Bioactivity of degradable polymer sutures coated with bioactive glass

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Novel bioactive materials have been prepared by coating violet resorbable Vicryl® sutures with a bioactive glass powder derived from a co-precipitation method. Two techniques have been chosen for the composite preparation: pressing the sutures in a bed of glass powder and slurry-dipping of sutures in liquid suspensions of bioactive glass powders. The uniformity and thickness of the coatings obtained by the two methods were compared. The bioactivity of the sutures with and without bioactive glass coating was tested by soaking in an inorganic acellular simulated body fluid (SBF). The composite sutures were characterised by XRD, SEM and FTIR analyses before and after soaking in SBF solution to assess the formation of hydroxyapatite on their surfaces, which is a qualitative measure of their bioactivity. The possible use of bioactive sutures to produce tissue engineering scaffolds and as reinforcement of resorbable calcium phosphates is discussed.

1. Introduction

Sutures are natural or synthetic textile biomaterials widely used in wound closure, to ligate blood vessels and to draw tissues together [1–5]. Surgical sutures (and meshes) are also used in augmentation devices to protect healing sutured ligaments or tendon transplants against excessive tensile loads [6] and in treatment of periodontal defects [7]. Most common sutures consist of a fibre or fibrous structure and they can be classified into two broad categories: absorbable and nonabsorbable. The most important properties of suture materials are physical and mechanical properties, handling properties, biological properties, and biodegradation properties, and all these properties are interrelated. Chu [1] has presented a comprehensive review of properties of the most common types of sutures in current medical praxis. Beyond their normal use in surgery, wound closure, augmentation devices and body wall repair, suture materials are attractive for the production of 3-D structures and meshes of variable pore size using textile technology for tissue engineering applications, that is, as resorbable scaffolds [8–10]. Sutures have been also proposed as reinforcement elements for brittle hydroxyapatite (HA) [11] and calcium phosphate cements [12, 13].

It has been suggested recently that the combination of surgical sutures and meshes with bioactive phases should result in useful bioactive composite materials with a wide range of applications in wound healing, augmentation devices and tissue engineering scaffolds [8, 14–16]. In the previous studies a commercially available bioactive glass powder (45S5 Bioglass®) has been used to produce bioactive coatings on biodegradable sutures, for example, Vicryl® [8, 15]. It was shown that coating Vicryl® sutures with Bioglass® affects the extent and rate of suture degradation in simulated body fluid (SBF) [8], thus providing a means of controlling the structural integrity of the sutures over times of exposure to body fluids. It was suggested that the rapid exchange of protons in water for alkali in the glass should provide a pH buffering effect at the polymer surface [8]. Moreover, after immersion in SBF for only a few days, it was found that the presence of the bioactive glass coating led to nucleation and growth of a crystalline HA layer on the sutures, thus demonstrating the enhanced *in vitro* bioactive behaviour of the composite sutures [8]. In the previous study however [8], it was also shown that as-received Vicryl® sutures exhibited slightly higher tensile strengths than Bioglass®-coated samples, which was thought to be due to mechanical damage on the sutures by the hard glass particles during the pressing operation used to prepare the coatings. It has been also reported that the use of a slurry dipping method allows to coat sutures with Bioglass® particles without damaging the outer surface of the sutures [15]. In general, the slurry dipping technique has been shown to have advantages

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over dry powder pressing routes for developing biodegradable polymer/Bioglass® composites [14, 15, 17]. In all previous investigations, the same melt-derived commercial 45S5 Bioglass® powder (mean particle size $< 5\,\mu m$) has been used. It is therefore interesting to explore the use of other types of bioactive glasses as coating of suture materials, in particular glasses derived by wet-chemistry routes because of the peculiar reactivity of these materials in comparison to melt-derived glasses [18].

In the present work composite suture materials were fabricated combining commercially available resorbable (Vicryl®) sutures with a bioactive glass powder produced by a modified coprecipitation procedure. Both powder pressing and slurry-dipping coating techniques were investigated to produce coatings. The *in vitro* bioactivity of the sutures coated by the different methods was assessed by studying the formation of hydroxypatite on sutures' surfaces upon immersion in SBF.

