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Cu-BASED CLAY MINERALS AS ENHANCING AGENTS OF MICROBIAL CONTROL IN CHRONIC WOUND HEALING

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Riassunto

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Chronic wounds are characterized by an impaired healing process and by high risk of microbial infections [1]. The employment of antimicrobial drugs in the treatment is controversial due to the possible rising of resistance. Hence, the use of antimicrobial nanotherapeutics is gaining interest [2].
Therefore, the aim of this study was the design and the development of chitosan-based microparticles to be used as a powder to enhance wound healing in chronic skin lesions. Two Cu-based clay minerals of natural and synthetic origin, montmorillonite and layered double hydroxide (LDH), respectively, were included in the systems to provide antibacterial properties.

The Cu-based MMT was prepared by means of an intercalation solution procedure, while the Cu-based LDH was obtained through the coprecipitation method. Chitosan carbamate was prepared by adding NH_4HCO_3 to a chitosan acetate salt solution [3,4]. Then, Cu-MMT or Cu-LDH were added to the chitosan carbamate aqueous blends. The microparticles were obtained using spray drying and subsequently characterized.

The formation of the MMT and LDH was evaluated by means of XRD analysis. The Cu loading in both clays was found to be around 25% w/w. To obtain a chitosan derivative which could be water soluble in a non-acidic environment and preserve the structure of the clay minerals, chitosan carbamate was correctly synthesized, as confirmed by NMR analysis. Then, starting from an aqueous solution of chitosan carbamate doped with copper-loaded clay minerals, water insoluble spray-dried chitosan microparticles were successfully obtained due to the removal of the carbamate moiety. The microparticles were characterized by smooth and spherical morphology, which was not altered by the clays doping. The presence of the Cu-based clays increased the antimicrobial properties on *E. Coli* and *S. Aureus*. Preliminary *in vitro* tests confirmed the enhanced cell proliferation and wound healing activity of normal human dermal fibroblasts. Moreover, the safety and efficacy of the systems was tested on a murine model *in vivo*.

To conclude, it was possible to manufacture water insoluble microparticles based on chitosan and doped with clay minerals containing Cu. The process allows to avoid the use of harmful crosslinkers In addition, the enhanced cell proliferation and the antibacterial properties suggest the promising use of these scaffolds for the treatment of chronic wounds and prevention of microbial growth.

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