DIPLÔME NATIONAL DE DOCTORAT

(Arrêté du 25 mai 2016)

Date de la soutenance : **04 octobre 2018**

Nom de famille et prénom de l'auteur : **FARANO Vincenzo**

Titre de la thèse : « *Une étude des différentes voies de traitement du verre de phosphaté et du rôle du verre de phosphate dans les échafaudages à base de collagène dentaire* »

Résumé

This thesis concerns the development of a new series of Sr-doped phosphate-based glasses for biomedical applications. Such glasses in powder form are envisaged to have applications in novel composite restorations where the following is achievable: dentin cell-mediated bioremineralization, dental pulp regeneration and as carrier for therapeutics or antibacterial ions.

The initial aim was to produce soluble porous phosphate glasses using the sol-gel method (phosphate-alkoxide based sol-gel process). Knowing the effect that the variation of Ca content has on the dissolution properties of the glass, a series of glasses where Ca was progressively increased at the expense of Na was produced. The structure of the prepared samples was probed by XRD, XRF and FTIR to confirm the successful synthesis of the target phosphate-based glass compositions. After that a promising methodology was established, attempts were made to replace Ca with Sr. Different Sr sources were used without success due to the difficulty to fully dissolve those precursors in the sol-gel mixture.

Subsequently, the issue of the toxicity of some precursors and solvents used in the sol-gel procedure was recognised. To overcome this obstacle, efforts were made to replace the toxic precursor chemicals with safer ones. Nevertheless, due to the low solubility of some new precursors and the low reactivity of others, the sol-gel process did not proceed in a predictable and reproducible fashion.

At this stage, the sol-gel route was put aside, and two alternative soft and water-based chemical approaches were experimented: the precipitation method and the coacervation process. The first one was found to be unsuitable for our needs for two main reasons: 1) the presence of Na in the composition generated a crystalline material (instead of a glassy amorphous one); 2) the Ca/P ratio of our composition fell in the range of crystalline phase by using this method. In addition, the yield was really low. The second method (coacervation process) was a complete success. The glassy nature of the materials obtained was proved by XRD and XRF and the surface features were tested by BET and SEM. The process was retained for a while as the preferred synthesis route and both the scale-up effect and the possibility to

add Sr were analysed. The production scale of the material was increased by 5 times and different Sr sources were tested to find the best one. XRD and XRF analysis proved both the success of the scale-up and the incorporation of the Sr in glass composition.

However, despite the promising results, due to both issues on the reliability of reaching the composition and lack of porosity / surface area meaning, in the end, the melt-quench technique was chosen as a definitive and reliable method to produce the above mentioned compositional series. Quaternary phosphate-based melt-quenched derived glasses in the P_2O_5–CaO–Na_2O–SrO system were synthesised in a way that by increasing Sr, Ca decreases. The glasses obtained have the general formula of (P_2O_5)53–(CaO)(32-x)–(Na_2O)15–(SrO)x, where x = 0, 5, 10 or 15 (mol%). Substituting Sr in place of Ca improves the stability and prolongs the degradation of these glasses.

To try to mimic the real architecture of deep dentine tissue and provide for a 3D support for cells, these glasses were mixed as powders with collagen fibres to make scaffolds. The presence of the collagen as an organic polymer guarantees the three-dimensionality of the structure and provides for an excellent and natural binding sites for cells to easily adhere and proliferate. The glass particles, on the other hand, ensure improved mechanical properties and release over time of important ions such as Ca, P and Sr to trigger and sustain cell differentiation.

In the end, to test the cytocompatibility of such prepared materials, hGFs were seeded in direct contact with the scaffolds and the viability checked at day 2, 4 and 7. As control, cells were seeded in an empty well. Although the control cells showed a high metabolic activity indicating the good health of the cells used, those in contact with the tested scaffolds displayed a significant low viability due to the acidification of the cell medium following glass particles dissolution.