2. Materials and methods

2.1. Starting materials

Violet braided resorbable 3/0 Vicryl® (polyglactin 910) sutures were obtained commercially from Ethicon Inc. (Edinburgh, Scotland). Vicryl® is a widely used suture made from the semi-crystalline polymer family, a poly(glycolide-L-lactide) (PGLA) random copolymer with 90–10 molar ratio. The mean diameter of as-received Vicryl® suture is 0.33 mm, with individual fibrils of diameters $\sim 10\,\mu m$. The suture is coated with equal parts of a copolymer of lactide and glactide plus calcium stearate to form an absorbable, adherent non-flaking lubricant. These components are water repelling, which slows tissue fluid penetration and absorption. A scanning electron microscopy (SEM) micrograph of the as-received Vicryl® suture is shown in Fig. 1.

The bioactive glass of composition (in wt %): 24.5% Na_2O, 24.5% CaO, 45% SiO_2 and 6% P_2O_5 was prepared using alkoxides and water-soluble salts. In this way the starting compounds are mixed at colloidal level and hence have a high-chemical homogeneity. The reagents were tetraethilortosilicate (TEOS), triethilphosphate (TEP), NaCl and $Ca(NO_3)_2 \cdot 4H_2O$. The hydrolysis reactions of alkoxides were acid cathalised using a 2 N HNO_3 solution, under magnetic stirring. The inorganic salts were dissolved in distilled water and then added very slowly to the prehydrolised alkoxides, under strong stirring. After the addition of every reactant, the solution was stirred for 1 h. The obtained sol was cast in a cylindrical Teflon container that was sealed and kept for three days at room temperature. During this step, the coprecipitation of very fine white powders occurred, and no gel formation was observed. The obtained powders were dried at 150 °C and analysed by X-ray diffraction (XRD). The XRD analysis revealed its semi-crystalline nature, with the presence of few peaks, mainly identified as NaCl, over an amorphous background. The precipitation of crystalline phases could not be avoided, even by modifying the sol-forming conditions in terms of pH, sequence of reagents mixing and sodium precursors. For this reason this method can be considered a coprecipitation-like one [19, 20]. Traditionally, coprecipitation is used to obtain very fine crystalline phases with a high degree of homogeneity, strong reactivity, high purity and lower processing temperatures if compared with traditional ceramics. In this case the aim was the production of an amorphous glass, therefore the dried powder was ground for 30 min, then melted in a platinum crucible at 1300 °C for 30 min in air atmosphere and finally poured on a copper plate. After cooling, the glass was milled in a magnetic ball mill and sieved. The glass was analysed by powder XRD in order to verify its amorphous state. The glass particle morphology was observed by SEM. The fraction of particles smaller than 20 μm was used for the coating experiments.

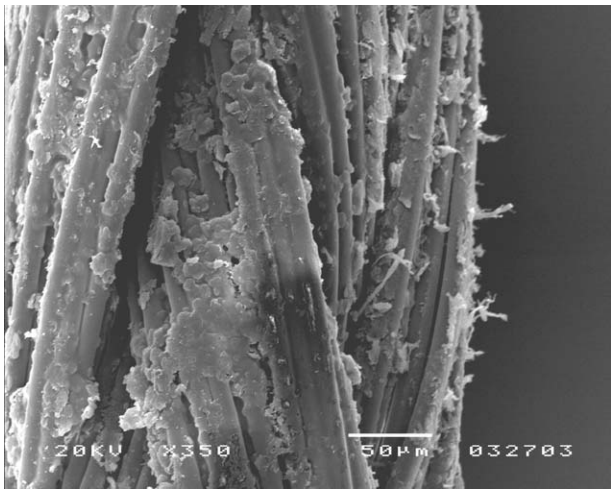

Figure 1 SEM micrograph showing the as-received Vicryl® suture.

2.2. Preparation of coated sutures

The composite sutures were prepared by two methods: pressing of sutures in a dried powder bed and slurry-dipping of sutures into a liquid suspension of glass particles.

In the pressing procedure, the glass powders were placed on a flat surface plate forming a uniform layer. The sutures (2 cm in length) were placed on the glass powder layer. A new glass powder layer was added, covering the sutures. A second similar plate was placed on top and the assembly was set in a uniaxial press. A pressure of 100 MPa was applied for 5 min. Subsequently, the sutures, which were covered by a layer of glass particles, were extracted manually. The uniformity of the coatings was characterised by SEM.

