1Cu and 46S6-10Cu. For Ti-doped glasses, ΔTS = 38 K between 46S6-0.1Ti and 46S6-10Ti. Szumera et al. [45] observed the same influence when MnO2 is introduced in glass matrix of silicate-phosphate glasses. The increase of the amount of MnO2 involves a decrease of the glass transition and an increase of the thermal stability.

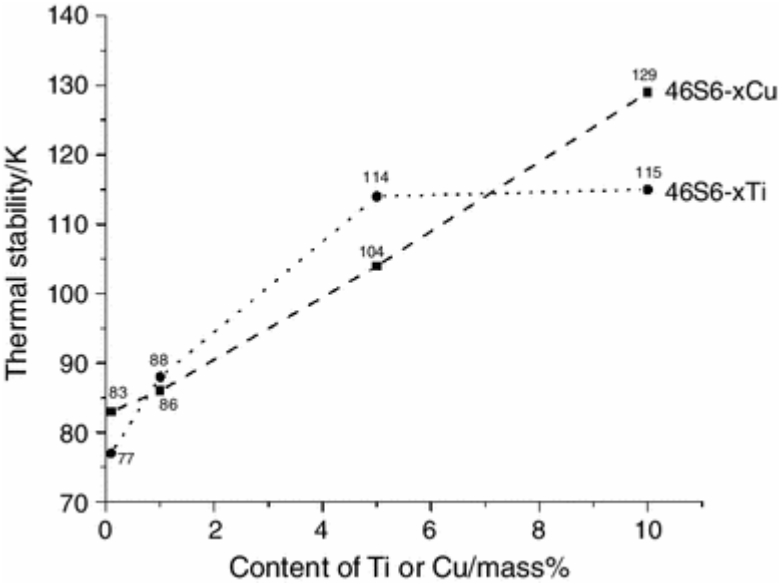

Fig. 6
Thermal stability function of the content of doping metal element

The most important impact of Ti and Cu is observed on the melting temperatures. Indeed, between 46S6-0.1Cu and 46S6-10Cu, ΔT_f = –128 °C and between 46S6-0.1Ti and 46S6-10Ti, ΔT_f = –117 °C. The differences of temperature are more important compared to T_g and T_c. Moreover, the increasing adding of Cu in the glass matrix decreases linearly the melting temperature following a mathematic relation: $T_f = 1{,}215.26 – 12.98\tau_{Cu}$ where τ_{Cu} is the content of copper.

Finally, the introduction of Cu or Ti in glasses involves a decrease of melting temperature: linear decrease for Cu-doped glasses and non-linear decrease for Ti-doped glasses. For Cu-doped glasses, T_c and T_g also decrease while for Ti-doped glasses, T_g and T_c increase. The doping elements introduced in high amount increase the thermal stability of glasses. When the doping metallic oxides are introduced in the amorphous matrix, the covalent Si–O–Si chemical bonds were broken to create metal–oxygen ionic bonds. As covalent bonds are stronger energetically than metal–oxygen bonds formed, changes in the thermal behavior of glasses are observed. Also, as in the works of Sitarz et al. [46] about MgO in phosphosilicate glasses, it would be possible that calcium ions Ca^{2+} are replaced by copper ions Cu^{2+} causing the reduction of thermal resistance of glasses which would explain the decrease of glass transition, crystallization, and melting temperatures. The changing character of domains structure may be the reason of different thermal behaviors [47, 48]. The chemical characteristics of Ti and Cu (Table 1) may also explain the changes in the thermal behavior. Indeed, the reduction of melting temperatures for Cu-doped glasses is rapid compared to those Ti-doped glasses which start to decrease as from 5 mass% of Ti introduced. The melting points of the introduced metal elements may explain this phenomenon. Copper and titanium have respectively melting points of 1,083 and 1,660 °C that is why the Ti-doped glasses present a slowly decrease of their melting temperature and present a non-linear evolution

compared to Cu-doped glasses. Moreover, titanium presents a high electronegativity compared to copper. Thereby, the Ti–O bonds are stronger than Cu–O bonds. The kinetic of decrease of the melting temperatures could be explained by these electronegativities. A metal having a high electronegativity could involve metal–oxygen bonds more important and have an impact on the kinetic of decrease of the melting temperatures.

