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Jonny J. Blaker, Aldo R. Boccaccini, Showan N. Nazhat. Thermal Characterizations of Silvercontaining Bioactive Glass-coated Sutures. Journal of Biomaterials Applications, 2005, 20 (1), pp.81-98. 10.1177/0885328205054264 . hal-00570762

HAL Id: hal-00570762 https://hal.science/hal-00570762

Submitted on 1 Mar 2011

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Thermal Characterizations of Silver-containing Bioactive Glass-coated Sutures

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ABSTRACT: This study utilized and compared a number of thermal analysis methods to characterize the thermal properties of commercial sutures with and without antimicrobial coatings of silver-doped bioactive glass (AgBG) interlocking particulates. The effect of a slurry dipping technique used to coat resorbable Vicryl[®] (polyglactin 910) and non-resorbable Mersilk[®] surgical sutures with AgBG was investigated using conventional differential scanning calorimetry (DSC), high speed calorimetry (or HYPERDSCTM), and modulated temperature DSC (MTDSC). These methods were compared in terms of their ability to resolve the thermal transitions of the types of suture materials. Differential thermal analysis (DTA) and thermogravimetric analysis (TGA) were used to verify the thermal degradation temperatures of these materials and to quantify the AgBG coatings on the sutures.

The use of complementary thermal analysis techniques enabled the understanding of the effect of the AgBG coating technique on the morphological properties of the sutures. The slurry dipping technique had no significant effect on the thermal transitions of both types of materials. The use of high speed calorimetry through DSC offered better resolution for the transitions that appeared to be weak through conventional heating regimes, and was able to separate broad double transitions. Furthermore, it was shown not to compromise either the melting temperature or the enthalpy of melting. Therefore this method allows for the accurate determination of thermal

JOURNAL OF **BIOMATERIALS APPLICATIONS** Volume 20 — July 2005

81

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^{0885-3282/05/01 0081–18 \$10.00/0} DOI: 10.1177/0885328205054264 $\ensuremath{\mathbb{C}}$ 2005 Sage Publications

transitions through much shorter experimental times thus allowing for an increased sample throughput. The combined DTA and TGA indicated that a greater AgBG coating was obtained in the case of the Mersilk[®] sutures.

KEY WORDS: suture, silk, bioactive glass, silver ion, antibacterial, MTDSC, HYPERDSCTM.

INTRODUCTION

D ioactive glasses of the general formula SiO_2 -CaO-P₂O₅-Na₂O D have been shown to form tenacious bonds to both hard and soft tissues, where bonding occurs by the rapid formation of a thin layer of hydroxycarbonate apatite (similar to biological apatite) on the glass surface with exposure to biological fluids [1]. By incorporating these bioactive glass particles as coatings or fillers into bioresorbable polymers, scaffolds of tailored biological and mechanical properties can be produced for potential applications in tissue engineering [2-4]. Furthermore, Hench and collaborators have recently reported [5–7] the inclusion of silver oxide (Ag₂O) into some bioactive glass compositions, aiming at reducing the risk of microbial contamination through the leaching of silver ion (Ag⁺). They have demonstrated that bioactive glass doped with 3 wt% Ag₂O elicits rapid bactericidal action without compromising the glass bioactivity [7]. Ag⁺ has a broad-spectrum antimicrobial property, and therefore significance for the polymicrobial colonization associated with biomaterial related infections [8]. Generally, it has been shown that bacteria have a low propensity to develop resistance to silver-based products, and these have therefore been incorporated into several biomaterials, such as hydroxyapatite [9], polyurethane [10] and bioactive glasses [5-7,11]. When metallic silver reacts with wound fluids, silver ions are released, damaging bacterial RNA and DNA, thus inhibiting replication [12–14].

