PhD Course in Models and Methods for Materials and Environmental Sciences – Cycle XXXIX

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Development of advanced biomedical devices for hard and soft tissue applications

A biomaterial is a material intended to interface with biological system to evaluate, treat, augment or replace any tissue, organ or function of the body. Biomaterials are divided according to their nature into different classes: biological, metallic, polymeric, composite and ceramic. Bioactive glasses (BGs), which will be used in this project, are ceramic biomaterials. A lot of studies demonstrate the ability of silicate-based BGs to form a hydroxyapatite-like (HA) layer on their surface when in contact with a simulated body fluid (SBF); an apatite layer is responsible of the bond with bone.

In recent years, interest in phosphate-based glasses (PGs) has increased, also PGs promote bone regeneration, because their composition is very similar to the composition of bone and teeth. Like silicate-based BGs, PGs can be used for hard and soft tissue regeneration. In *Figure 1* it is possible to see the formation of apatite-like layer on the surface of silicate (A) and phosphate (B) based glasses.

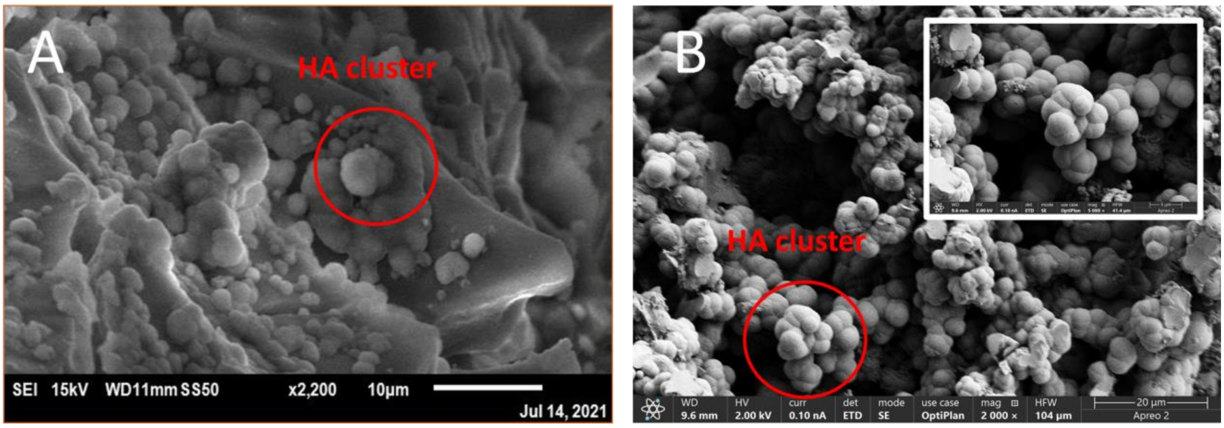

Figure 1. Apatite-like layer on the surface of silicate-based BGs (A) and on the surface of PGs (B).

PGs are a completely bioresorbable material, they dissolve over time and are completely replaced by the regenerated tissue. Silicate-based BGs have a very slow solubility, which makes them suitable only for long-term implants. The tetrahedral structure of phosphates and silicates-based glasses look like quite similar, but their chemical behaviour is very different. This is mainly due to the double bond of oxygen with phosphorous, which allows it to have three bridging oxygens as opposed four in the case of silicon. The hydrolysis reaction of phosphates is similar to that of silicates; however, phosphorus is more electronegative than silicon, and this reveals a greater positive charge for silicon and a much slower rate of hydrolysis.

During my PhD, I will work on silicate and phosphate-based glasses in order to improve their properties. In this respect, the proposed project involves the use of materials (biomolecules with therapeutic properties) which refer to waste of diverse origins, e.g., polyphenols extracted from plant waste, and which can be reintegrated for applications in the regenerative medicine field.

Applications of BGs in hard tissues are based on their ability to bind to the host bone, promoting bone regeneration (bioactivity); for soft tissues, appropriate textural properties and degradation rates are required to match the recovery rates of the host tissues. A frequent complication after BGs insertion is postoperative inflammation, which involves harmful reactive oxygen species (ROS) and can significantly delay recovery. To overcome these problems, the BGs must act as an antioxidant, converting ROS into non-damaging species; this can be achieved by doping with therapeutic inorganic ions (TIIs) and/or loading with organic molecules (drugs and biomolecules).

The addition of TIIs to the composition of the BGs can improve the osteogenesis (e.g., Fe, Mg, Zn, Ce), angiogenesis (e.g., Co, Cu), antibacterial activity (e.g., Zn, Ce, Ag) and cementogenesis (e.g., Li, Sr) of the BG. Among the biomolecules studied, some are of natural origin (especially polyphenols) and represent an important opportunity for biomedical research. The polyphenols have functional properties of interest for health, such as antioxidant, antibacterial and anti-tumour effects, but due to their reduced bioavailability and stability in the physiological environment there are limitations in therapeutic applications. BGs could also be functionalised with antibiotic or anti-inflammatory molecules like gentamicin, amoxicillin, paracetamol and ibuprofen.

Therefore, the synthesis and physicochemical characterisation of a series of hybrid materials derived from silicate and phosphate-based glasses containing drugs and naturally occurring biomolecules will be performed. The new materials will thus combine their characteristic bioactivity and biocompatibility with modulable antioxidant properties and also function as drug delivery systems (DDS).

This study will therefore provide know-how for the development of advanced biomedical devices and ideally provide prototypes for both hard and soft tissue applications.