CALCIUM PHOSPHATE NANOSYSTEMS AS VEHICLES FOR CONTROLLED DRUG DELIVERY

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Systemic drug administration to bone tissue has several drawbacks as low drug absorption, which leads to supplying high concentrations that damage other tissues. Calcium phosphate (CaP)-based nanosystems can be used for drug transport and delivery to calcium-containing surfaces, as bone mineral matrix, due to its high affinity for hydroxyapatite. With this basis we developed nanospheres based on liposomes of 1,2-Dioleoyl-sn-glycero-3-phosphate (DOPA), coated with a CaP amorphous layer (CaPLi) which provides them with stability, stiffness and affinity in the biological media. The antibiotic Levofloxacin (Lx) was used as a model drug for encapsulation (CaPLiLx), tracking and release studies, which allowed monitoring by fluorescence spectroscopic methods.

The CaPLi were characterized by TEM, SEM, AFM and HR-STEM microscopies, among other techniques.

The CaPLiLx charge release was studied in the PBS and acetate buffers and in simulated body fluid (SBF), following the concentration of Lx by fluorescence. A faster release was evidenced in SBF, where Ca^{2+} and Mg^{2+} ions are present, and we proposed that the divalent cations can complex the surface of the CaP nanolayer, stimulating the release of the drug. The interaction with surfaces (Ca^{2+}modified mica surface, hydroxyapatite nanoparticle (Ap) films on glass, and Ap modified 45S5® bioactive glassbased scaffolds) was evaluated, showing the preferential accumulation of the CaPLi on the calciumenriched ones, the disruption of the inorganic structure and release of molecules contained in the nanospheres.

Furthermore, biological studies were performed. Bacterial susceptibility and time killing assays with Staphylococcus aureus suspensions demonstrated the bactericidal potential of the nanoshells containing Lx (1.0 µg/ml, corresponding to 2x MIC). Moreover, cell viability was analyzed in MC3T3 cell cultures exposed to nanospheres, concluding that they are not cytotoxic under the performed conditions (CaP 200 µgCa/ml and CaPLiLx 100µM Lx dilutions up 20% in cell culture). Finally, zebrafish model will be used to assess the in vivo biocompatibility and localization aiming to develop stable and functional vehicles that contribute to the optimization of the treatment of bone diseases.