These data are important in the understanding of thermal behavior of glasses. The introduction of metal elements Cu and Ti have a high impact on the melting temperature and a less impact on the crystallization and glass transition temperatures. In a previous work [25], the effect of Zn was studied in order to elaborate a protocol of synthesis of a porous biomaterial. This present study can bring information about the behavior of glasses during in vitro assays and their capacity to exchange ionic elements to form hydroxyapatite crystals. Therefore, we could adapt the use of Cu and Ti in the porous biomaterial to improve its physiological properties and to use it into broader medical applications.

Excess entropy of doped bioactive glasses

The aim of this part is to calculate the excess entropy of each glass and to evaluate the effect of the content of doping metal elements on this value. The entropy at 0 K was calculated. In a previous work [25], the excess entropy formula was established at a temperature $T < T_f$:

$$\Delta S = \frac{\Delta H_f}{T_f} - 2.09 Ln \frac{T_f}{T_g} + 0.48 \times 10^{-3} [T_f - T_g]$$

Obtained results show that values obtained for doped bioactive glasses are not equal to zero. However, the excess entropy of pure glass is 79 J K^{-1} [25]. The obtained excess entropy is from 37 up to 14 J K^{-1} for Cu-doped glasses and from 73 up to 5 J K^{-1} for Ti-doped glasses. The presence of metal elements Cu or Ti in the amorphous matrix reduces this excess entropy which varies depending on the content of metal element in the glass matrix as shown in Fig. 7. Moreover, up to 3 mass/% of metal element introduced, Cu allows decreasing faster the excess entropy than Ti. Beyond 3 mass% added, there is an inversion and the excess entropy decreases faster with titanium.

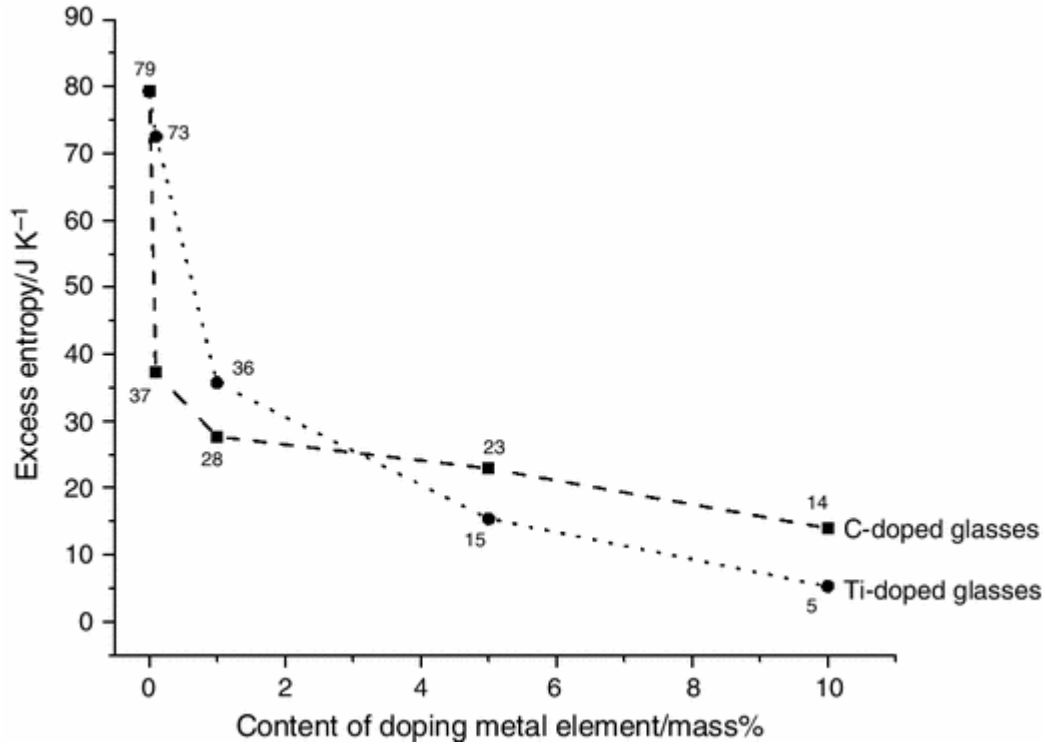

Fig. 7
Excess entropy function of the content of doping metal element

The results are in agreement with the Zarzycki theory. We conclude that the third principle of thermodynamic is not applicable to bioactive glasses elaborated in the quaternary system SiO_2–CaO–Na_2O–P_2O_5. This result will contribute on the comprehension of the changes of the kinetic of bioactivity of doped bioactive glasses compared to pure glass [25-49].

