

Analysis of Bioactive Glasses Obtained by Sol-Gel Processing for Radioactive Implants

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This paper presents the chemical and physical characterizations of SiO₂ and SiO₂-CaO bioactive glasses incorporated with samarium atoms, produced by sol-gel synthesis. The objective is to provide biocompatible and biodegradable radioactive seeds as an alternative to be used in Brachytherapy for the treatment of prostate cancer. The glasses were produced and analyzed by X-ray fluorescence spectroscopy (XRF), energy dispersive X-ray spectroscopy (EDS), scanning electron microscopy (SEM), He picnometry and nitrogen adsorption analysis. A theoretical evaluation of the specific activity of the samples upon neutron activation is proposed. The XRF and EDS results demonstrate the incorporation of samarium atoms in the glass matrix. The experimental data coupled with the theoretical studies in neutron activation suggest that it is possible to obtain radioactive seeds with activities equivalent to ¹²⁵I seeds used in brachytherapy prostatic.

Keywords: *sol-gel, biodegradable glasses, biodegradable seeds, brachytherapy, radioactive seeds, samarium seeds*

1. Introduction

The first bioactive material described was the glass composed of SiO₂, CaO, Na₂O and P₂O₅ by Hench in 1971¹. Bioactive glasses have been successfully used in various clinical applications for over 10 years². Then main feature of bioactive glasses is a well-known controlled reaction in the physiological environment, leading to the formation of a continuous interface connecting the tissue with the implanted material. Among the production methods of bioactive materials stands out the sol-gel processing. The possibilities of processing materials with high purity, homogeneity and lower processing temperatures provide insights in the research area of ceramic and glass processing by sol-gel³⁻⁶. Glasses obtained by this method have been recommended for several applications such as bioactive materials; encapsulation of proteins, enzymes and biomolecules for controlled drug delivery; and, incorporation of nuclear waste. A new generation of ceramic materials with great structural properties has emerged with the sol-gel processing due to the possibility of manipulation and control of the nanostructures^{7,8}.

The present approach proposes the production of bioactive and biodegradable glasses incorporated with radioactive elements, seeking an alternative for the treatment of prostate cancer. The technique is denominated brachytherapy. Indeed brachytherapy on the prostatic gland applies radioactive metallic wires or seeds, containing radioisotopes such as ¹⁰³Pd, ¹³⁷Cs, ¹⁹²Ir, ¹²⁵I. These implants may be temporary (in which case they must be removed after treatment) or permanent⁹. Relevant tumor control has been obtained with ¹²⁵I seeds, that emits 27-keV γ -rays at a half-life of 59.4 days¹⁰. Considering the high cost of the treatment, the sophisticated technology involved in the metallic seeds production, and the fact that the seeds should stay or be removed from the prostatic gland after the therapy, the idea of a bioactive and biodegradable material in substitution for the metallic seeds is attractive. Bioactive seeds, manufactured by the sol-gel technique, with the isotope ¹⁵²Sm incorporated, may be activated by neutrons. The choice of this radioisotope is justified by its short half-life of 46.27 h, which will impart more energy on the gland in a shorter time compared to ¹²⁵I⁵. The reduced volume of the organ (~25 cm³) and the high number of seeds usually im-

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planted (~200) justify the introduction of biodegradable materials that can recompose the original structure of the organ after treatment.

The possibility of obtaining glasses with controlled composition and structures makes the sol-gel processing a potential technique for the encapsulation of radioactive materials for therapeutic applications. The higher porosity and surface area associated with the typical structure of the glasses produced by sol-gel, allied to the compositional variation, allows to obtain materials with different solubility and, therefore, different degradation rates and absorption *in vivo*. Previous work show the largest degradability of bioactive glasses produced by sol-gel compared to dense glasses obtained by conventional processing⁸.

