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SiO_2-CaO-K_2O coatings on alumina and Ti6Al4V substrates for biomedical applications

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Alumina and Ti6Al4V alloys are widely used for orthopedics and dental applications due to their good mechanical properties and biocompatibility. Unfortunately they can not provide a satisfactory osteointegration when implanted. In fact, both alumina and Ti6Al4V are not bioactive and thus they can only guarantee a morphological fixation with the surrounding tissues without a suitable chemical anchorage. Aiming to impart bioactive properties to these materials a coating can be proposed. At this purpose, a bioactive glass belonging to the SiO_2-CaO-K_2O system was selected and prepared. This glass, named SCK, possess a thermal expansion coefficient matching with the alumina ($8.5 \times 10^{-6}/^{\circ}C$) and Ti6Al4V ($9 \times 10^{-6}/^{\circ}C$) ones and thus is a good candidate to produce coatings on both of them. Simple and low-cost enameling and glazing techniques were used to realize the coatings. Structural, morphological and compositional characterizations of the coatings were carried out by means of X-ray diffraction, optical and scanning microscopy and compositional analyses. The *in vitro* properties of the coatings were investigated by soaking them in a simulated body fluid (SBF) in order to study the precipitation, on their surfaces, of a biologically active layer of hydroxylapatite (HAp).

1. Introduction

Alumina and Ti alloys are widely used as biomaterials due to their attractive mechanical properties. Specifically, alumina is used in several orthopedics and maxillofacial applications due to its excellent wear resistance, fracture toughness and very high compressive strength [1–3]. Titanium alloys are utilised in many applications where an extensive load carrying ability is required [4, 5]. Despite their significant properties, alumina and Ti alloys lack of osteointegration which is known to be a key requirement for many biomedical applications. When implanted *in vivo*, these biomaterials, particularly alumina, show the formation of a non-adherent fibrous capsule at the tissue-device interface [2]. The presence of this fibrous capsule is not desirable for devices in which, actually, a direct interaction with the surrounding tissue would be preferable. At this purpose, a suitable modification of their surface properties thorough a coating deposition, is of great scientific interest as can lead to a substantial improvement of their osteointegration [6–22]. The crucial requirement to assure a chemical bond with the surrounding tissues is related to the coating ability of forming a biologically active hydroxylapatite layer on its surface. This requisite can be satisfied by bioactive glasses and glass-ceramics that are known to promote new tissue formation on their surfaces and to encourage positive interactions between cells and implanted devices [23–28]. Coating a substrate with a bioactive glass offers also several advantages in terms of protection of the substrate from corrosion and degradation phenomena and thus can hamper eventual adverse interactions between the tissues and the degradation products [29].

On these bases, alumina and Ti6Al4V substrates were coated with a bioactive glass of tailored composition. The choice of the glass was done considering the need of matching the substrate thermal expansion coefficient to avoid extensive residual stresses that would negatively affect the coating adhesion.

Several methods can be used to coat a substrate with a glassy layer: enameling, glazing, plasma-spray, casting, electrophoresis and sputtering [8–10, 13–16, 21, 30–34]. Due to their low-cost and relative simplicity, enameling and glazing were used in this study.

The reactivity of glasses at the high temperatures involved is often an issue when a bioactive coating with good mechanical and biological properties is needed. In fact, silica-based glasses have a random network structure with many open pathways for ions diffusion. As far as bioactive compositions are concerned, this property is strictly related to their high ability of forming HAp on their surfaces when in contact with physiological fluids.

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On the other hand, due to their open network, bioactive glasses are prone to cations diffusion from the substrate (i.e. Al^{3+}, Ti^{4+}) towards the coating surface. If these cations reach the surface, they can severely hamper the nucleation of the calcium-phosphate rich layers and thus the subsequent formation of HAp. Actually, only few percent of multi-valent cations are sufficient to completely hinder the bioactivity of a glass and thus its bone bonding ability [35–37].

As far as this study is concerned, the presence of Al^{3+} is recognized to be highly detrimental for the bioactivity of a glass, even at very low concentrations (1.5 wt%) [29, 35, 37], due to its effect of stabilization of the glass network. In fact, a more closed network strongly reduces the leaching process, which is fundamental for the bioactivity. Moreover, some authors suggested that alumina retards bone mineralization *in vivo* due to the precipitation of multivalent ions as hydroxides or carbonates, not compatible with the bone growth process [29].

In this study, a SiO_2-CaO-K_2O glass (SCK) with a thermal expansion coefficient congruent with the alumina and Ti6Al4V ones was prepared. The SCK composition was tuned in order to attain a high degree of bioactivity of the realized coatings. The processing parameters for the coatings preparation (time and temperature) have been separately optimized for the two substrates, in order to realize adherent and flawless coatings, by means of reproducible and low-cost techniques.

2. Materials and methods

A glass belonging to the system SiO_2-CaO-K_2O (SCK) was prepared by melting the raw products (SiO_2, $CaCO_3$, K_2CO_3) in a platinum crucible at 1500 °C for 1 h. The chosen glass composition (% mol. of the oxides) was the following: 50%SiO_2-44%CaO-6%K_2O. The molten glass was quenched in cold water to avoid undesired crystallization phenomena. After quenching the glass was grounded by ball milling and sieved to a final grain size below 40 μm. The SCK thermal expansion coefficient was calculated using a computational program (Sci-Glass) whereas its glass transition (T_g) and crystallization (T_x) temperatures were determined on powders by means of a differential thermal analysis (DTA7 Perkins Elmer). SCK was also characterized by means of X-ray diffraction and compositional analysis (EDS) in order to assess its amorphous nature and its chemical composition.

2.1. Preparation of coatings on alumina

Full-density medical grade α-alumina was used as substrate.