The entropy of a crystal is zero at 0 K, i.e., there is more thermal agitation of the atoms within the material and they became motionless. The decrease of the entropy of glasses with the increase of doping elements means that the disorder is reduced in the glass matrix and the atoms present become increasingly immobile. This decrease of the disorder is related to the size of atoms constituting the glass matrix and their electronegativity (property explaining the ability of an atom to attract another and the formation of bonds between atoms).

Titanium is bigger than that of copper (176 pm vs 146 pm). On the contrary, the electronegativity of copper is greater than that of titanium (1.90 vs 1.54). Thereby, the values of excess entropy 46S6-10Cu glasses (14 J K^{-1}) and 46S6-10Ti (5 J K^{-1}) may be explained by these properties. The size of atoms is a more important characteristic than the electronegativity. Indeed, for Ti-doped glasses, when the titanium content increases, titanium atoms cannot be thermally agitated compared to copper atoms which would reduce the entropy up to a value of 5 J K^{-1} for 46S6-10Ti. For copper, which has a smaller atomic radius, the entropy decreases by adding of copper, but the entropy of 46S6-10Cu is greater by a factor of 2.8 compared to 46S6-10Ti. The atomic radius being smaller than that of titanium, copper atoms can easily move in the glass matrix hence largest entropy. The capacity of copper created chemical bonds in the glass matrix, due to its important electronegativity, may explain the decrease of entropy in the Cu-doped glasses. The chemical bonds formed tend to order the glass network

hence a decrease. These properties of the introduced doping elements are important characteristics to explain the variations of entropy.

Conclusions

The physico-chemical methods of characterization of doped bioactive glasses highlight the amorphous character of all glasses whatever the amount of metal elements introduced in the glass matrix. However, new chemical bonds appear according to the doping element introduced in the glass network.
The introduction of copper or titanium in the glass matrix involves several changes in the thermal characteristics. Melting temperatures clearly decrease when the amount of these metal elements increases. According to the introduced element, melting temperatures may vary linearly. Changes are observed on the crystallization and glass transition temperatures. The introduction of copper decreases these temperatures, and the introduction of titanium increases them. Moreover, the introduction of metal elements increases the thermal stability of glasses.

The calculated excess entropy shows that the pure glass has more important excess entropy compared to doped glasses. The presence of metal elements in the glass matrix reduces the excess entropy according to the amount of metal introduced. The disorder of the material defined by the entropy decreases with the adding of metal elements in the glass matrix probably due to the formation of metal–oxygen chemical bond that "structure" the glass network.

The present study allows us to understand the thermal behavior of bioactive doped glasses which could have an influence on their chemical reactivity and on their bioactivity. Biomaterials could be adapted in different medical applications by introducing chemically interesting elements having good physiological properties.

References

[1] Hench LL. Bioceramics: from concept to clinic. J Am Ceram Soc. 1991;74:1487-1510.

[2] Daculsi G, Malard O and Goyenvalle E. Efficacité et performance des substituts osseux pour remplacer les allogreffes et autogreffes. ITBM-RBM. 2005;26:218-22.

[3] Wers E et al.. Effect of copper and zinc on the bioactivity and cells viability of bioactive glasses. Bioceram Dev Appl. 2013. doi: 10.4172/2090-5025.S1-013

[4] Oudadesse H, Dietrich E, Le Gal Y, Pellen P, Bureau B, Mostafa AA, Cathelineau G. Apatite forming ability and cytocompatibility of pure and Zn-doped bioactive glasses. Biomed Mater. 2011;6:11-16

[5] Dietrich E, Oudadesse H, Lucas-Girot A, Mami M. In vitro bioactivity of melt-derived glass 46S6 doped with magnesium. Biomed Mater. 2007;2:59-64.

[6] Kansal I, Tulyaganov DU, Goel A, Pascual MJ, Ferreira JMF. Structural analysis and thermal behavior of diopside-fluorapatite- wollastonite-based glasses and glass-ceramics. Acta Biomater. 2010;6:4380-4388.

[7] Watts SJ, Hill RG, O'Donnell MD, Law RV. Influence of magnesia on the structure and properties of bioactive glasses. J Non Cryst Solids. 2010;356:517-524.