The goal of the present work is the characterization of SiO₂ and SiO₂-CaO glasses incorporated with the element Sm, produced through sol-gel route. The viability of incorporation of this element, the amount of Sm incorporated in the seeds, and the physical and structural characteristics of the materials produced are evaluated. Also, an analysis of the activation potential of the seeds is presented.

2. Materials and Methods

Pure silica (SiO₂) or silica-calcia (SiO₂-CaO) glasses, with nominal compositions presented in Table 1, were prepared *via* sol-gel technique. The systems were chosen due to a possibility of selecting an adequate solubility and, therefore, potentially, acceptable degradation rates and absorption *in vivo*. Each synthesis was repeated three times. The samples were prepared from tetraethylorthosilicate (TEOS), deionized water, samarium oxide, nitric acid (2N) and calcium nitrate. All reagents were analytic grade. The samarium was introduced during the sol-gel synthesis as a solution prepared by solubilization of the oxide with nitric acid. After mixing, the sol was cast in polyethylene containers, and placed in an oven for gelation and aging at 60 °C. The samples were then dried with a schedule ending at 130 °C and thermally treated for 4 h at 700 °C.

After the processing stages, the samples were photographed and than grinded. To verify the samarium incorporation and the chemical composition, the samples were analyzed by X-ray fluorescence spectroscopy (XRF), en-

ergy dispersive X-ray spectroscopy (EDS), and neutron activation analysis (NAA). X-ray diffraction (XRD), N₂ adsorption and He pycnometry were used for determination of the phases present, characterization of the pore structure and density of the samples.

The activity of the seeds in units of $\frac{\text{mCi.cm}^2 \cdot \text{s}}{\text{mg.n}}$ was

evaluated theoretically versus the samarium concentration in the samples. For such, Eq. 1 provides the activity, A_m is after the neutronic activation (in Ci), as follows

$$A_m = 0,6025 \frac{ma}{A} (\phi_{ep} \sigma_{ep} + \phi_{th} \sigma_{th}) (1 - e^{-\lambda t}) e^{-\lambda \theta} \quad (1)$$

in which m is the mass of the activated material (g); a is the isotopic abundance ($\%$); A is the atomic mass (g); ϕ_{ep} and ϕ_{th} represent the thermal and epithermal neutron flux (n/cm^2s), respectively; σ_{ep} and σ_{th} represent the thermal and epithermal neutron cross-sections ($barns$), respectively, λ is the disintegration constant expressed in s^{-1} ; t is the exposition time (s) of the material to the neutrons flux and θ is the decaying time (s) to of the material after the activation process¹¹. The theoretical evaluation of the neutronic activation allows to estimate the ideal amount of Sm in the seeds, to obtain activities equivalent to values used in brachytherapy of prostatic cancer.

3. Results And Discussion

Figure 1 illustrates the aspect of the samples. Samples synthesized with and without samarium presented distinct colors. The appearance of the samples suggests the presence of samarium atoms when compared with the samples of pure SiO₂ and pure SiO₂-CaO. The presence of samarium atoms was detected in the samples by XRF analysis, confirming the incorporation and maintenance of these elements in the vitreous matrix, after thermal treatment at 700 °C.

Table 1 presents the semi-quantitative results of the chemical composition obtained by the EDS analysis. The measured samarium content differs from the nominal value in less than 10% in the samples S50 and S70. In the samples S100 however, the measured value differs from the nominal in 100%. It was possible to observe in the EDS analyses that there is a heterogeneous distribution of the chemical elements in the samples with higher content of calcium. In agreement with Pereira *et al.*³ this heterogeneity is due the use of the salt of calcium as precursor of the CaO in the sol-gel glass. Adjustments in the drying cycle of the material can be made to reduce the heterogeneity level.