Specimens with 1 cm^2 surface were ultrasonically cleaned in ethanol for 10 min to remove eventual contaminants. A glazing technique was chosen to realize the coatings. At this purpose, a slurry of SCK powders, using ethanol as liquid medium, was prepared and then uniformly applied on the substrate with a spatula. The slurry was left drying for about 30 min at room temperature to allow a complete evaporation of the liquid medium. Subsequently, the specimens were thermally treated at temperatures high enough to allow a good SCK softening and thus a sufficient wetting on alumina. The choice of the thermal parameters was done considering the need of minimizing Al^{3+} diffusion from the substrate towards the coating to maintain the SCK bioactivity. At this purpose, an optimization of the glazing treatment in the temperatures range of 1200–1300 °C and for times of a few minutes was carried out. In fact, preliminary tests showed that lower temperatures and shorter times did not allow a proper wetting of SCK on alumina obtaining non-continuous, scarcely adherent coatings. After firing, the coatings underwent an annealing treatment at 650 °C for 2 h to release residual thermal stresses that would negatively affect the coating adhesion and its quality.

2.2. Preparation of coatings on Ti6Al4V alloy

Ti6Al4V plates with 1 cm^2 surface were used as substrates. The plates were polished using a 600 grit SiC paper and then cleaned in ethanol. In this way, the titanium oxide layer that naturally forms on these substrates was completely removed. To coat the Ti alloys plates, an enameling technique was used and an SCK slurry was applied on them with a spatula and left drying at room temperature for about 30 min. On the dried coatings, a thermal treatment was carried out trying to fulfill the following requirements:

- to use the lowest temperature that would allow a good softening of SCK while completely avoiding the $\alpha \rightarrow \beta$ transformation of Ti6Al4V (980 °C) that negatively affects the mechanical properties of the alloy.
- to reduce as much as possible the treatment time preventing the formation of a thick titanium oxide at the coating interface which will lead to poor adhesion and easiness of delamination of the coating.

On the basis of these considerations, different conditions were tested in the temperatures range within 850–950 °C and for times varying from 30″ to 90″. For the coatings on Ti6Al4V, the annealing phase was avoided in order to limit the substrate oxidation due to the high reactivity of the glass with the metallic substrate at the temperatures involved. The coatings were prepared in air as preliminary tests showed that the substrate oxidation will occur also in an inert atmosphere due to the presence of high amount of oxygen in the glass.

2.3. Morphology, composition and structure of the realized coatings

The coatings quality was evaluated by scanning electron microscopy (SEM Philips 525M). Specifically, the investigations were focused on the following topics: thickness of the coating, adhesion to the substrate, existence of a reaction layer at the substrate

interface, presence of cracks and residual porosity. Furthermore, semi-quantitative compositional analyses (EDS, Philips- EDAX 9100) were carried out to verify if the coating process and the temperatures involved caused compositional modifications. In fact, the diffusion of ions coming from the substrate towards the coating can lead to the crystallization of phases different than those predicted by the equilibrium ternary diagram of SiO_2-CaO-K_2O. These unexpected crystalline phases can negatively affect the coatings properties from the thermo-mechanical and biological point of view. In any case, the presence of diffused ions, also if they remain in the amorphous phase, would influence the mechanism of ions exchange when the biomaterial is in contact with physiological fluids, due to changes in the glass composition and/or network stabilization. These latter considerations were particularly important for the coatings on alumina. In fact, in this case, the temperatures and times involved in the coating process were noticeably higher than the ones used for Ti6Al4V specimens and thus greater ions diffusion (i.e. Al^{3+}) was expected. Moreover, Al^{3+}ions show a peculiar detrimental effect, as even the presence of small quantities of these ions, can stabilize to a great extent the glass network and thus strongly lower the coating bioactivity.

As far as the coatings on Ti alloys are concerned, the reactivity at the interface with the glass and the ions inter-diffusion can lead to the formation of a reaction layer that can result in poor coating adhesion. For the above mentioned reasons, the ions diffusion from the substrate, and thus the whole coating process, should be carefully controlled and optimized.

For both substrates, the effects of the thermal treatment and of the eventual ions diffusion on the final coating structure were investigated by means of X-ray diffraction (X'Pert Philips diffractometer) using the Bragg Brentano camera geometry and the Cu K_α incident radiation. In this way, the presence of crystalline phases was assessed and their nature was investigated.

The *in vitro* behavior of the realized coatings was studied by soaking them in 25 ml of a simulated body fluid (SBF) [24] for periods up to one month. The samples were maintained for the whole soaking period at 37 °C without any refresh of the solution. This test was useful to assess the *in vitro* bioactivity of the realized coating by verifying the presence, morphology and thickness of a precipitated HAp layer on their surfaces. At this purpose, after soaking, the samples were characterized by means of X-ray diffraction, compositional analysis and scanning electron microscopy.

3. Results and discussion

The SCK thermal expansion coefficient (9.5×10^{-6}/ °C) showed that this glass is suitable to realize coatings on both alumina and Ti6Al4V.

Fig. 1 reports the results of the SCK thermal characterization: three exothermic signals within 750° and 950 °C can be observed (Tx_1, Tx_2 and Tx_3).

Besides, as shown by the endothermic signal (T_d), the phases that crystallize at lower temperatures decompose before the crystallization of the third one and thus above 950 °C only one phase is present. These latter considerations are in good accordance with the ternary diagram reported in Fig. 2 [39].

The analysis of the SiO_2-CaO-K_2O diagram showed that, for the chosen composition, β-$CaSiO_3$ is a stable phase above 900 °C.

3.1. Coatings on Al_2O_3

The glazing process to realize coatings on alumina required an optimization of the thermal treatment to achieve the best compromise between two different requirements. In fact, sufficiently high temperatures and times are needed to enhance the wettability of the softened SCK powders on alumina, and thus the coating adhesion, but they would also increase the Al^{3+} diffusion toward the coating surface affecting its *in vitro* properties.