Sutures are natural or synthetic textile biomaterials widely used in wound closure, to draw tissues together and ligate blood vessels and can be classified into two broad categories: resorbable and non-resorbable [15]. Sutures can also be attractive materials for the production of 3D structures and meshes of controlled and variable pore size; using textile technology in the production of resorbable scaffolds [16–18]. Recently, composites based on AgBG particulate coatings on surgical sutures have been reported [19] on the surface of resorbable (Vicryl[®]) and nonresorbable (Mersilk[®]). The sutures were coated using an optimized aqueous slurry dipping procedure, whereby sutures are dip-coated in stable slurries of the particulates in water for various times, then removed, and dried. The *in vitro* bioactivity of sutures coated with silver-doped bioactive glass (AgBG) has been demonstrated, where the dissolution of the glass after only 3 days in simulated body fluids lead to the formation of a crystalline hydroxyapatite layer on the suture surface [19]. The benefits of an apatite coating on textiles for potential applications in tissue engineering have been highlighted [20]. Furthermore, the antibacterial properties of AgBG-coated Mersilk[®] against *Staphylococcus epidermidis* have recently been demonstrated [21].

In this work, complementary thermal analysis techniques were used to investigate the thermal properties of both 'as received' and 'coated' suture materials in order to investigate the effect of the slurry dipping technique on the morphological properties of the sutures. Furthermore, differential scanning calorimetry (DSC) was undertaken using a variety of heating regimes, where conventional constant heating rates, high speed calorimetry (or HYPERDSCTM) and modulated temperature DSC (MTDSC) were assessed in terms of resolving the thermal transitions. HYPERDSCTM is a form of high speed calorimetry and a relatively new tool in thermal analysis that has been shown to provide quantitative measurement at very high controlled heating and cooling rates of up to hundreds of degrees per minute of (sub)milligram amounts of material, thus also facilitating high throughput DSC. The technique has been shown to minimize instrument drift during measurement where extremely high heating rates reduce or eliminate reorganization during heating [22]. Comparisons were made with the more established MTDSC method which can be regarded as a slow scan rate. Differential thermal analysis (DTA) and thermogravimetric analysis (TGA) were used to verify the thermal degradation temperatures of the materials and to quantify the AgBG coatings on the sutures. These thermal investigations should provide relevant data regarding the effect of AgBG coatings on the effective thermal and therefore morphological properties of composite sutures. These must be known to assess the potential application of the sutures in wound healing, and to serve as a model for applications other than suturing, such as tissue engineering scaffolds.

EXPERIMENTAL METHODS

Materials Preparations

Braided sutures, in the form of resorbable 3/0 Vicryl[®] (polyglactin 910) sutures and non-resorbable 2/0 Mersilk[®] (W775) sutures were obtained commercially from Ethicon Inc. (Edinburgh, Scotland). Vicryl[®], which is a semicrystalline polymer composed of a poly(glycolide-co-L-lactide) (PGLA) random copolymer with a 90:10 molar ratio.

The suture is also coated with equal parts of a copolymer of lactide and glycolide plus calcium stearate to form an absorbable, adherent non-flaking lubricant. Mersilk[®], on the other hand, is a braided silk suture, from the silkworm Bombyx mori, and consisting of two proteins: sericin, the antigenic gum-like protein surrounding a fibroin core. Fibroin is composed of highly crystalline β -sheet crystal regions and semicrystalline regions [23,24]. Once braided the suture is coated with beeswax.

The sol-gel derived AgBG particles were fabricated following a process similar to that reported by Bellantone et al. [5,7]. The composition of the bioactive glass used in the present investigation was (in mol%): 60% SiO_2 , 2% Ag₂O, 34% CaO, and 4% P₂O₅, with a particle size <38 μ m. Composite sutures were prepared using a slurry dipping technique, which has been described in detail, elsewhere [19]. Briefly the technique involved the preparation of stable slurries of AgBG particles in deionized water. AgBG particles were added slowly to a 50 ml beaker containing deionized water and continuously agitated using a magnetic stirrer to prevent particle sedimentation, and left to stabilize for 30 min. Suture lengths ($\sim 25 \text{ mm}$) were lowered into the slurry for 2 and 5 min for Vicryl® and Mersilk® sutures, respectively, and removed at a withdrawal velocity of $10 \,\mathrm{mm \, s^{-1}}$. Samples were slowly dried at room temperature (left for 7 days) on glass plates to minimize microcrack development in the glass-coating. It was anticipated that some inhomogeneities would be introduced on the coating surface during this drying procedure.