Figure 2 shows the diffraction patterns for samples S50, S70 and S100. Low intensity peaks are observed indicating the presence of a small amount of a crystalline phase in the sample with larger calcium content. These peaks were ob-

Table 1. Nominal and measured (EDS) composition of the samples

	% Nominal			% Measured		
	Si	Ca	Sm	Si	Ca	Sm
S50	40.44	57.71	1.85	35.28	62.74	1.98
S70	60.35	36.91	2.74	51.40	45.59	3.02
S100	95.66	0.00	4.34	91.15	0.00	8.85

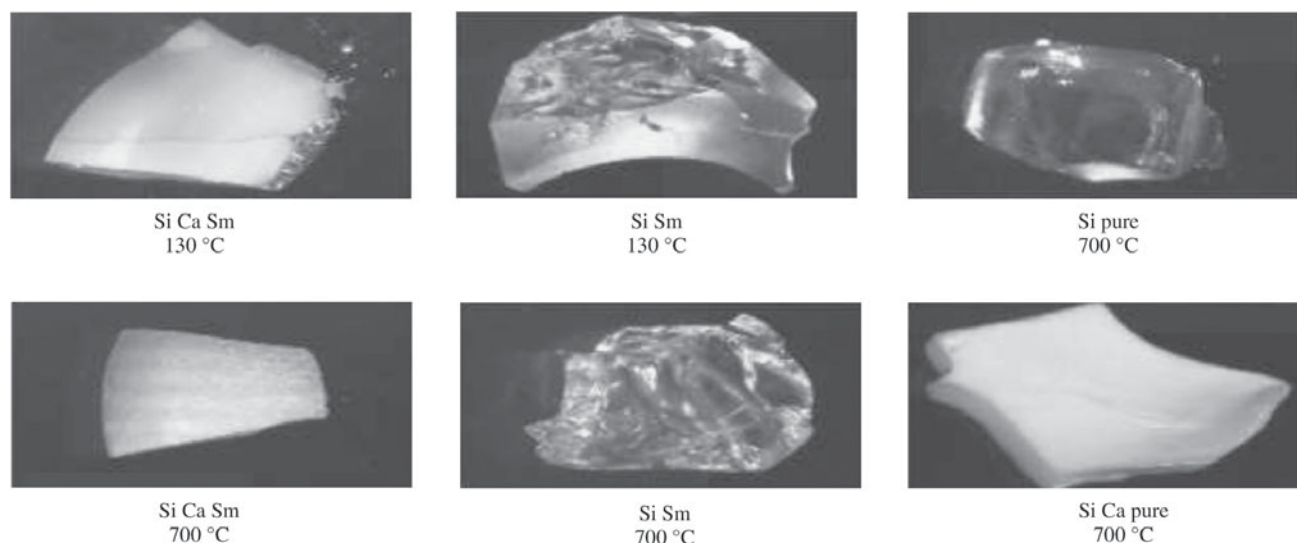


Figure 1. Glass samples containing Samarium obtained by the sol-gel process (size \approx 3 mm).

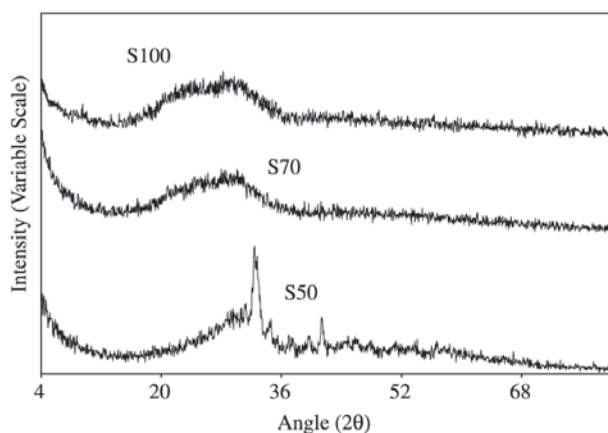


Figure 2. X-ray diffraction spectra of the samples S50, S70 and S100.

served in all the samples S50 and the analysis suggests that they represent the phase Ca_2SiO_4 . These peaks were also identified in samples with similar SiO_2 and CaO content of in the SiO_2 - CaO - P_2O_5 system, reported by Li *et al.*⁸. The diffraction pattern for the other compositions studied in this work S70 and S100 showed that there are not crystalline phases present.