In the slurry-dipping procedure two different slurries were compared: the first one was prepared by mixing the glass powder with distilled water in a 1 : 1% vol. ratio, the second one was prepared using isopropanol in the same volume ratio. Both procedures were carried out under magnetic stirring for 15 min. The sutures (2 cm in length) were immersed in the slurries and they were not removed until water or isopropanol had evaporated. Thus the drying process took place at room temperature at a very slow rate. This was important to minimise the appearance of microcracking in the coatings. The

TABLE I Ionic composition of SBF and blood plasma [21]

Ion	SBF	Blood plasma
Na^+	142.0	142.0
K^+	5.0	5.0
Mg^{2+}	1.5	1.5
Ca^{2+}	2.5	2.5
Cl^-	147.8	103.0
HCO_3^-	4.2	27.0
HPO_4^{2-}	1.0	1.0
SO_4^{2-}	0.5	0.5

uniformity and quality of the coatings was characterised by SEM observations.

2.3. *In vitro* tests and surface chemistry

The uncoated (2 cm in length) and coated sutures prepared as described above were immersed in SBF in order to assess their bioactivity by detecting the formation of HA on their surfaces, as proposed by Kokubo *et al*. [21]. The composition of the SBF solution is given in Table I. The tests were carried out by soaking the samples in 15 ml SBF at 37 °C in polyethylene ware. The pH of the SBF solution was buffered at 7.40. The SBF solution was refreshed twice a week. The specimens were removed from the fluid after given soaking times (7, 14, 22 and 28 days) and gently washed with distilled water. After drying in air atmosphere, the formation of apatite on the surface of the samples was studied by XRD, SEM and Fourier transform infrared spectroscopy (FTIR). The ability of HA formation in contact with SBF is considered a qualitative measure of the materials' bioactivity [21, 22].

The surfaces of each specimen before and after immersion in SBF were studied by XRD (Philips X'Pert diffractometer), using the Bragg–Brentano geometry and the Cu K_α radiation (30 mA and 40 kV), SEM coupled with energy dispersive spectroscopy (Philips 515, EDAX PV 9900EDS) and FTIR. FTIR spectra were acquired in a Bruker Equinox 55 IR-IF spectrometer with attenuated total reflection (ATR) cell.

3. Results and discussion

In order to prepare the bioactive glass used in this work, a wet-chemistry procedure was developed. The precursors selected for this synthesis are commonly used in sol–gel routes. In this way, the starting materials were mixed at colloidal or molecular scale, producing a sol. However, in the system investigated in this work, the stability of the sol was severely affected by the addition of NaCl, which has a great influence on the repulsive forces between colloidal particles, as many other electrolytes [23]. For this reason, after the sol casting, it was impossible to observe any gelification, but only the precipitation of uniform particles as observed in many co-precipitation routes, commonly used to prepare fine-dispersed ceramic powders [19]. The so produced particles were characterised by a microstructure not completely adequate for the goal of this work, that is, the production of amorphous glass particles. For this reason a further thermal treatment was necessary to produce the final

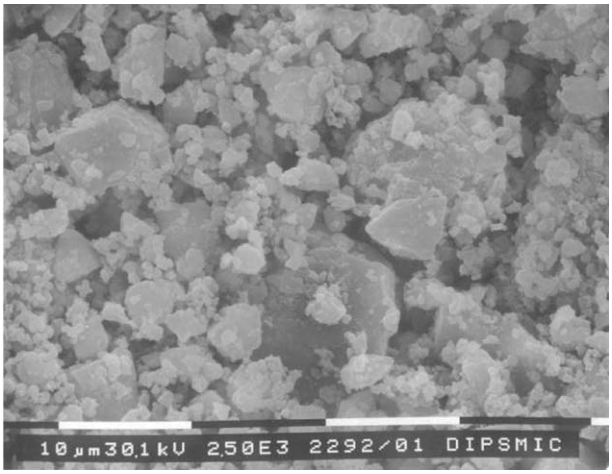

Figure 2 SEM micrograph showing the morphology of the bioactive glass powder prepared in this work.

glass powder. Neverthesess, the preparation of the starting powders by wet-chemistry still has advantages with respect to the conventional melting of commercially available reagents, particularly regarding the better homogeneity (in molecular scale) and better purity of the raw materials and enhanced reactivity of the obtained powders.