A series of samples were prepared using glazing treatments at different temperatures and times: their

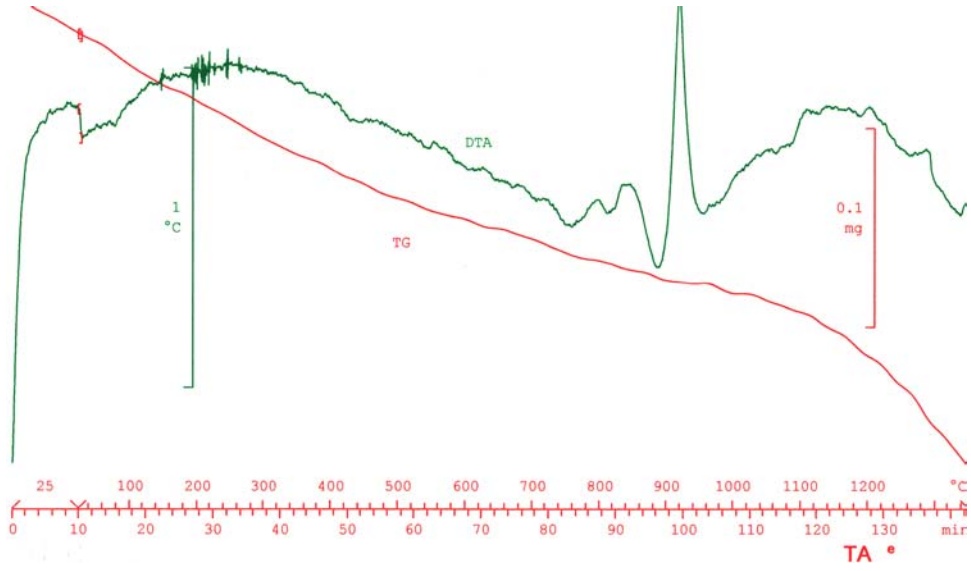

Figure 1 Differential thermal analysis on SCK powders.

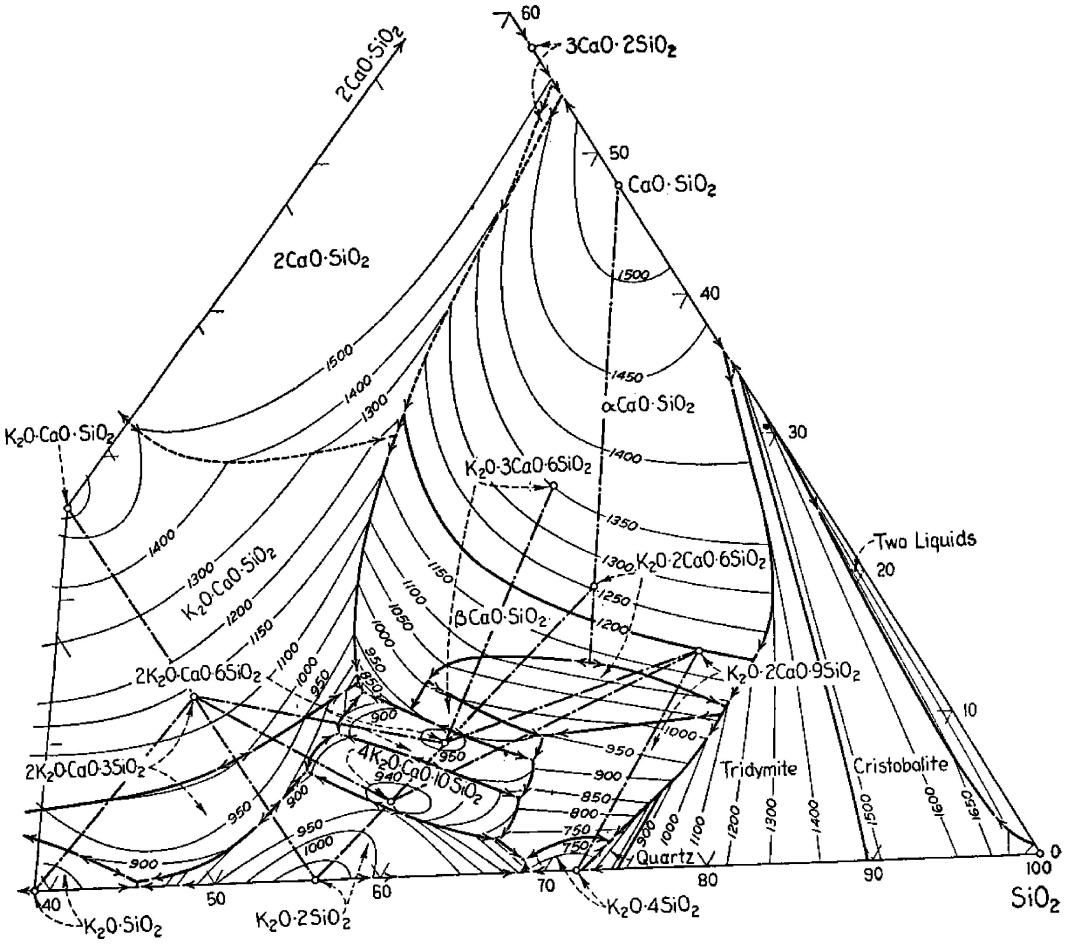

Figure 2 Ternary diagram for the SiO_2-CaO-K_2O system.

cross sections were evaluated by SEM and EDS to assess the quality of their interfaces with alumina, the coating cohesion and the eventual, undesired presence of Al^{3+}.

Specifically, the coating composition was deeply investigated in the outer 50 μm, as normally the thickness of the layer involved in the bioactivity mechanism is about a few tenths of microns.

The glazing treatment that allowed obtaining flawless, well adherent and Al^{3+} free coatings, was selected as the optimized one and used to prepared samples that underwent a more complete characterization. On these specimens, a structural characterization was performed to verify the presence of crystalline phases in the coating and *in vitro* tests were carried to document its bioactivity.

The optimized glazing treatment consisted of a thermal treatment in air at 1300 °C for 5 min followed by 2 h at 650 °C to anneal the coating.