Table 2 presents the N_2 adsorption and He picnometry results. Figure 3 exhibits the pore size distribution in the produced glasses. The total surface area of the samples was in the range of 50 to 531 m^2/g while the total pore volume in the range of 0.06 to 0.37 cm^3/g . The work of Saravanapavan *et al.*¹ and Li *et al.*⁸ indicates that the sur-

Table 2. N_2 adsorption and He picnometry results for sol-gel glasses obtained.

Sample	Surface Area (m^2/g)	Pore Volume (cm^3/g)	Average Pore Size (nm)	Density (g/cm^3)
S50	50.39	0.06	2.55	2.77
S70	92.49	0.37	7.85	2.61
S100	531.53	0.29	1.1	2.31

face area increases and the pore size decreases with the Si content, in samples in the SiO_2 - CaO - P_2O_5 system. Similarly, it is also observed a smaller surface area and a larger pore size in the produced samples with smaller Si content. However, this tendency is not proportional to the Si content. The sample with intermediate Si content presented a pronouncedly increase in the medium pore size. It can be observed in the Fig. 3 that the distribution of pore sizes was different for the several compositions. Samples S100 and S50 presented a decreasing pore size distribution, with medium pore size of 1.2 and 2.5 nm, respectively. The range of pore sizes is narrower in the sample S100. The sample S70, however, presented two different pore size ranges, one of smaller pores, below about 1.7 nm, and another of larger pores centered around 6.0 nm.

Figure 4 shows the possibility to generate radioactive seeds with activities similar to values used in ^{125}I brachytherapy, based on a theoretical evaluation. Natural samarium has ^{152}Sm and ^{144}Sm nuclides with large neutron

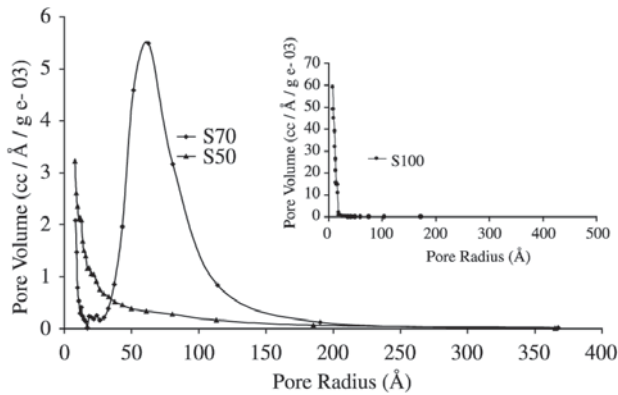


Figure 3. Pore size distribution for the samples S50, S70 and S100, obtained by N_2 adsorption

Table 3. ^{153}Sm content in the sol-gel glasses, determined by EDS and NAA.

Sample	EDS		NAA
	% natural Sm	% natural Sm	% ^{152}Sm
S70	3.02	4.08	1.09
S100	8.85	5.65	1.51

cross section, among others. Neutronic activation will lead the production of the radioisotopes ^{153}Sm and ^{145}Sm , with half-life of 46.27 h and 340 days respectively. ^{153}Sm is suggested here for the permanent implants. In this case, ^{145}Sm should be considered as a contaminant. Figure 4a and 4c exhibits the area namely as “ ^{125}I implants” whose activities values in the vertical axis are similar to those found ^{125}I seeds. The adopted neutrons flux was in the order of

$10^{12} \frac{n}{\text{cm}^2 \cdot \text{s}}$. Figures 4a and 4c show that the Sm concentrations in the samples must be between 4.5 and 11.5% for natural Sm, or between 1.5 and 4.5% for enriched one, to present activities similar to the ^{125}I seeds.