[8] Fredholm YC, Karpukhina N, Law RV, Hill RG. Strontium containing bioactive glasses: glass structure and physical properties. J Non Cryst Solids. 2010;356:2546-2551.

[9] Aina V, Bertinetti L, Cerrato G, Cerruti M, Lusvardi G, Malavasi G, Morterra C, Tacconi L. On the dissolution/reaction of small-grain Bioglass® 45S5 and F-modified bioactive glasses in artificial saliva (AS). Appl Surf Sci. 2011;257:4185-4195.

[10] Brauer DS, Mneimne M, Hill RG. Fluoride-containing bioactive glasses: fluoride loss during melting and ion release in tris buffer solution. J Non Cryst Solid. 2011 ;357 :3328-3333.

[11] Goel A, Rajagopal RR, Ferreira JMF. Influence of strontium on structure, sintering and biodegradation behavior of CaO-MgO-SrO-SiO2-P2O5-CaF2 glasses. Acta Biomater. 2011;7:4071-4080.

[12] Hill RG, Stamboulis A, Law RV, Clifford A, Towler MR, Crowley C. The influence of strontium substitution in fluorapatite glasses and glass-ceramics. J. Non Cryst Solids 2004;336: 223-229.

[13] Lusvardi G, Malavasi G, Menabue L, Aina V, Morterra C. Fluoride-containing bioactive glasses: surface reactivity in simulated body fluids solutions. Acta Biomater. 2009;5:3548-3562.

[14] Lusvardi G, Zaffe D, Menabue L, Bertoldi C, Malavasi G, Consolo U. In vitro and in vivo behaviour of zinc-doped phosphosilicate glasses. Acta Biomater. 2009;5: 419-428.

[15] Handke M, Sitarz M, Rokita M, Galuskin EW. Vibrational spectra of phosphate-silicate biomaterials. J Mol Struct. 2003;39:651-653.

[16] Sitarz M, Handke M, Fojud Z, Jurga S. Spectroscopic studies of glassy phospho-silicate materials. J Mol Struct. 744-747 (2005) 621.

[17] Sitarz M. Influence of modifying cations on the structure and texture of silicate-phosphate glasses. J Mol Struct. 2008;887:237-248.

[18] Sitarz M, Bulat K, Olejniczak J. Structure and microstructure of glasses from a $NaCaPO_4$-SiO_2-BPO_4 system. Vib Spect. 2012;61:72-77.

[19] Niinomi M. Mechanical properties of biomedical titanium alloys. Mat Sci Eng A. 1998;243:231-36.

[20] Barbucci R, Lamponi S, Magnani A, Piras FM, Rossi A, Weber E. Role of the Hyal-Cu(II) complex on bovine aortic and lymphatic endothelial cells behavior on microstructured surfaces. Biomacromolecules. 2005;6:212–19.

[21] Hoppe A, Guldal NS, Boccaccini AR. A review of the biological response to ionic dissolution products from bioactive glasses and glass–ceramics. Biomaterials. 2011;32:2757–74.

[22] Giavaresi P, Torricelli PM, Fornasari R, Giardino RB , Leone G. Blood vessel formation after soft-tissue implantation of hyaluronan-based hydrogel supplemented with copper ions. Biomaterials. 2005;26:3001–8.

[23] Erol MM, Mourino V, Newby P, Chatzistavrou X, Roether JA, Hupa L, Boccaccini AR. Copper-releasing, boron-containing bioactive glass-based scaffolds coated with alginate for bone tissue engineering. Acta Biomater. 2012;8:792–801.

[24] Hu GF. Copper stimulates proliferation of human endothelial cells under culture. J Cell Biochem. 1998;69:326–35.

[25] Wers E, Oudadesse H. Thermal behaviour and excess entropy of bioactive glasses and Zn-doped glasses. J Therm Anal Calorim. 2013. doi: 10.1007/s10973-013-3280-3.

[26] Barton J, Guillemet C. Le verre: science et technologie. Les Ulis: EDP Sciences; 2004

[27] Mosner P, Vosejpkova K, Koudelka L. Thermal properties and stability of lithium titano-phosphate glasses. J Therm Anal Calorim. 2009;95:53-8.

[28] Pospisil J, Mosner P, Koudelka L. Thermal behaviour and crystallization of titanium–zinc borophosphate glasses. J Therm Anal Calorim. 2006;84:479-82.