Materials Characterization

Scanning Electron Microscopy

AgBG-coated sutures were characterized using scanning electron microscopy (SEM) to study the thickness, morphology, homogeneity, and structure of the coatings. Samples were gold-coated and observed at an accelerating voltage of 10-20 kV.

Thermal Analysis

DIFFERENTIAL SCANNING CALORIMETRY (DSC)

Thermal analysis through DSC was conducted using a power compensation Perkin-Elmer Pyris Diamond DSC (Perkin-Elmer Corp). Comparative techniques under constant and high speed calorimetry (high performance DSC or HYPERDSCTM), and modulated temperature DSC (MTDSC) were used to identify the thermal transitions of the suture materials, assess the effect of different heating rates on resolving

the transitions, and to investigate the effect of coating method on the sutures. Sutures were cut into 5 mm length pieces and weighed to give samples of 1.9 ± 0.1 mg and placed in aluminum pans. Nitrogen gas was used as purge. Temperature and energy calibrations were carried out on indium standards under manufacturer instructions.

The constant heating rate and HYPERDSCTM was carried out at heating rates of 10, 20, 50, and 100° C min⁻¹. Three repeats were used in the 20° C min⁻¹. Samples were cooled to 0° C and held for 1 min prior to heating and a temperature range of $0-220^{\circ}$ C and $0-250^{\circ}$ C for Vicryl[®] and Mersilk[®], respectively. The output of this method is heat flow versus temperature. Glass transition temperature (T_g) was characterized by a change in the upward direction of the heat flow, the value being calculated by the onset of change in the heat flow.

The MTDSC (using the Perkin-Elmer Pyris StepScan software) was carried out by heating at 2°C steps at a rate of 50°C min⁻¹ from 20 to 220°C and 0 to 250°C for Vicryl[®] and Mersilk[®], respectively. At the end of each heating step the temperature was maintained isothermally for 4 min. Since T_g is accompanied by an increase in the heat capacity (Cp), it was measured using the onset of change in the Cp calculated through MTDSC. However, it should be noted that these calculated Cp were not absolute as a baseline run was not carried out first, but were only used to locate T_g . Therefore the results here should only be considered as qualitative.

DIFFERENTIAL THERMAL ANALYSIS (DTA) AND THERMOGRAVIMETRIC ANALYSIS (TGA)

DTA/TGA was conducted using a Stanton Redcroft STA-780 Series Thermal Analyzer, to determine the thermal and degradation profiles of 'as received' and 'coated' sutures. Scans were performed between 20 and 500° C and at a rate of 5° C min⁻¹ for Vicryl[®], and between 20 and 550° C at a rate of 10° C min⁻¹ for Mersilk[®]. Measurements were collected over three repeats using a sample mass of 4 ± 0.5 mg.

Statistical Analysis

Data was subjected to one-way analysis of variance (ANOVA) and least square difference tests, with a significance level of 0.05.

RESULTS AND DISCUSSION

Commercially available, resorbable Vicryl[®] and non-resorbable Mersilk[®] sutures were coated with AgBG, through the use of an aqueous slurry dipping technique. This study carried out a number of

complementary thermal analysis techniques to characterize the thermal properties of suture materials in order to investigate the effect of this coating method. Initial qualitative analysis of the morphology, uniformity, and thickness of the coatings were conducted by SEM as shown in Figure 1(a) and (b) for the optimally coated Vicryl[®] and Mersilk[®] sutures, respectively. Relatively homogeneous and well-adhered AgBG layers were observed along the length of the sutures. There appeared to be less adhesion of the AgBG particles into the voids



Figure 1. (a) SEM micrograph of AgBG-coated Vicryl $^{\circledast}$ and (b) SEM micrograph of AgBG-coated Mersilk $^{\circledast}.$

of the Vicryl[®] suture, probably due to the PLGA and calcium stearate coating on this suture, whereas the individual fibers in the Mersilk[®] sutures were more easily adhered to.