The morphology of the bioactive glass powders prepared in this work is shown in Fig. 2. The particle size appears uniformly distributed in the range 1–20 µm. XRD analyses performed on these powders showed that they are almost completely amorphous. Fig. 3 shows the XRD pattern of the glass powders after sieving. A broad amorphous halo between $2\theta = 20°$ and $2\theta = 40°$ can be observed, on which two very weak signals are seen. These are attributed to HA.

Fig. 4 shows the SEM micrographs of the uncoated sutures before and after 28 days soaking in SBF. It is seen that after nearly one month in SBF the sutures are severely degraded. This is in agreement with previous results [8]. Degradation of these polymers occurs first by dissolution of the amorphous region, followed by the erosion of the crystalline region [8, 24]. By soaking such materials into an aqueous solution, the water molecules penetrate first the amorphous region. As degradation proceeds, tie-ends, chain-ends and chain folds comprising the amorphous region of the polymer degrade into fragments, until a point where the fragments start to dissolve in the aqueous medium [8, 24]. Since Vicryl® sutures are not bioactive materials, HA did not grow on the surface of the uncoated sutures in contact with SBF.

The surfaces of the coated sutures fabricated by the

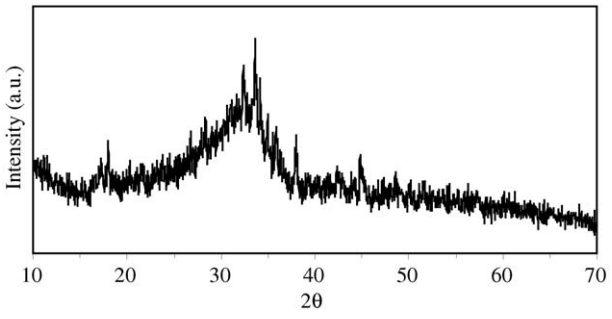

Figure 3 X-ray diffraction pattern of the glass powder after sieving.

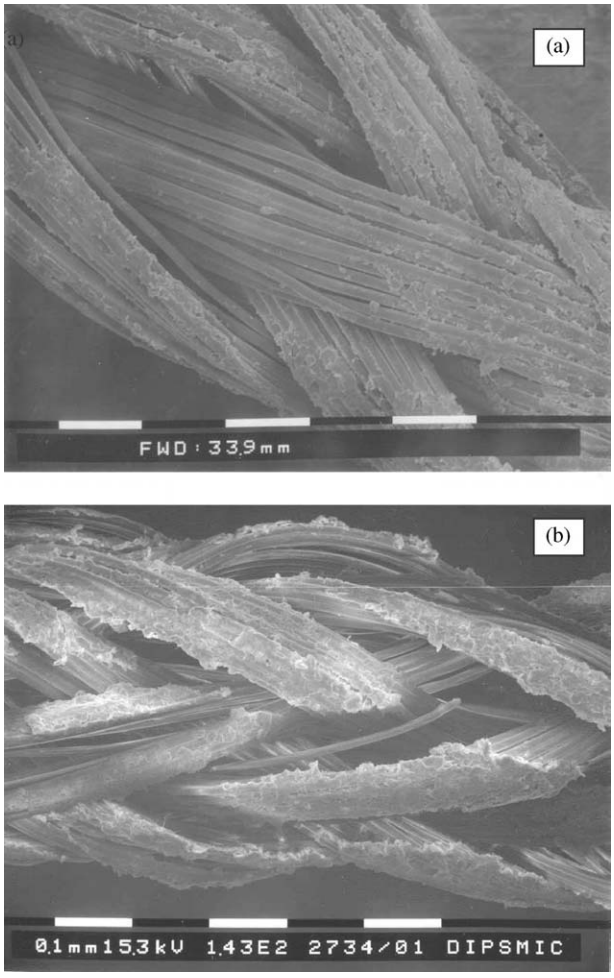

Figure 4 SEM micrographs of the uncoated sutures (a) before and (b) after 28 days soaking in SBF.