Fig. 3(a) reports a cross section of an SCK coating on alumina: there are not pores or bubbles at the interface and the adhesion is satisfactory as any discontinuity can

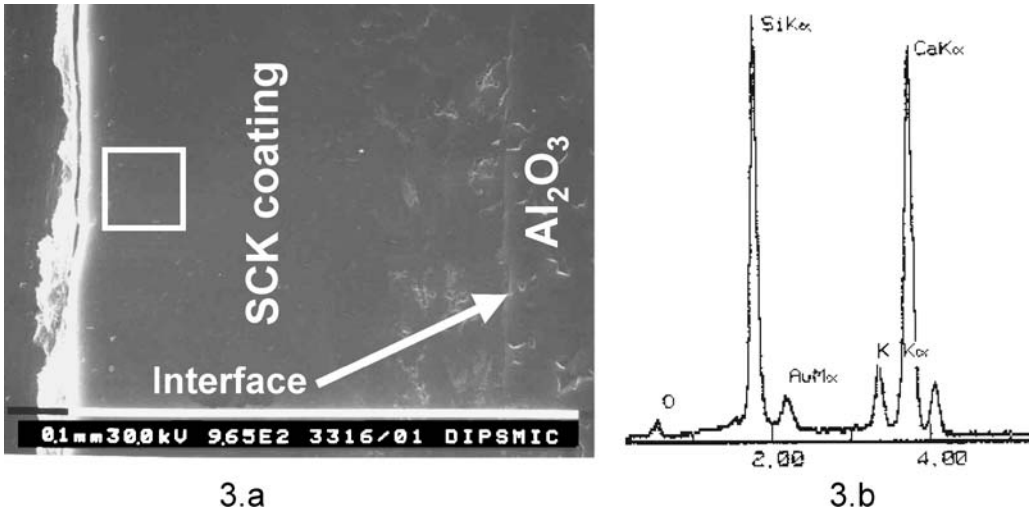

Figure 3 (a) Cross section of an SCK coating on alumina, (b) EDS analysis of the area reported in Fig. 3(a).

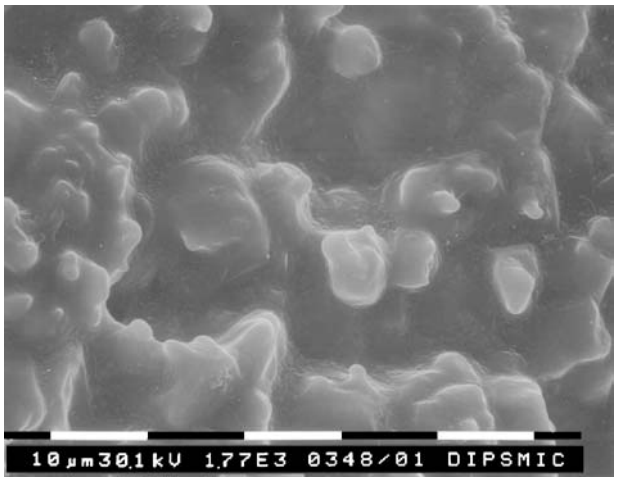

Figure 4 Top view of a SCK coating on Alumina.

be seen. The coating is flawless as any cracks or other defects were detected. For the obtained coatings, an average thickness of 70–100 μm was found; (Fig. 3(a)) shows a coating thickness of about 80 μm: in good accordance with the values reported above). Fig. 3(b) shows the result of an EDS analysis carried out on the area labeled with a white rectangle in Fig. 3(a), which is about 100 μm^2 and is positioned at the coating outer surface. The only elements detected were the SCK components in amounts according with the theoretical glass composition. The presence of Au was also detected and is only due to the sample preparation for SEM observation. The EDS results assessed that the Al^{3+} diffusion from the substrate, if present, was not high enough to reach the outer part of the coating which is the one directly involved in the leaching phase during the *in vitro/in vivo* tests. The absence of Al^{3+} is a crucial result as these ions will strongly alter and hinder the bioactivity mechanism.

Fig. 4 depicts a top view of the coating in which the lack of pores and cracks can be observed supporting the considerations coming out from Fig. 3(a). Moreover, Fig. 4 shows a not smooth and rich in crystal surface due to the glass–ceramic structure of the realized coating.

The nature of the observed crystals was further investigated by means of X-ray diffraction and the results are reported, in the next paragraph, in Fig. 11.

Fig. 5(a) and (b) show two micrographs, at different magnifications, of the SCK coatings surface after 1 months of soaking in SBF without any refresh of the solution.

Fig. 5(a) shows a continuous layer of globular HAp that completely covers the coating surface. The presence of a thick HAp layer is a reliable index of the high *in vitro* bioactivity of these coatings. Besides, as any refresh of the solution was performed, an even higher *in vivo* bioactivity might be expected. A magnification of this globular HAp is reported in Fig. 5(b) and shows the presence of sub-micronic leaf-like crystals that are typical of precipitated hydroxylapatite.

To ascertain the thickness and the coherence of this HAp layer, cross sections of the coatings after SBF were prepared and polished for microscopical evaluations. At this purpose, Fig. 6(a) reports a micrograph of the cross section after SBF showing the presence of a 10–20 μm thick layer well tied up on top of the coating. The EDS results on the area labeled with the white rectangle in Fig. 6(a) are reported in Fig. 6(b). Only Ca and P were detected, in amounts according to hydroxylapatite (1.67 atomic ratio); analogous results were found carrying out the compositional analysis on the whole area shown in Fig. 5(a).

On the basis of these evidences, we could confirm the morphological observations assessing that the overlapping layer was effectively HAp. Moreover, as any other element was detected, we verified that this HAp layer is uniform and quite thick, as the electron beam did not reach the coating layer below it. The thickness of this HAp layer was also measured during the SEM evaluations on different cross sections after soaking in SBF (as in Fig. 6(a)) and was about 10–20 μm.

A further evidence of the presence of the HAp layer was achieved by means X-ray diffraction and will be reported in the next paragraph with the data obtained for the coatings on Ti6Al4V. Shorter soaking times, less than a week, would be necessary to confirm the truly bioactive behavior of the coatings.