The DSC investigations carried out in this study utilized a number of methods by using a constant heating rate and modulated temperature DSC to resolve the thermal transitions in both types of sutures. Under the constant heating method the effect of heating rate on resolving transitions was assessed up to 100° Cmin⁻¹ as shown in Figures 2(a)–(d) and 3(a),(b), and summarized in Tables 1 and 2 for Vicryl[®] and Mersilk[®] sutures, respectively. The MTDSC data are



Figure 2. (a) DSC scan, showing the effect of heating rate on 'as received' Vicryl[®] sutures; (b) expanded box highlighted in Figure 2(a); (c) DSC scan, showing the effect of heating rate on 'coated' Vicryl[®] sutures; and (d) expanded box highlighted in Figure 2(c).



Figure 2. Continued.

presented in Figure 4(a) and (b) for Vicryl[®] and Mersilk[®] sutures, respectively. (Here, the Cp measurements were not absolute and were calculated only to estimate the T_g values, which were measured as the onset of change in this parameter, and are also given in Tables 1 and 2.) Throughout this study, the mass of the samples were not compensated for with regard to increasing the heating rate or when using MTDSC. Overall, as can be expected, the measured glass transition temperatures increased with increasing heating rates. Generally it was also found that by using high speed calorimetry, the resolution of the transitions was increased. Thereby the results suggest that high speed calorimetry

88



Figure 3. (a) DSC scan, showing the effect of heating rate on 'as received' Mersilk[®] sutures and (b) DSC scan, showing the effect of heating rate on 'coated' Mersilk[®] sutures.

allowed the possibility of locating thermal transitions for low mass samples (in the sub-milligram range) that otherwise appeared weak and with faster end results. Conversely, MTDSC data gave consistently lower transition temperatures for the same sample mass as this slower method of heating allowed relaxation processes to occur in the samples during the testing period.

As shown in Figure 2(a),(b) and (c),(d) for 'as received' and 'coated' Vicryl[®] sutures, apparently, two T_g transitions (as demonstrated by the respective enlarged insets) were found in each of the materials, where

Heating rate (°C/min)	1st transition onset (°C)		2nd transition onset (°C)		3rd transition onset (°C)		Melt peak (°C)		(X _c %)	
	As received	Coated	As received	Coated	As received	Coated	As received	Coated	As received	Coated
10	57.0	56.2	67.3	65.2	119.2	117.6	197.2	198.1	35.7	35.3
20	60.1	59.6	67.7	66.6	117.2	118.3	196.9	197.6	33.4	32.8
	(±0.1)	(±0.6)	(± 1.4)	(±0.9)	(± 1.4)	(± 1.1)	(±0.1)	(±0.9)	(±0.9)	(±1.8)
50	62.7	62.7 [´]	71.5	69.8 [´]	118.8	121.4	196.1	196.6	33.1	33.2 [´]
100	67.3	64.9	76.8	77.4	122.2	122.6	198.0	198.8	33.3	29.8
MTDSC	59.9	56.6			110.8	111.0	195.8	196.1		
	(±0.5)	(±1.8)			(±2.8)	(±1.3)	(±1.1)	(±0.1)		

Table 1. Summary of DSC data of 'as received' and 'coated' Vicryl $^{\mbox{\tiny \$}}$ sutures.

Table 2. Summary of DSC data of 'as received' and 'coated' Mersilk[®] sutures.

