Student Speech Contest 2024

Strontium-doped apatitic bone cement for the treatment of bone infections

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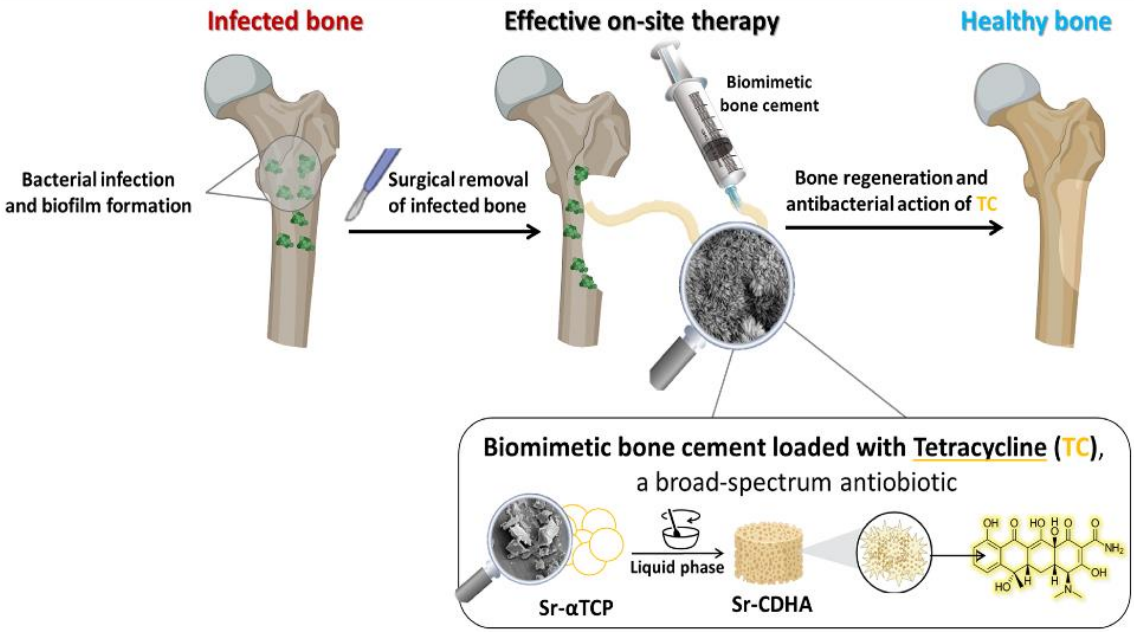

Abstract

Current therapies for the treatment of bone infections can involve the surgical removal of the affected bone and systemic administration of high doses of drugs, to achieve an effective concentration at the bone target site. The development of devices that can combine bone regeneration with effective drug delivery ability without reaching toxic levels in the blood is an area of active research. Injectable apatitic bone cements (CPCs)

are promising biomaterials for hard tissue regeneration as they are biocompatible, bioabsorbable, osteoconductive, and osteoinductive. Moreover, because of their ability to self-harden under physiological conditions, they can find wide applicability in clinic, especially in minimally invasive surgery. The possibility of obtaining bioactive ceramics through low temperature self-hardening processes allows the incorporation of biomolecules, paving the way for the development of multifunctional medicated scaffolds, with enhanced therapeutic ability, suitable to be moulded and adapted to complex shape bone defects. Specifically, strontium-doped CPCs have been the subject of recent studies due to the inherent anti-osteoporotic properties of strontium. Hence, CPCs represent promising candidates for the regeneration of complex-shape bone defects, thanks to self-hardening ability, bioactive composition and nanostructure offering high specific surface area for cell attachment and conduction. In this regard, direct-ink-writing (DIW) is a three-dimensional (3D) printing technique that can be used to extrude self-hardening pastes with appropriate visco-elastic properties and produce complex-shaped devices. In this work, a SrCPC previously reported as osteointegrative and capable to modulate the fate of bone cells was enriched with hydroxyapatite nanoparticles (HA) functionalized with tetracycline (TC) to provide antibacterial activity. We found that HA functionalized with TC (TC/HA) can act as modulator of the drug release profile when embedded in SrCPCs, thus providing a sustained and tenable TC release. In vitro microbiological tests on Escherichia coli and Staphylococcus aureus strains proved effective bacteriostatic and bactericidal properties, especially for the TC/HA loaded SrCPC formulations. Overall, these results indicate that the addition of TC/HA on CPC acted as effective modulator towards a tenable drug release control in the treatment of bone infections. Moreover, a preliminary study was carried out on the optimization of the ink composition, based on Sr-αTCP, and 3D-printing parameters. Particularly, Sr-doped αTCP and Mg-doped hydroxyapatite nanoparticles (MgHA) or tetracycline-loaded MgHA (TC/MgHA) were used as solid component of the inks, whereas a sodium alginate solution enriched with carboxymethylcellulosa or pluronic® as the liquid component.