

# Abstract

---

The activities performed during the present PhD thesis were focused on the production, synthesis process optimisation and characterisation of calcium silicate mesoporous bioactive glasses (MBGs) that could be used for designing advanced biomedical devices to promote tissue regeneration when the normal healing process is hindered (*i.e.* in the case of a delayed bone healing and non-healing skin wounds).

In particular, the efforts were devoted to enrich the binary composition of these MBGs with different therapeutic ions in order to impart and enhance specific biological functions. The possibility to include these therapeutic species in the MBGs and to tailor their release allows to consider these materials as valid and potent alternatives to the traditional treatment in bone and wound healing applications.

In this context, a library of ion-containing nanomatrices was developed by substituting small amount (1%, 2% or 5% mol) of CaO with the specific ion precursor.

In detail, the following two types of nanomatrices were developed:

- Nano-sized particles (100-200 nm) with pore size of about 4 nm;
- Micro-sized particles (0.5-5  $\mu\text{m}$ ) with pore size of about 8 nm.

Both types of nanomatrices were characterized by ordered mesoporous structure with high specific surface area and pore volume, especially for the nano-sized particles, demonstrating that the successful ion incorporation occurred without hampering the formation of the mesostructure. Moreover, the bioactivity test performed on the nanomatrices demonstrated their good reactivity when soaked in Simulated Body Fluid (SBF), confirming that the incorporation of different metallic ions did not affect their ion exchange ability. The ion release test proved that all the nanomatrices were able to release the therapeutic ion with specific kinetics depending on the amount of the incorporated ion, the structural features of the nanomatrices and the release medium.

The second aim was to find the best synthesis procedures in terms of material properties, scalability, safety and cost-efficiency.

In order to achieve this goal, different synthesis procedures were tested. In particular, following the objective of avoiding the use of toxic solvents and enhancing the synthesis yield, a water-based sol-gel procedure using ammonia as

catalyst without sonication was selected as the best route to produce the nano-sized particles.

By following the same aim, the second type of nanomatrices (micro-sized particles) was produced by an aerosol-assisted spray-drying approach under mild acidic conditions due to its scalability and repeatability in an industrial environment.

To reach the final target of developing multifunctional platform able to promote tissue regeneration in the presence of bacterial infection, the MBGs in the SiO<sub>2</sub>-CaO system were enriched by the following selected therapeutic ions:

- Copper for its antibacterial, pro-osteogenic and pro-angiogenic effect
- Cerium for the pro-osteogenic and antibacterial potential
- Silver for its well-known antibacterial effect

In this frame, the third aim was to investigate the therapeutic potential of these nanomatrices, in particular their antibacterial effect which was tested through the viable count test using both *Gram positive* (*S. Aureus*) and *Gram negative* (*P. aeruginosa*).

In details, the different sensitivity to Cu-containing samples shown by the bacteria strains was attributed to the differences in the bacteria structure and surfaces. For what concerns the Ce-containing nanomatrices, although the antibacterial test demonstrated a reduction of both *Gram positive* and *Gram negative* bacteria strains, it was not possible to find a clear correlation between the results, the experimental conditions and the bacteria structure. Finally, the antibacterial results of the Ag-containing particles were ascribed to the presence of accessible metal Ag compounds which, through the direct contact and the formation of interactions between silver and the sulfhydryl groups of the bacterial wall, led to the reduction of bacterial viable species by blocking their respiration.

The biological assessment performed on the optimized ion-containing nanomatrices leads to consider the Cu-containing MBGs as the most promising systems due to the possibility to find a proper therapeutic window within which they resulted both biocompatible and antibacterial. Among the Cu-containing MBGs, the MBG\_SG\_Cu0.5% and MBG\_SD\_Cu0.5%, providing the best results in terms of biocompatibility, deserve to be taken into account for further investigations, especially in terms of multifunctional systems able to release both therapeutic ion and specific drugs.