[29] Mosner P, Vosejpkova K, Koudelka L. Thermal behaviour and properties of Na_2O-TiO_2-P_2O_5 glasses. J Term Anal Calorim. 2009;96:469-74.

[30] Sulowska J, Waclawska I, Szumera M. Effect of copper addition on glass transition of silicate–phosphate glasses. J Therm Anal Calorim. 2012;109:705-10.

[31] Sulowska J, Waclawska I, Szumera M, Olejniczak J. Characterization of thermally induced of crystalline phases in CuO containing silicate-phosphate glasses. J Therm Anal Calorim. 2012;108:657-63.

[32] Lu XC, Li HY. Kinetics of non-isothermal crystallization in $Cu_{50}Zr_{43}Al_7$ and $(Cu_{50}Zr_{43}Al_7)_{95}Be_5$ metallic glasses. J Therm Anal Calorim. 2013. doi: 10.1007/s10973-013-3364-0.

[33] Kivelson D, Reiss H. Metastable systems in thermodynamics: consequences, role of constraints. J Phys Chem. 1999;103:8337.

[34] Gupta PK, Mauro JC. On the reality of residual entropies of glasses and disordered crystals. J Phys Chem. 2008;129:067101.

[35] Lewis GN, Randall M, Nemilov SV. Zero-point entropy of glasses as physical reality. J Non Cryst Solid. 2009;355:607-16.

[36] Nemilov SV. Zero-point entropy of glasses as physical reality. J Non Cryst Solid. 2009;355:607-616.

[37] Tropin TV, Schmelzer JWP, Schick C. On the dependence of the properties of glasses on cooling and heating rates: I. Entropy, entropy production, and glass transition temperature. J Non Cryst Solid. 2011;357:1291-302.

[38] Zarzycki J. Les verres et l'état vitreux. Paris: Masson; 1982.

[39] Dietzel A. Glasstruktur und Glaseigenschaften. Glass Technol. 1968;22:41.

[40] Jastrzębski W, Sitarz M, Rokita M, Bulat K. Infrared spectroscopy of different phosphates structures. Spectrochimica Acta Part A. 2011;79:722-727.

[41] Sitarz M. The structure of simple silicate glasses in the light of Middle Infrared spectroscopy studies. J Non Cryst Solid. 2011;357:1603-1608.

[42] Silva AMB, Correia RN, Oliveira JMM, Fernandes MHV. Structural characterization of TiO_2–P_2O_5-CaO glasses by spectroscopy. J Eur Ceram Soc. 30 (2010) 1253–1258.

[43] Sitarz M, Bulat K, Szumera M, Wajda A. Direct crystallization of silicate–phosphate glasses of NaCaPO4–SiO2 system. J Therm Anal Calorim. 2013;113:1363-1368.

[44]Abou Neel EA, Chrzanowski W, Knowles JC. Effect of increasing titanium dioxide content on bulk and surface properties of phosphate-based glasses. Acta Biomater. 2008;4:523-34.

[45] Szumera M, Waclawska I. Thermal study of Mn-containing silicate–phosphate glasses. J Therm Anal Calorim. 2012;108:583-588.

[46] Sitarz M, Bulat K, Szumera M. Influence of modifiers and glass-forming ions on the crystallization of glasses of the $NaCaPO_4$–SiO_2 system. J Therm Anal Calorim. 2012;119:577-584.

[47] Szumera M, Wacławska I. Spectroscopic and thermal studies of silicate-phosphate glass. J Therm Anal Calorim. 2007;88:151-156.

[48] Szumera M, Wacławska I. Effect of molybdenum addition on the thermal properties of silicate–phosphate glasses. J Therm Anal Calorim. 109 (2012) 649.

[49] Dietrich E, Oudadesse H, Lucas-girot A, LeGal Y, Jeanne S, Cathelineau G. Effects of Mg and Zn on the surface of doped melt-derived glass for biomaterials applications. Appl Surf Sci. 2008;255:391-5.

Figures Captions

Figure 1 Diffractograms of pure and doped glasses

Figure 2 FTIR spectra of pure and doped glasses

Figure 3**a** Thermal curves of Cu-doped glasses, **b** thermal curves of Ti-doped glasses

Figure 4 T_c and T_g function of the content of doping metal element

Figure 5 T_f function of the content of doping metal element

Figure 6 Thermal stability function of the content of doping metal element

Figure 7 Excess entropy function of the content of doping metal element