Hydrophilic Sponges loaded with Curcumin solid lipid nanoparticles and Metronidazole applied on L-PRF clot to promote tissue regeneration in dentistry.

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Leukocyte-and platelet-rich fibrin (L-PRF) technology allows for the preparation of strong fibrin membranes enriched with cells (activated platelets, leukocytes, circulating cells) and platelet growth factors [1]. In dentistry, the use of this autologous platelet concentrates such as L-PRF, also in association with Metronidazole (MTR), seems an innovative approach for vestibular bone grafting on the alveolar ridges [2]. In addition, Curcumin (CUR), a natural polyphenol derived from the rhizome of the Curcuma longa, could be effectiveness on tissue regeneration due to its well-known antioxidant and anti-inflammatory properties [3].
The aim of the present work was the development of bioerodible sponges loaded with CUR-solid lipid nanoparticles (NLC) and MTR, assessing *in vitro* and *ex vivo* performance together with L-PRF, for future *in vivo* applications for tissues regeneration in oral surgeries.
Curcumin (CUR) loaded solid lipid nanoparticles (NLC) were prepared using Glycyrrhetic acid, hexadecanol, isopropyl palmitate and Tween 80 as surfactant. As method, the homogenization followed by high-frequency sonication was used. After dialysis, NLC dispersion was evaluated in term of drug loading (DL, 2.2 % w/w) and drug recovery (DR, 88% w/w). NLC, characterized by Dynamic Light Scattering, exhibited an average particle size of 121.6 nm and PDI value of 0.235, considered optimal for a colloidal nanoparticle dispersion. The PZ value of -37 mV also indicated a good stability of the system. Subsequently, a hydrophilic sponge was obtained by lyophilization of a gel based on Trehalose, Natrosol, PVP, CUR-NLC dispersion and MTR (10% w/w of solid components). The ability of sponge to release CUR and MTR when applied on L-PRF clot, obtained according to the FDA and CE approved protocol (Intra-spin®, Intra-lock, Salerno, Italy) and the aptitude of actives to penetrate and/or permeate the membrane were evaluated. L-PRF clot was mounted as membrane in Franz type diffusion cells and to the apical side the sponges were applied. At the end of experiments, the residual drugs entrapped into the L-PRF membrane were quantified by extraction. The results showed that after 3 h CUR is not able to cross the L-PRF clot, whereas a significant percentage of dose (11.4%) remains trapped inside it. MTR cross L-PRF membrane and reaches the acceptor compartment gradually. After 3 h, the 16.8% of dose reaches plasma whereas 6.5% was entrapped in membrane.
In conclusion, both the CUR-NLC and the hydrophilic sponge containing MTR and CUR-NLC have been successfully prepared. When applied on L-PRF membrane, the sponges release the actives promoting CUR penetration and MTR permeation. The obtained results encourage further studies about the possibility to use these sponges to delivery antioxidant and antimicrobial agents to support bone regeneration on surgical sites of teeth extraction treated with L-PRF.

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