Injectable composite made of nano tubular clays and polysaccharide matrix

The research in the bone medication field is constantly aiming at developing effective strategies and new materials to treat bone defects. Minimally invasive surgery, for instance, represents a valuable option since it ensures several benefits, such as lower total cost of care, shorter recovery times, lower pain and lower medical risks. In this perspective, the *in-situ* injection of biomaterials able to combine adequate mechanical properties with bioactivity can be of particular relevance.

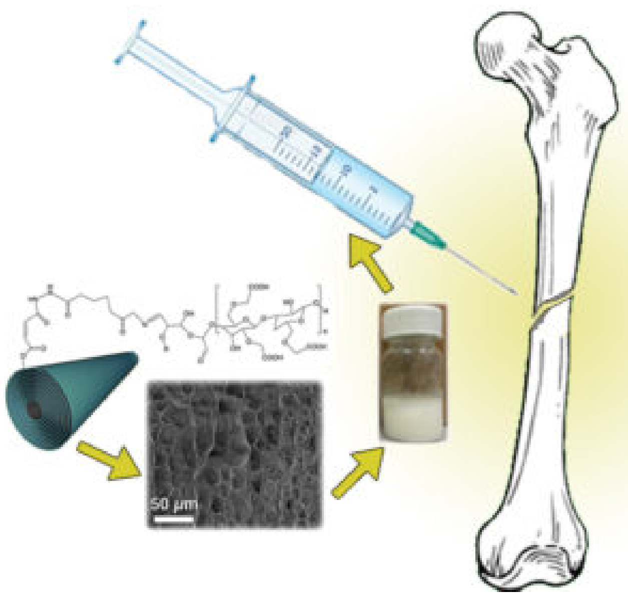

Fig. 1.

Halloysites (*i.e.*, naturally occurring clay nanotubes) are widely recognized as promising platforms for multiple purposes in tissue engineering and biomedicine, thanks to their biocompatibility, structure and physico-chemical properties.

We integrated Halloysite nanotubes within a cellulose matrix, in order to prepare an injectable composite for the local treatment of bone defects. Structural and rheological properties of the obtained hybrid are driven by chemical design. The nanotubular shape of Halloysite provides a strong thickening power, while their hollow structure avoids a large increase in the density of the composite. On the other hand, the use of a shear-thinning polymer matrix is especially appealing to minimal invasive surgery: in fact, the viscosity of the material decreases during the injection (*i.e.*, shear stress), while it recovers its initial rheological state at the injection site when the stress is relieved. As a result, the material is able to conform and effectively adhere to the treatment site.

A practical evaluation of the material's injectability is crucial to a reliable application. To this aim, we injected our composite through needles with inner diameters spanning from 510 to 180 µm, commonly employed for intramuscular and subcutaneous injections, observing no clogging and homogenous flow also at very low applied loads (*i.e.,* less than 1 Kg). In spite of the presence of inorganic nanostructures that could in principle aggregate and obstruct the orifice, the injectability is mostly dictated by the polymer matrix, with Halloysite nanotubes tending to align with the direction of the flow causing a strong change in the structure of the polymer matrix. This is especially interesting in view of the application in minimal invasive surgery: in fact, once injected, the structuring of the material takes to an increase of its viscosity, eventually reducing its spreading from the injection site. Together with the very small size of the needles and the low flow achievable, this could result in the possibility to robotically apply our composite at the damaged site with a high spatial resolution.

We believe that these results could represent a significant contribution to extend the use of composite hydrogels in the bone medication field. However, further studies are needed to validate the *in-vivo* application of our material and they must concern with the evaluation of its biodegradation, its toxicological effects, and its influence on the bio-mineralization process.

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