	1st peak	(°C)	2nd peak (°C)		
Heating rate (°C/min)	As received	Coated	As received	Coated	
10	_	_	75.0	82.3	
20	54.4	52.9	94.3	96.7	
	(±3.9)	(±0.1)	(±3.8)	(±7.5)	
50	53.9	55.2	102.2	104.6	
100	65.5	64.4	117.0	122.6	
MTDSC	50.4 (±0.4)	51.3 (±0.6)	_	-	

(a) ⁸ Melting peak 7 6 Specific heat (J.g⁻¹.°C⁻¹) 5 Onset of glass transition temperatures 4 Coated 3 2 As received 1 0 -0 50 100 150 200 250 Temperature (°C) (b) 3.5 Single low temperature peak 3 Coated 2.5 Specific heat (J.g⁻¹°C⁻¹) 2 As received 1.5 1 0.5 0 -50 100 250 300 0 150 200 Temperature (°C)

Figure 4. (a) Cp vs temperature through MTDSC for 'coated' and 'as received' Vicryl[®] sutures and (b) Cp vs temperature through MTDSC for 'coated' and 'as received' Mersilk[®] sutures.

at 20° C min⁻¹ there were no statistically significant differences (P < 0.05) when comparing the 'as received' and 'coated' materials. These transitions were due to the different regions of the amorphous polymeric chains for this semicrystalline polymer. Interestingly however, these double glass transitions were only apparent through the constant heating rates, and became stronger with increasing rates and not evidenced by MTDSC (see Figure 4(b) and Table 1). This double transition is in agreement with literature, where Taddei et al. [25] found two similar transitions in a study using DSC to characterize Vicryl[®] membrane (monofilament) that were guoted at 48 and 63°C. A third transition in the region of 120°C found for the 'as received' and 'coated' Vicryl[®] suture is also in agreement with the work carried out by Taddei et al. [25]. Here, the higher heating rates enhanced the resolution of the transition at around 120°C. Both the 'as received' and 'coated' Vicryl[®] sutures exhibited a significant melting peak that appeared at $196.9 \pm 0.1^{\circ}$ C and $197.6 \pm 0.9^{\circ}$ C, respectively. From this melting peak, the percentage crystallinity $(\% X_c)$ of these sutures as obtained through the different heating rates was determined using the measured enthalpy of melting (ΔH_m) and calculated according to the equation given below:

$$X_{\rm c}\% = \frac{\Delta H_{\rm m}}{\Delta H_{\rm m^{\circ}}} \times 100 \tag{1}$$

where $\Delta H_{\rm m}$ was measured from the area under the melting peak, and $\Delta H_{\rm m^{\circ}}$ is the enthalpy of melting of a 100% crystalline PGA (assumed to be 139 J g⁻¹) [25]. As given in Table 1, the crystallinity values were of similar order obtained for rates up to $100^{\circ} {\rm C\,min^{-1}}$ and no statistically significant differences ($P \leq 0.05$) were observed at $20^{\circ} {\rm C\,min^{-1}}$ between the 'as received' and 'coated' Vicryl[®], which were similar to the ones obtained by Taddei et al. [25] who reported a crystallinity of 31.5% with the rate of $2^{\circ} {\rm C\,min^{-1}}$.

The DSC results obtained under the constant heating rates for Mersilk[®] sutures showed a double peak region that gave a broad endothermic transition (between 30 and 120° C), which corresponded well with the low temperature peak previously indicated by DMA [19]. These peaks appeared to separate with higher heating rates, suggesting two separate processes. These processes may be due to the combined loss of integrity of the beeswax coating, and water loss from the sericin gumcoating [26] as a result of increasing temperature. Therefore it can be suggested that high speed calorimetry resolved these transitions (Figure 2(a)–(d)), whereas the MTDSC, which eliminates the loss of water effect on a DSC thermogram resulted in one peak as shown in

Figure 4(b). However, none of the DSC heating regimes were able to confirm the high temperature transition that previously appeared through DMA (at around 220° C) [19] that were related to the silk phase.

DTA/TGA was conducted to assess the thermal degradation of the sutures, and to quantify the AgBG coating. Figure 5(a) and (b) show the results and Tables 3 and 4 summarize the transition regions obtained for Vicryl[®] and Mersilk[®] sutures, respectively. For the Vicryl[®] sutures the $T_{\rm g}$ regions indicated both DMA, previously, and DSC were not



Figure 5. (a) DTA/TGA scan (normalized with respect to suture mass) for 'as received' and 'coated' Vicryl[®] sutures and (b) DTA/TGA scan (normalized with respect to suture mass) for 'as received' and 'coated' Mersilk[®] sutures.