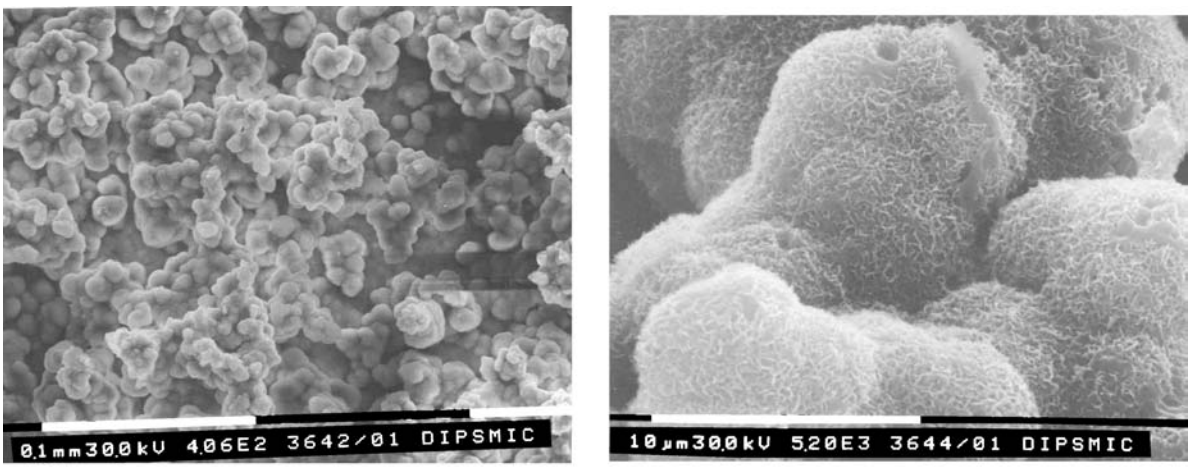

Figure 5 (a) and (b) surface after 1 month in SBF of a coating on Alumina at different magnifications.

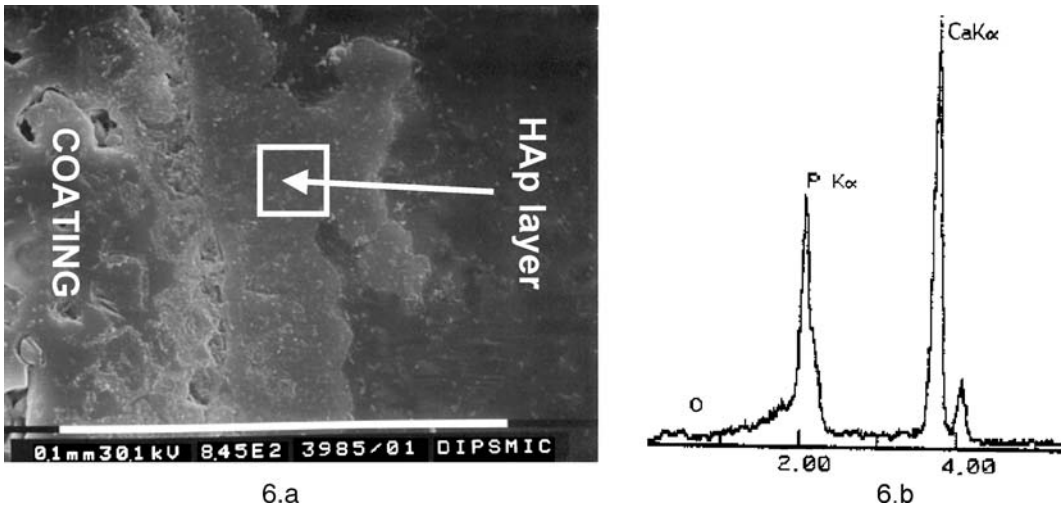

Figure 6 (a) Cross section of an SCK coating on alumina after soaking in SBF and (b) EDS analysis on the white area of Fig. 6(a).

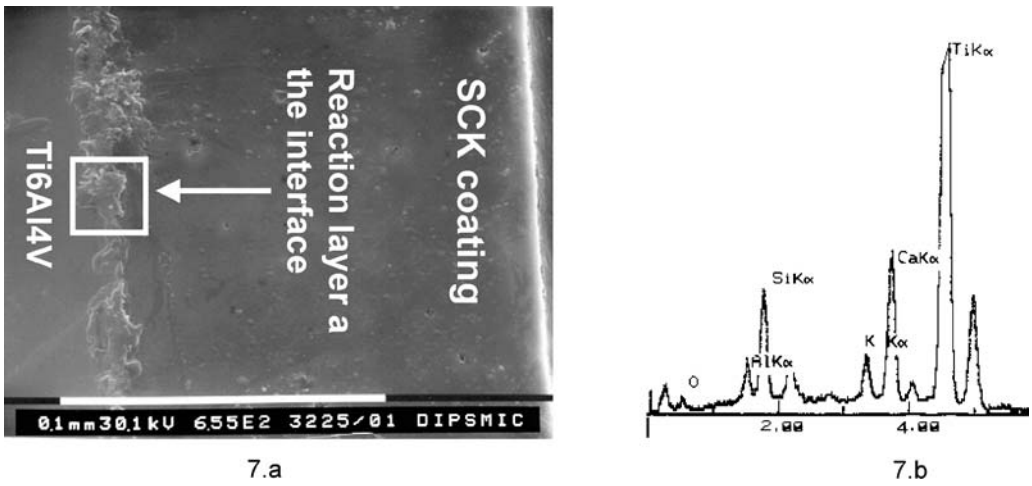

Figure 7 (a) Cross section of an over-reacted coating on Ti6Al4V and (b) EDS analysis on the area reported in Fig. 7(a).

3.2. Coatings on TI6AL4V

A careful optimization of the enameling treatment was carried out to realize successful coatings on Ti6Al4V substrates. The basic requirement was to obtain a continuous, well adherent and crack free coating avoiding the $\alpha \rightarrow \beta$ transformation of the alloy as well as an over-reaction of SCK with the substrate which would cause delamination of the coating itself.

The more promising results were obtained applying a SCK slurry directly on the polished substrate and by thermally treating it at 900 °C for 60″.

Firing treatments below this temperature, specifically at 850° and 875 °C resulted in insufficient SCK softening and thus coatings weakly adherent to the substrate due to inadequate wetting.

On the other hand, longer times or higher temperatures would cause an extensive reaction between the glass and the substrate, with the formation of Ti oxides and silicides at the coating interface and thus would lower the coating adhesion. These reactions can be observed when a silica-based glass is used as coating on Ti substrates according to [40]:

$$8\mathrm{Ti}_{(\mathrm{substrate})} + 3\mathrm{SiO}_{2(\mathrm{glass})} \rightarrow \mathrm{Ti}_5\mathrm{Si}_{3(\mathrm{interface})} + 3\mathrm{TiO}_{2(\mathrm{interface})}$$

At this purpose, Fig. 7(a) reports a cross section of a SCK coating that, due to the too high temperatures used (950 °C), strongly reacted with the substrate: the presence of a reaction layer of some microns is clearly observable. Fig. 7(b) reports the results of an EDS analysis carried out on a 100 μm^2 area across this reaction layer (white rectangle of Fig. 7(a)).

