

# **New formulation of functionalized bioactive glasses to be used as carriers for the development of pH-stimuli responsive biomaterials for bone diseases**

Valentina Aina<sup>\*,a</sup>, Claudio Magistris<sup>a</sup>, Giuseppina Cerrato<sup>a</sup>, Gianmario Martra<sup>a</sup>, Guido Viscardi<sup>a</sup>, Gigliola Lusvardi<sup>b</sup>, Gianluca Malavasi<sup>b</sup>, Ledi Menabue<sup>b</sup>

<sup>a</sup>Department of Chemistry, Centre of Excellence NIS (Nanostructured Interfaces and Surfaces); INSTM (Italian National Consortium for Materials Science and Technology), University of Torino, Via P. Giuria 7, 10125 Torino, Italy.

<sup>b</sup>Department of Chemical and Geological Science, University of Modena and Reggio Emilia, Via Campi 183, 41125 Modena, Italy.

**\* Corresponding author:**

Valentina Aina

[valentina.aina@unito.it](mailto:valentina.aina@unito.it)

## Supporting Information

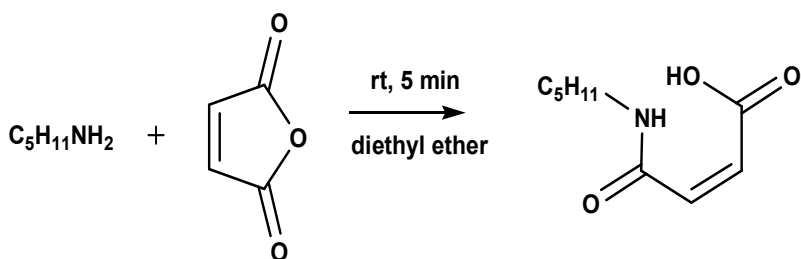
### Synthetic procedures and characterization

#### *Synthesis of maleic acid N-pentylmonoamide*

Pentylamine (0.10 g, 1.15 mmol) was slowly dropped in a solution of maleic anhydride (0.11 g, 1.15 mmol) in diethyl ether (2 mL); the reaction mixture was let under stirring at rt for 5 min, when TLC (EtOAc) showed disappearance of the maleic anhydride spot.

MS (ESI):  $m/z$  184  $[M-1]^-$

**Scheme 1 SM:** Reaction of pentylamine and maleic anhydride.



### **Additional text**

**Comment to Figure 1 SM.** In Figure 1 SM XRD pattern were reported for the studied materials. All sample showed a broad band centered at  $23.3^\circ$  in  $2\theta$ . In particular SG873 pattern present the broad band in the same position of APTS25SG423 and APTS50SG423 samples suggesting that the amorphous network of all samples is the same. In particular, calcium ions enter to take place in the network of the sample heated to 423K in the same way of the sample heated at 873K. If calcium ions were not entered in the silicate network, XRD spectrum should be similar to that of amorphous silica which has a band centered at  $22.2^\circ$  in  $2\theta$ . (Materials Research Bulletin Volume 45, Issue 9, September 2010, Pages 1330–1333 Immobilization of nanofibrous A- or B-site substituted LaMnO<sub>3</sub> perovskite-type oxides on macroscopic fiber with carbon nanofibers templates Qiang Wu, Masahiro Sadakane, Hitoshi Ogihara, Wataru Ueda).

**Comments to Figure 2 SM.** In Figure 2 SM FTIR spectra carried out on pure self-supported pellets after outgassing in-vacuo at 373K for 1 hour are reported. This treatment allows to remove the physisorbed species from the materials.

The peak centered at  $\sim 3744\text{ cm}^{-1}$  is typical of free OH stretching vibration typical of silanol groups; this band is clearly evident only in the case of SG873 sample, the high temperature of calcination allows to remove all the residues deriving from the synthesis.

The broad band in the  $3700\text{--}3400\text{ cm}^{-1}$  spectral range is due to the OH stretching vibration of OH groups involved in hydrogen bonds. Concerning the samples calcined at 423K (see spectra a, b, c and d) increasing the amount of APTS in the glass composition the intensity of this band decreases.

The band at  $3425\text{ cm}^{-1}$  is ascribable to N-H stretching vibration; this band is clearly evident in the case of post-synthesis functionalized sample and in the APTS25SG423 and APTS50SG423 samples.

The bands in the  $2900\text{--}2800\text{ cm}^{-1}$  region are typical of C-H stretching modes. These organic components derived from the APTS chains, TEOS and TEP organic residues and also from the solvent residues.