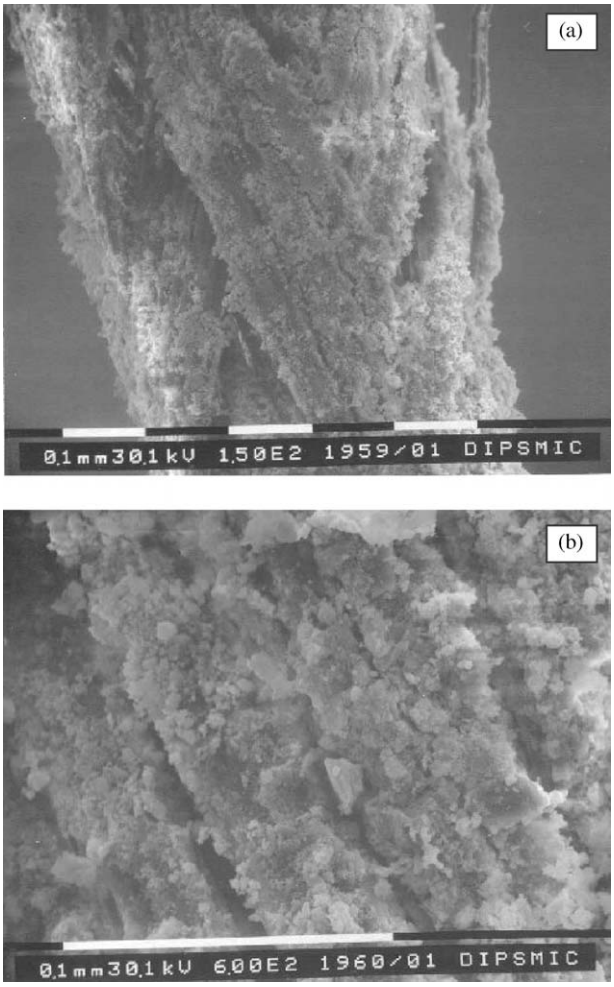

Figure 5 SEM micrographs showing the surfaces of bioactive glass coated sutures fabricated by the pressing method, at (a) low and (b) high magnifications.

pressing method are shown in Fig. 5(a) and (b) at low and high magnification, respectively. The thickness of the coating of glass particles on the sutures is not uniform. Fig. 5(b) shows a detail of the surface. In this image the glass particles appear mechanically attached to the surface of the sutures. After 28 days of soaking in SBF crystals of HA began to cover the surface of the sutures, as shown in Fig. 6. The HA composition was confirmed by EDS analysis.

The SEM micrographs corresponding to the composites prepared by slurry dipping in distilled water and isopropanol are shown in Fig. 7(a) and (b), respectively. An excellent coating quality is achieved by using distilled water (Fig. 7(a)). A uniform layer of glass particles of thickness 15–20 μm is deposited on the surface of the sutures. On the contrary, using isopropanol as suspension medium, the coating quality appeared very poor, as seen in Fig. 7(b). In this case very few glass particles still adhere to the suture surface. For this reason, only the composites produced by slurry dipping in distilled water were characterised in terms of bioactivity.

The XRD patterns of the surfaces of coated sutures produced by the slurry-dipping method before and after soaking in SBF are presented in Fig. 8 (patterns (b)–(e)). For comparison, the XRD pattern of as-received sutures is also shown in Fig. 8 (pattern (a)). The as-received sutures present a microcrystalline structure. Three main signals, quite wide, at $2\theta = 14.2°$, 17° and 25.8° can be detected. In all cases the XRD diagrams are almost

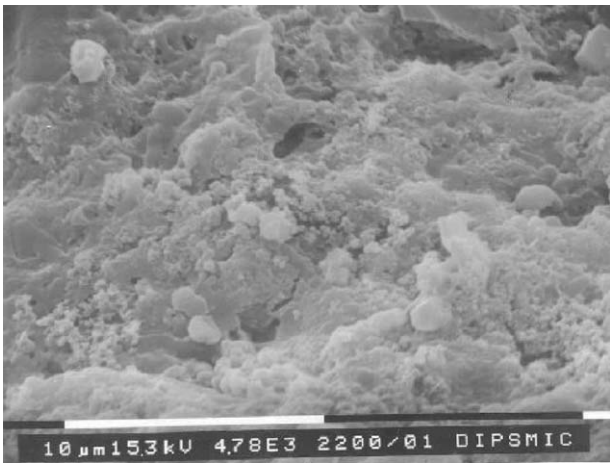

Figure 6 SEM micrograph showing a suture fabricated by the powder pressing method after 28 days in SBF, showing small crystals of HA have began to cover the surface of the sutures.