Figure 8 Cross section of a non over-reacted coating on Ti6Al4V.

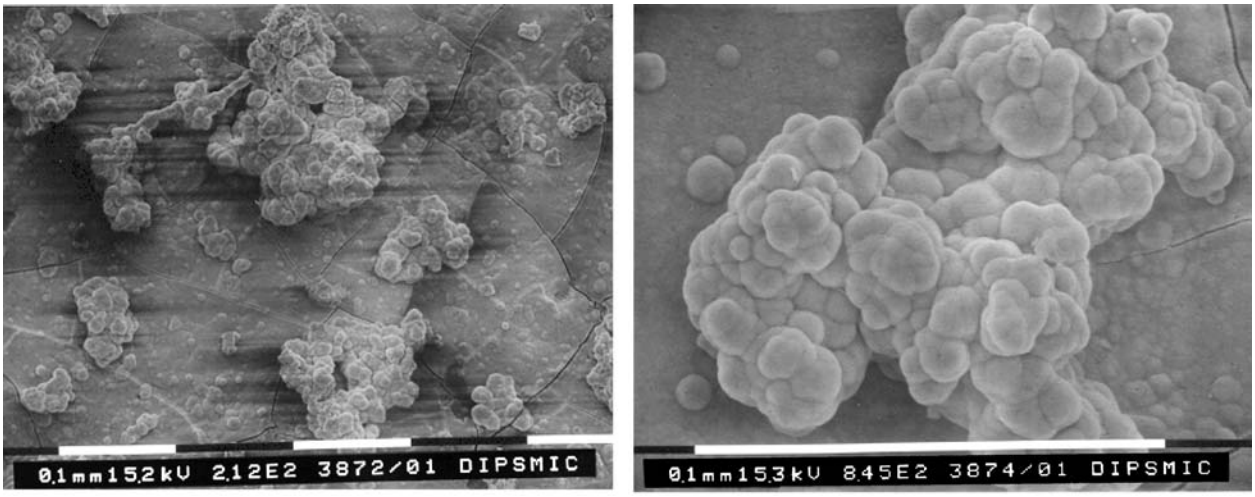

Figure 9 (a) and (b) Micrographs of an SCK coating on Ti6Al4V after 1 month in SBF at different magnifications.

As can be observed, apart from Si, Ca and K, which are the SCK components, the most relevant element was Titanium proving that an extensive ions diffusion and interaction occurred at the coating interface.

A certain amount of Al was also found, due to its presence in the alloy composition and to its diffusion in the glass coating. On the other hand, the quality of the coating was satisfactory as any cracks, pores or other defects were observed and thus, only the reaction at the interface needed to be optimized.

Fig. 8 reports a micrograph of a SCK coating on Ti6Al4V that did not over-react with the substrate and that shows better characteristics than the one reported in Fig. 7(a). An EDS analysis carried out on an area at the coating surface resulted in Si, Ca and K in relative amounts according with the SCK theoretical composition.

An enameling treatment at 900 °C but for longer times (90″) resulted in coatings with almost the same characteristics of the one reported in Fig. 7(a) due to the presence of an over-reaction layer at the interface.

On the basis of these results, it was assessed that the reaction at the coating interface could be successfully controlled by a careful optimization of the enameling treatment and that both time and temperature played an equally important role on the final coating properties. It should be also underlined that both time and temperature of the firing treatment used for coating Ti alloys were substantially lower than the one proposed for the glazing on alumina. In fact, lower times and temperatures were necessary in order to limit the reaction at the interface and to avoid the $\alpha \rightarrow \beta$ transformation. The times and temperatures requirements could be accomplished due to the excellent SCK wetting on Ti6Al4V substrates and to its low softening temperature.

Fig. 9(a) and (b) report two micrographs at different magnifications of the coating surface after 1 month of soaking in SBF.

A continuous layer was observed on the coating surface and many agglomerates with a globular morphology were found. The cracks that can be observed in this precipitated layer are due to its drying after the soaking phase and of course they would not occur *in vivo*.

The layer on top of which the globular HAp are present might be HAp itself or a silica gel which naturally forms before the HAp precipitation, according to the theories proposed by Hench and co-workers [25]. Fig. 9(b) reports the magnification of one of these conglomerates where the typical shape of sub-micronic crystals of precipitated HAp can be observed. For further controls, an EDS analysis was carried out on the whole area of Fig. 9(a), in order to have a validation of the nature of these aggregates and to ascertain if the layer below them was silica gel or HAp. On the basis of the EDS results reported in Fig. 10 (almost no Si was detected) and of the relative amounts of atomic Ca and P, we could confirm that an extensive HAp formation occurred on the coating surface during its soaking in SBF. In fact, this HAp precipitation was so important that after 1 month, it completely covered the silica gel that forms on these biomaterials when they are in contact with a simulated body fluid.

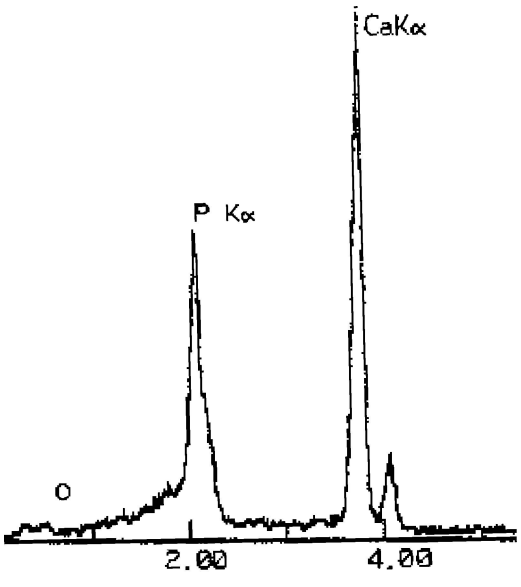

Figure 10 EDS analysis on the whole area reported in Fig. 9(b).