The three bands in the  $2000\text{--}1600\text{ cm}^{-1}$  spectral region are characteristic of Si-O-Si overtones; increasing the amount of APTS and decreasing the amount of TEOS (see

spectra c and d) these bands gradually disappeared. In fact with the addition of APTS molecules the  $1480\text{ cm}^{-1}$  is ascribable to CO stretching vibrations typical of carbonates species adsorbed onto the glasses surface. This band is clearly evident in the samples calcined at 423K with no APTS or low APTS content; increasing the amount of APTS the SSA of the samples decreases and at the same time the amount of surface carbonates decreased.

**Comments to Figure 3 SM.** Figure 3 SM reports FTIR spectra carried out on the bioactive glasses after the previously mentioned soaking times in SBF. KBr pellets of samples before and after SBF contact were prepared by mixing under controlled conditions (glovebox) 1 mg of either starting powder or filtered reacted powder with 50 mg of specpure KBr. Spectra are reported in the spectral range between  $1800\text{-}400\text{ cm}^{-1}$  spectral range.

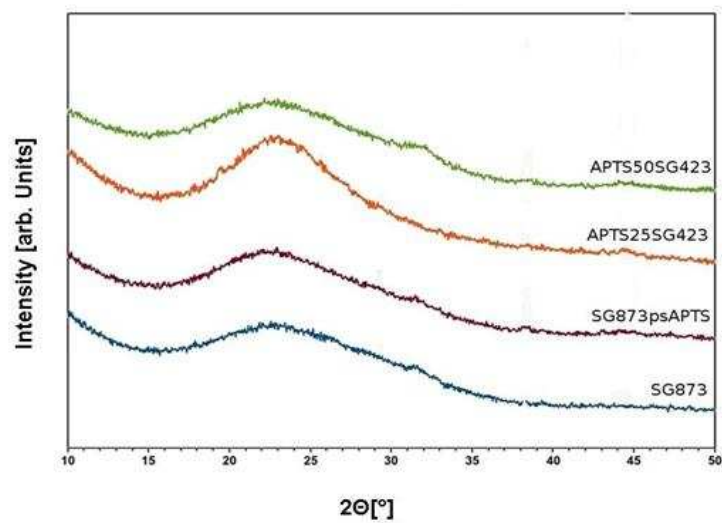
Starting from the spectra of the SG873 glass (Section A of Figure 3 SM) it can be noted that, after 1 day of reaction (spectrum A'), there is the appearance of two well resolved peaks at  $\sim 610$  and  $\sim 560\text{ cm}^{-1}$ , these are typical of crystalline HA/HCA formation. Calcium phosphate on the glass surface are amorphous before the reaction (see the broad band at  $\sim 600\text{ cm}^{-1}$  on the un-reacted sample) and already after 1 day of SBF soaking they become crystalline. One additional aspect of the gradual formation of a crystalline phosphate phase is the gradual resolution of a sharp peak at  $\sim 1040\text{ cm}^{-1}$ , this feature is evident after 15 days of reaction in SBF. This latter peak is due to both Si-O-Si and P-O-P stretching vibrations. In parallel on the low- $\nu$  side of the peak at  $\sim 1070\text{ cm}^{-1}$ ; the shoulder at  $\sim 940\text{ cm}^{-1}$  due to the so-called non-bridging oxygen species (NBO) disappeared after 7 days of reactions. The declining intensity of this latter spectral component as a function of reaction time is an indication of the release of cations ( $\text{Ca}^{2+}$  ions) from the glass to the SBF solution.

**Comment to Figure 4 SM.** For what concern SG423 glass (Section A of Figure 4 SM), the scenario is quite different. Only after 7 days of reaction there is the formation of crystalline HA/HCA; In the case of APTS25SG423 sample (Section C of Figure 4 SM) on the un-reacted sample a broad band at  $\sim 1350\text{ cm}^{-1}$  appears, this is due to the presence of amorphous carbonate species; increasing the reaction times this band becomes sharper