Sample compositions based on the NAA analysis are presented in Table 3. Matching sample composition data from Table 3 with the graphic in Fig. 4a, it is verified, for the samples produced in this work with natural samarium, that only the seeds S100 present appropriate Sm content with possible induced activity adequate for a temporary implant. However, if enriched Sm152 is used instead of Sm natural, all produced samples will be adequate for implants. In conclusion, with an appropriate preparation of the glasses with incorporated samarium, by the sol-gel processing route,

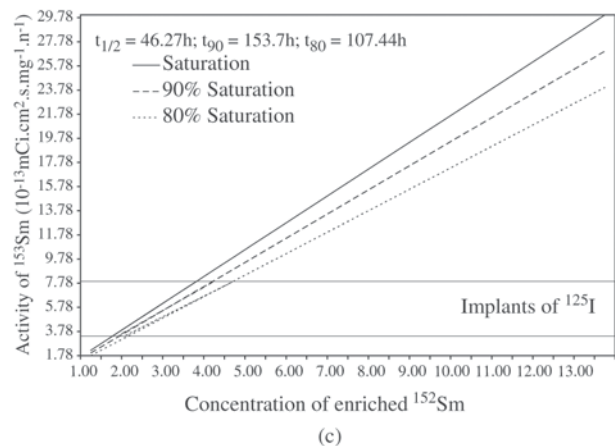
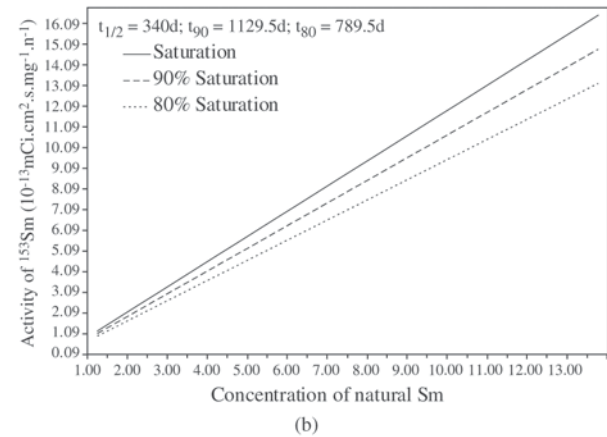
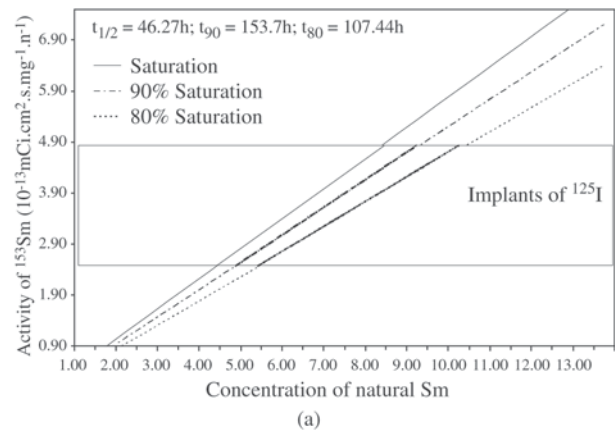


Figure 4. Theoretical activity as a function of natural and enriched Samarium concentration in the seeds. The terms t_{90} and t_{80} mean time at which 90 and 80% of the maximum activity were reached. The marked area indicates the ^{125}I seed activity used in brachytherapy.

it is possible to obtain seeds with activities similar to the ^{125}I currently used seeds.

4. Conclusions

The XRF and EDS analysis demonstrated the incorporation of samarium atoms in the SiO_2 and $\text{SiO}_2\text{-CaO}$ matrixes obtained by sol-gel processing. The XRD analysis indicated that the materials produced are non-crystalline, with the presence of a small amount of a crystalline phase in the samples with higher calcium content, identified as Ca_2SiO_4 . The glasses have high surface areas and pore size distribution dependent on the composition of the glass. The theoretical and experimental neutronic activation studies allowed the determination of the appropriate Samarium concentrations in the sol-gel glasses to produce seeds with activities equivalent to ^{125}I seeds used in current prostate cancer brachytherapy treatment.

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