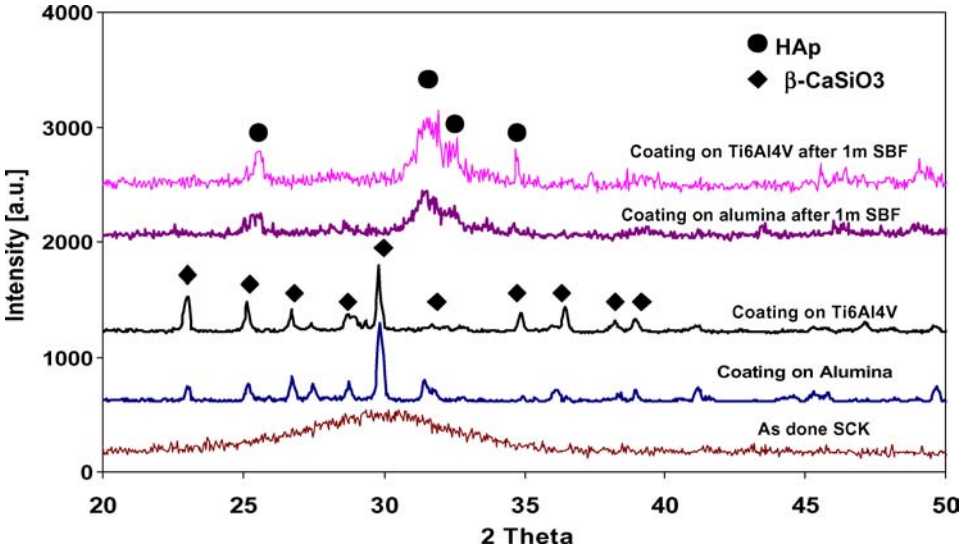

Figure 11 Diffraction patterns of the coatings before and after 1 month in SBF.

Fig. 11 depicts the diffraction patterns of the coatings on alumina and Ti6Al4V before and after soaking in SBF and of the as done SCK.

The diffraction pattern of SCK shows only an amorphous halo between 25 and 35 degree two theta and thus proved that the starting SCK powders were completely amorphous. On the other hand, on the realized coatings, many diffraction peaks were found and thus the proposed glazing/enameling treatments resulted in a glass crystallization. Actually, the glass-ceramic nature of the coatings was expected as the proposed thermal treatments were both above the SCK crystallization temperatures. No differences of significant relevance were found between the two coatings as they both crystallized the same phase which do not contain at all elements of the substrates. Specifically, all the diffraction peaks were identified as β-wollastonite (β-$CaSiO_3$), which is known for its good biological behavior [23, 26, 28, 41]; the crystallization of (β-$CaSiO_3$) is in good accordance with the data found in the ternary diagram of Fig. 2. Moreover, the thermal expansion coefficient of β-wollastonite is close to that of the substrates (9.4×10^{-6} between 100 and 200 °C) [42] and thus its formation should not involve residual thermal stresses.

As a general conclusion, it is possible to assess that the proposed coating process did not affect the composition of the coating (see Fig. 3(b)) and the crystalline phase that nucleates at the temperature involved.

The coatings bioactivity was further corroborated by the diffraction patterns obtained for the coating surfaces after 1 month in SBF. In fact, for both coatings, as can be observed in Fig. 11, broad signals were found at degrees typical of HAp. These diffraction peaks are broad as the nucleated and grown HAp crystals are partially crystalline and very small.

The evaluations of Figs. 6(a) and 9(a) and of the EDS data reported in Fig. 10, indicated that this HAp layer is thick and continuous and that it completely covers the coating surface. This latter consideration is also corroborates by the diffraction signals of β-$CaSiO_3$ that are observable in the as done coatings and are instead completely hidden by the presence of the HAp layer in the soaked samples.

This very high *in vitro* bioactivity it is likely to be found also *in vivo* as others workers showed a significant correspondence between the *in vitro/in vivo* results [43]. Further investigations at shorter soaking times would be of great interest to complete the bioactivity study.

4. Conclusions

Well adherent, flawless, glass-ceramic coatings on alumina and Ti6Al4V substrates were realized. The obtained results were reproducible and the applied techniques are low-cost and not complex.

The issues related to ions diffusion from the substrate, oxidation of the metallic substrate and $\alpha \rightarrow \beta$ transformation of the alloy were overcame by a careful optimization of the enameling/glazing treatments.

When tested *in vitro*, the coatings showed an extensive precipitation of a thick HAp layer, well adherent to the coatings.

On the basis of these results, the optimized procedure and the tailored SCK composition can be proposed as a low-cost, effective method to impart bone bonding ability to both alumina and Ti6Al4V inert substrates.

References

1. S. F. HULBERT, in "An Introduction to Bioceramics" edited by L. L. Hench and J. Wilson (World Scientific Pub, 1993) Vol. 1, p. 25.
2. L.L. HENCH, *J. Am. Ceram. Soc.* **74** (1991) 1487.
3. *Idem.*, *ibid.* **81** (1998) 1705.
4. A. SCHROEDER, F. SUTTER and G. KREKELER, in "Oral Implantology" (New York, Thiem Medical, 1991) p. 37.
5. M. LONG and H. J. RACK, *Biomat.* **19** (1998) 1621.
6. A. RAVAGLIOLI, A. KRAJEWSKI, A. PIANCASTELLI, G. BERGER, K. ADAM and R. GILDENHAAR, *Interceram.* **41** (1992) 41.
7. E. VERNÉ, C. VITALE BROVARONE, A. RAVAGLIOLI and A. KRAJEWSKI, in "Bioceramics" edited by H. Ohgushi, G. W. Hastings and T. Yoshikawa (World Scientific Publishing, 1999) Vol. 12, p. 491.