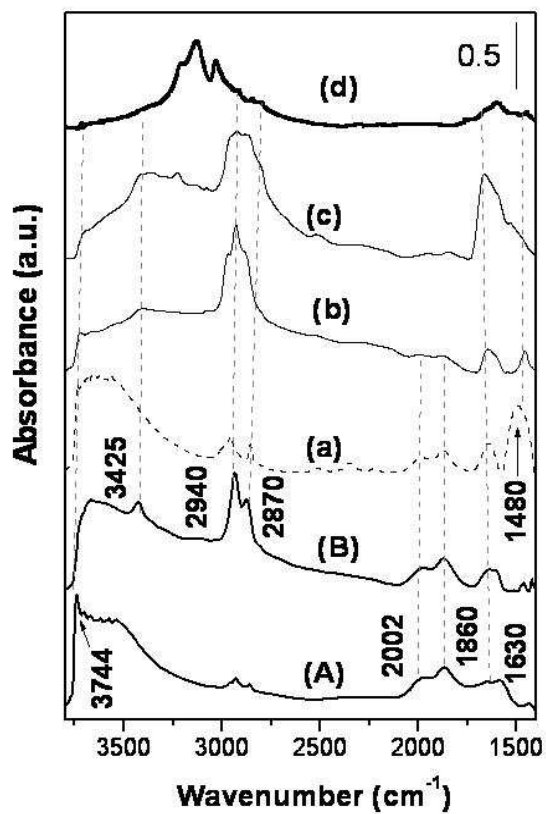
indicating the formation of crystalline carbonate (see bands at  $\sim 1430$  and  $\sim 1380$  of the sample reacted 15 days, spectrum b'''). These bands are characteristic of calcite.<sup>21</sup> The presence of APTS in the glass structure increased the amount of carbonate-like species. Only after 15 days of reaction it is possible to single out the two peaks at  $\sim 611$  and  $\sim 560$   $\text{cm}^{-1}$  typical of HA/HCA crystallization. The crystalline forms of crystalline Ca-phosphate (resolved doublet at  $\sim 610$  and  $\sim 560$   $\text{cm}^{-1}$ , resolved sharp peak at  $\sim 1038$   $\text{cm}^{-1}$ ) is evident only after 15 days of reaction. The behaviour of the APTS50SG423 sample (Section C of Figure 4 SM) is similar to what described in the case of APTS25SG423 one.

## Figures SM

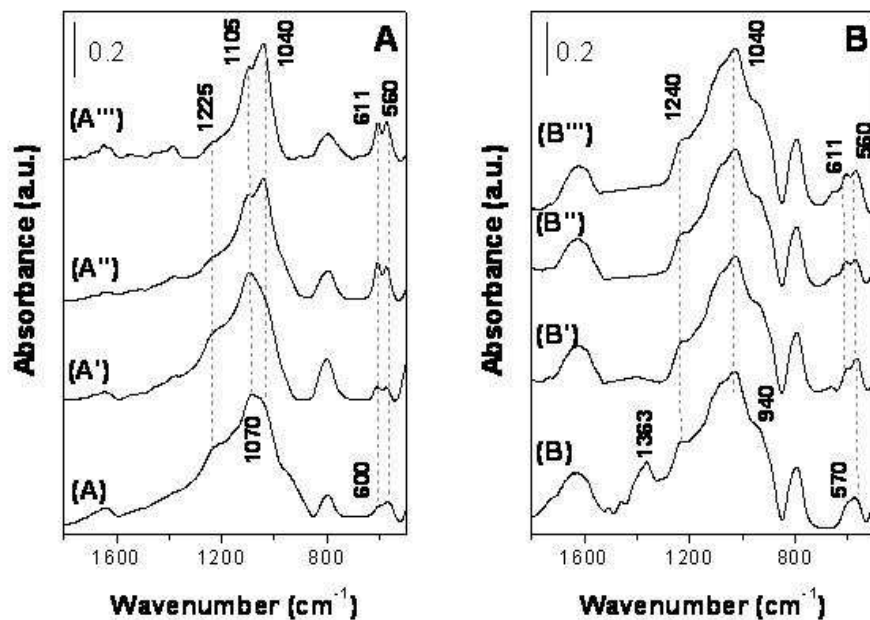
**Figure 1 SM.** XRD patterns of as synthesized samples.



**Figure 2 SM.** FTIR spectra on as-synthesized samples: (A) SG873, (B) SG873psAPTS; (a) SG423, (b) APTS25SG423, (c) APTS50SG423 and (d) APTS100SG423. FTIR spectra, reported in the 3850-1400  $\text{cm}^{-1}$  spectral range, are collected on self-supported pellets outgassed in vacuo at 373K for 1h.



**Figure 3 SM.** FTIR spectra in the 1800-400 spectral range carried out on the samples as-synthesized and after different times (1,7 and 15 days) of SBF soaking. Section A SG873; Section B SG873psAPTS (A), and (B) samples as-such; (A') and (B') samples after 1 day of reaction; (A'') and (B'') samples after 7 days of reaction; (A'''), and (B''') samples after 15 days of reaction in simulated body fluids.





**Figure 4 SM.** FTIR spectra, in the 1800-400 spectral range, carried out on the samples as-synthesized and after different times (1, 7 and 15 days) of SBF soaking. Section A BG423; Section B APTS25BG423 and Section C APTS25BG423. (a), (b) and (c) samples as-such; (a'), (b') and (c') samples after 1 day of reaction; (a''), (b'') and (c'') samples after 7 days of reaction; (a'''), (b''') and (c''') samples after 15 days of reaction in simulated body fluids.