identical and no HA peaks could be evidenced. Therefore, using this experimental technique it was not possible to detect the presence of any crystalline phase precipitated on the surface of the coated sutures from the solution.

A SEM micrograph of the surface of a coated suture produced by slurry dipping in distilled water after soaking in SBF for 28 days is presented in Fig. 9. The suture shows a degraded structure. A high magnification

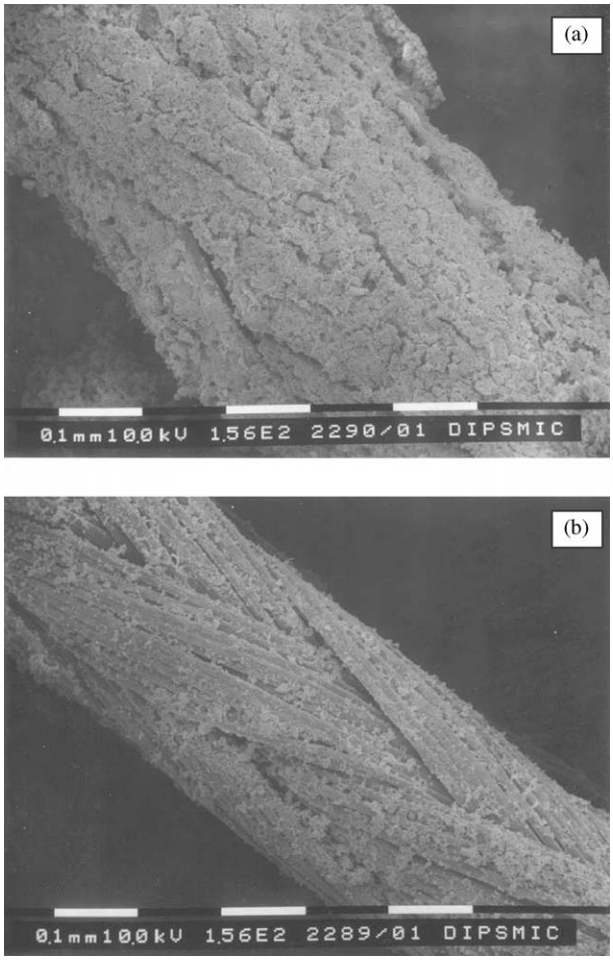

Figure 7 SEM micrographs of coated sutures prepared by slurry dipping in (a) distilled water and (b) isopropanol.

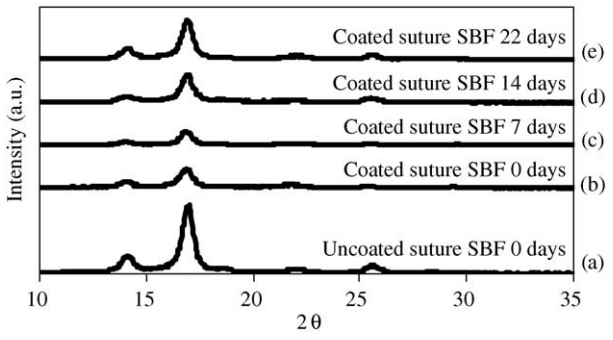

Figure 8 XRD patterns of the surfaces of coated sutures produced by the slurry-dipping method before and after soaking in SBF for different days (patterns (b)–(e)). For comparison, the typical XRD pattern of as-received sutures is also shown (pattern (a)).

of the sample shown in Fig. 9 is presented in Fig. 10(a). Several spherical precipitates can be observed, which exhibit an appreciable degree of uniformity. These precipitates were analysed by EDS (Fig. 10(b)) and they were identified as HA, due to the presence of calcium and phosphorus as predominant elements in a ratio close to the right Ca/P ratio of HA (1.67). The difference between the estimated experimental ratio (~ 2) and the theoretical one is due to the presence of the gold peak (gold coating was used for SEM observation), which partially covers the phosphorus peak and affects the accuracy of the measure (see Fig. 10(b)).