8. E. VERNÉ, C. VITALE BROVARONE, C. MOISESCU, E. GHISOLFI and E. MARMO, *Acta Materialia* **48** (2000) 4667.
9. C. VITALE BROVARONE, E. VERNÉ, F. LUPO, C. MOISESCU, L. ZANARDI, M. BOSETTI and M. CANNAS, in "Key Engineering Materials" (Trans. Tech. Publications Switzerland, 2001) Vols. 192–195, p. 123.
10. C. VITALE BROVARONE, E. VERNÉ, A. KRAJEWSKI and A. RAVAGLIOLI, *J. Eur. Ceram. Soc.* **21** (2001) 2855.
11. E. VERNÈ, M. BOSETTI, C. VITALE BROVARONE, C. MOISESCU, F. LUPO, S. SPRIANO and M. CANNAS, *Biomat.* **23** (2002) 3395.
12. C. VITALE BROVARONE and E. VERNE', in 7th meeting and Conference on Ceramics, Cells and Tissues, Biomimetic Engineering, a New Role for Ceramics, edited by A. Ravaglioli and A. Krajewski (ISTEC-CNR Faenza, 2002) p. 137.
13. M. FERRARIS, P. RABAJOLI, F. BROSSA and L. PARACCHINI, *J. Am. Ceram. Soc.* **79** (1996) 1515.
14. E. VERNÉ, M. FERRARIS, A. VENTRELLA, L. PARACCHINI, A. KRAJEWSKI and A. RAVAGLIOLI, *J. Eur. Ceram. Soc.* **18** (1998) 363.
15. E. VERNÉ, M. FERRARIS, C. JANA and L. BARACCHINI, *ibid.* **20** (2000) 473.
16. M. FERRARIS, P. RABAJOLI, F. BROSSA and L. PARACCHINI, *J. Am. Ceram. Soc.* **79** (1996) 1515.
17. C. JANA, W. NISCH and G. GRIMM, in "Advances in Science and Technology," edited by Vincenzini (Materials in Clinical Applications, Techna, Faenza, 1995) Vol. 12, p. 257.
18. J. M. GOMEZ VEGA, E. SAIZ, A. P. TOMSIA, G. W. MARSHALL and S. J. MARSHALL, *Biomat.* **21** (2000) 105.
19. A. PAZO, E. SAIZ and A.P. TOMSIA, *Acta Mater.* **46** (1998) 2551.
20. J. M. GOMEZ-VEGA, E. SAIZ and A. P. TOMSIA, *J. Biomed. Mater. Res.* **46** (1999) 549.
21. T. SOHMURA, H. TAMASAKI, T. OHARA and J. TAKAHASHI, *J. Biomed Mater Res (Appl Biomater)* **58** (2001) 478.
22. L. L. HENCH, in "An Introduction to Bioceramics," edited by L. L. Hench and J. Wilson (World Scientific Publ., 1993) Vol. 1, p. 41.
23. C. KIM and S. JEE, *J. Eur. Cer. Soc.* **23** (2003) 1803.
24. T. KOKUBO, H. KUSHITAI, C. OHTSUKI, S. SAKKA and T. YAMAMURO, *J. Mater. Sci.: Mater. Med.* **3** (1992) 79.
25. O. PEITL, E. ZANOTTO and L.L. HENCH, *J. Non. Cryst. Sol.* **292** (2001) 115.
26. T. KOKUBO, M. SHIGEMATSU, Y. NAGASHIMA, M. TASHIRO, T. NAKAMURA, T. YAMAMURO and S. HIGASHI, *Bull. Inst. Chem. Res. Kyoto. Univ.* **60** (1982) 260.
27. T. KOKUBO, *J. Non Cryst. Solids* **120** (1990) 138.
28. T. KOKUBO, H. KIM and M. KAWASHITA, *Biomat.* **24** (2003) 2161.
29. L. L. HENCH and O. ANDERSSON, in "Introduction to Bioceramics," edited by L. L. Hench and J. Wilson (World Scientific Pub., 1993) Vol. 1, p. 261.
30. S. W. K. KWEH, K. A. KHOR and P. CHEANG, *Biomat.* **21** (2000) 1223.
31. E. S. THAIN, K. A. KHOR, N. H. LOH and S. B. TOR, *ibid.* **22** (2001) 1225.
32. K. YAMASHITA, K. E. YONEHARA, X. DING, M. NAGAI and T. UMEGAKI, *J. Biomed. Mater. Res. (Appl Biomater)* **43** (1998) 46.
33. C. C. MARDARE, A. I. MARDARE, J. F. R. FERANDES, E. JOANNI, S. C. A. PINA, FERNANDES and R. N. CORREIRA, *J. Eur. Cer. Soc.* **23** (2003) 1027.
34. X. NIE, A. LEYLAND and A. MATTHEWS, *Surf. Coat. Techn.* **125** (2000) 407.
35. F. BRANDA, F. ARCOBELLO-VARLESE, A. COSTANTINI and G. LUCIANI, *Biomater.* **23** (2002) 711.
36. M. FERRARIS, E. VERNÉ, C. MOISESCU, A. RAVAGLIOLI and A. KRAJEWSKI, in "Bioceramic Coatings for Guided Bone Growth," edited by A. Ravaglioli and A. Krajewski (Gruppo Editoriale Faenza Editrice, 1996) p. 31
37. K. OHURA, T. NAKAMURA, T. YAMAMURO, Y. EBISAWA, T. KOKUBO, Y. KOTOURA and M. OKA, *J. Mater. Sci: Mater. Med.* **3** (1992) 95.
38. H. M. KIM, F. MIYAJI, T. KOKUBO, C. OHTSUKI and T. NAKAMURA, *J. Am. Ceram. Soc.* **78** (1995) 2405.
39. G. W. MOREY, F. C. KRACEK and N. L. BOWEN, *J. Soc. Glass. Technol.* **14** (1930) 158.
40. I. W. DONALD, *J. Mat. Sci.* **28** (1993) 2841.
41. C. OHTSUKI, Y. AOKI, T. KOKUBO, Y. BANDO, M. NEO and T. NAKAMURA, *J. Ceram. Soc. Jpn.* **103** (1995) 449.
42. P. W. MCMILLAN, in "The Properties of Glass-Ceramics," edited by J.P. Roberts and P. Popper (Academic Press Inc., London, 1979) p. 225.
43. S. FUJIBAYASHI, M. NEO, H. KIM, T. KOKUBO and T. NAKAMURA, *Biomat.* **24** (2003) 1349.

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