		Regio	n I				
Material	Rate I (%/°C)	$\begin{array}{c c} T_{I \rightarrow II} & \text{Residue at} \\ (^{\circ}C) & T_{I \rightarrow II} \ (\%) \end{array}$		Rate II (%/°C)	T _{II–III} (°C)	Residue at T _{II–III} (%)	Residue at 475°C (%)
As received Vicryl [®]	0.03	268	92.76	0.89	361	9.80	6.35
Coated Vicryl [®]	0.03	267	92.88	0.88	358	12.37	7.61
Wt% AgBG							1.26

Table 3. DTA/TGA data for 'as received' and 'coated' Vicryl[®] sutures.

highlighted using this method, however, the melting region was indicated for both the 'as received' and 'coated' material at 201.3 ± 2.4 and $202.4 \pm 4.1^{\circ}$ C, respectively, as confirmed by the endothermic peaks (endothermic in the downward direction). At temperatures above 268° C the onset of degradation of the polymer commenced. In terms of the Mersilk[®] suture, there was a continuous loss in weight up to 100° C, which was due to water loss and corresponded well to the broad peak obtained in the DSC analyses. Silk sericin possesses a moisture-retaining property and this loss in weight corresponds to the dehydration of water molecules from the semi-crystalline host [27]. The loss in weight at 220° C was due to the decomposition of the silk sericin (corresponding to the peak previously obtained with DMA [19]) whereas that in the region of $280-400^{\circ}$ C corresponds to the irreversible dissociation of the crystallites and the decomposition of amorphous silk fibroins [28].

The weight percentage of AgBG coating was estimated from the difference in percentage mass of the 'as received' and 'coated' sutures obtained at the end of each DTA run, where the polymer was assumed to be totally thermally degraded. The weight percentage of AgBG coating was found to be 1.26 and 1.75 for Vicryl[®] and Mersilk[®] sutures, respectively, suggesting more adhesion of the coatings in the silk-based sutures, thus confirming the SEM observations.

CONCLUSIONS

AgBG coatings on the surfaces of Vicryl[®] (polyglactin 910) and Mersilk[®] surgical sutures were achieved using a slurry dipping technique. The use of a number of complementary thermal analysis techniques enabled the thermal characterizations and therefore an understanding of the effect of the AgBG coating technique on the

		Region I			Region II			Region III		
Material	Rate I (%/°C)	T _{I–II} (°C)	Residue at T _{I-II} (%)	Rate II (%/°C)	T _{II–III} (°C)	Residue at T _{II-III} (%)	Rate III (%/°C)	T _{III–IV} (°C)	Residue at T _{III-IV} (%)	Residue at 550°C (%)
As received Mersilk [®] Coated Mersilk [®] Wt% AgBG	0.04 0.04	143 143	94.97 95.85	0.01 0.02	245 237	94.48 94.01	0.41 0.36	458 444	6.71 18.53	5.90 7.65 1.75

Table 4.	DTA/TGA	data for	'as received'	and	'coated'	Mersilk®	sutures.	

morphological properties of different suture materials. The slurry dipping technique had no significant effect on the thermal transitions of both types of suture materials. The use of high speed calorimetry through DSC offered better resolution for the transitions that appeared to be weak through conventional heating regimes and separated double transitions. By using the onset of transition for T_{g} generally there was a slight increase in temperature for the transition temperatures that appear for Vicryl[®] since the sample weight was not compensated. However, high speed calorimetry did not compromise either the melting temperature or the enthalpy of melting for these materials. Therefore this method allows for the accurate determination of thermal transitions through much shorter experimental times, thus allowing for an increased sample throughput. The combined DTA and TGA verified the high temperature degradations of the materials and gave estimates of the AgBG coatings indicating that a greater coating was obtained in the case of the Mersilk[®] sutures.

ACKNOWLEDGMENTS

The glass powder used was kindly supplied by Dr I. Thompson (Department of Materials, Imperial College). The financial support of the UK EPSRC is gratefully appreciated.

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