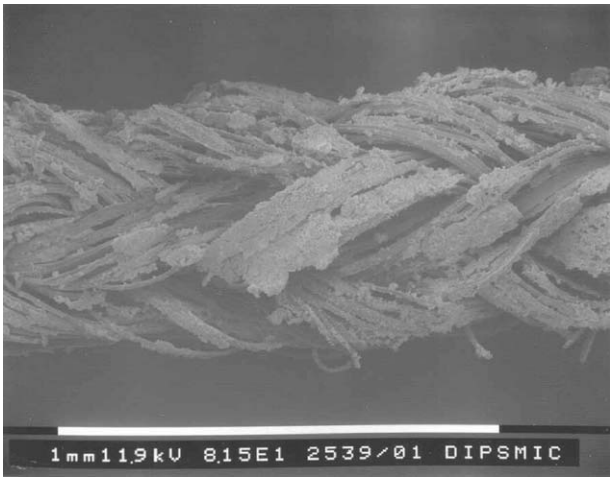

Figure 9 SEM micrograph of the surface of a coated suture produced by slurry dipping in distilled water after soaking in SBF for 28 days.

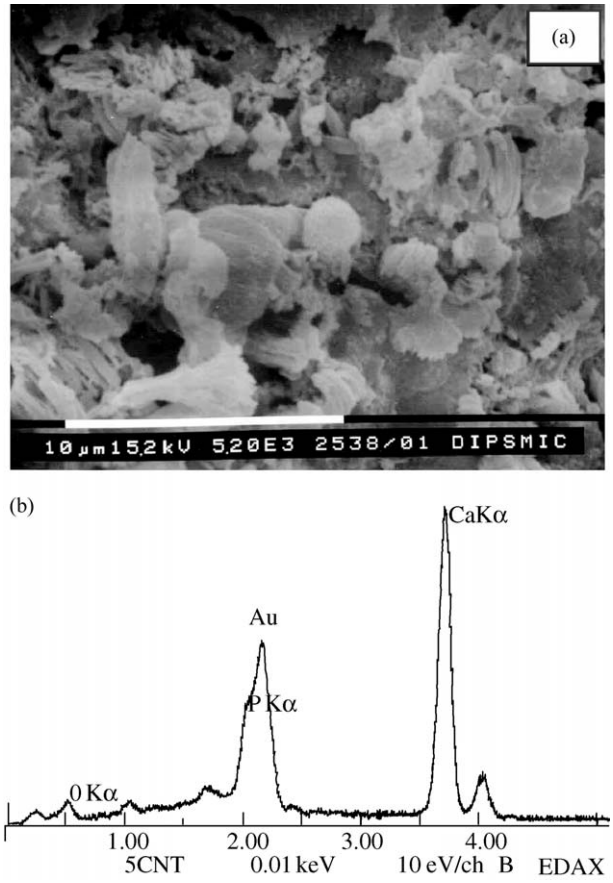

Figure 10 (a) High magnification SEM micrograph of the suture shown in Fig. 9 showing spherical uniformly distributed precipitates. (b) EDS analysis of the precipitates, which are identified as HA, due to the presence of calcium and phosphorus as predominant elements.

In Fig. 11 the FTIR–ATR spectra of the sutures produced by slurry-dipping in distilled water before soaking and after 14, 22 and 28 days in SBF are shown. The two spectra corresponding to the as-received sutures before and after 28 days immersion in SBF are added in Fig. 11. After coating, before soaking in SBF, the major part of the peaks corresponding to the as-received sutures is covered and a new peak at $1085\,cm^{-1}$ can be seen. This band corresponds to the vibrational mode of the asymmetric stretch of Si–O–Si. After 14 days soaking in

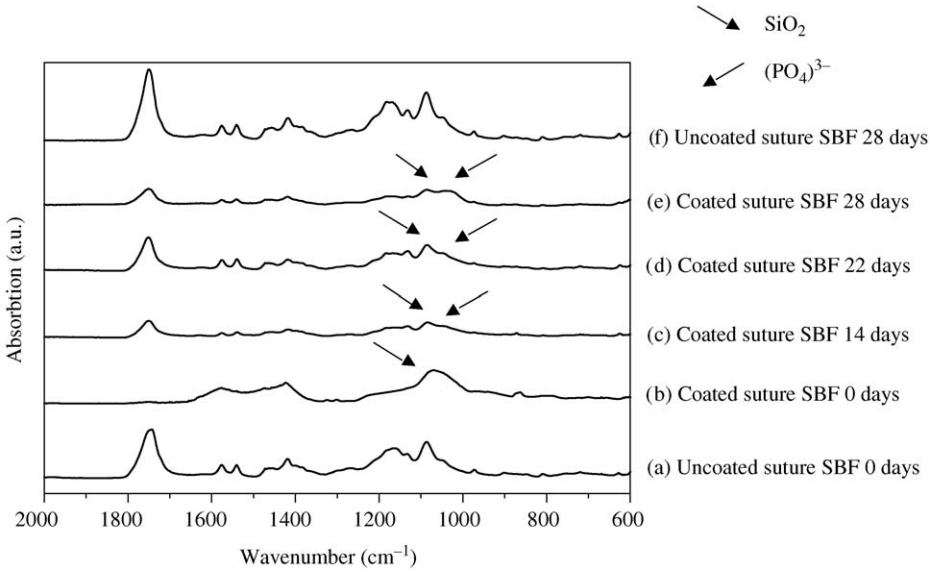

Figure 11 FTIR–ATR spectra of sutures produced by slurry-dipping in distilled water. Results on sutures before soaking in SBF and after 14, 22 and 28 days in SBF are shown. Typical spectra for noncoated sutures are also presented for comparison.

SBF, a slight variation in the band shape at 1035 cm^{-1} can be observed. This variation could be due to the appearance of a P–O anti-symmetric stress band. After 22 days of soaking in SBF, the IR spectrum is analogous to that observed after 14 days. However, minor differences can be observed, such as an increasing of 1035 cm^{-1} peak. After 28 days in SBF, the IR spectrum shows a widening of the band at 1035 cm^{-1}, which may be attributed to the phosphate group. The spectrum of the uncoated sutures after 28 days in SBF is similar to that observed before soaking and the peaks are characteristic for both the crystalline and amorphous structure of the suture [7].

The results of the present work confirm the effect of the bioactive glass coating on bioactivity and degradation behaviour of Vicryl® sutures, as discussed in previous studies for 45S5 Bioglass® coatings [8, 15, 16]. Bioactive glass coated sutures, as developed here, should increase the value of sutures and so extend their function beyond the traditional role in wound closure. For example, resorbable sutures with bioactive coating, in conjunction with textile technology, may provide cost effective materials for producing 3-D scaffolds with controlled variable porosity for bone tissue engineering applications. The bioactive glass coating may provide graded or localised bioactivity and control over degradation and mechanical properties of the scaffold. Moreover resorbable bioactive sutures are attractive reinforcement elements for resorbable bioceramics such as calcium phosphates and HA, as it has been suggested in the literature [11–13]. Further research should be carried out in order to compare the reactivity and degradation behaviour of sutures coated with wet-chemistry derived glasses (as developed here) and those prepared using conventional melt-derived glasses, investigated in previous works (e.g. Boccaccini *et al*. [15]).

4. Conclusions

Composites based on violet resorbable Vicryl® sutures coated with bioactive glass were prepared. The bioactive glass was produced by a coprecipitation-derived method. Two coating procedures were compared: dry powder pressing and slurry-dipping in different suspension media. The slurry-dipping in distilled water gave the best results in terms of production of uniform and reproducible bioactive glass coatings (15–20 μm thickness), and provided a better bioactive behaviour of the coated sutures in terms of kinetics of HA precipitation and quality of the precipitated layers.

Biodegradable polymer sutures with bioactive glass coatings, forming bioactive composite materials, as developed in this investigation, are attractive materials which could be used to develop 3-D scaffolds for bone-tissue engineering. They may be also interesting reinforcing elements for resorbable calcium phosphate matrices, with the bioactive glass coating providing an optimal interface between the bioceramic matrix and the reinforcing polymeric suture.

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