A Multifunctional Levan Hydrogel Platform with CBD and IGF-1 Liposomes for Bone Regeneration

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INTRODUCTION: Oral bone regeneration after trauma or surgery due to periodontitis or oral cancer remains challenging because autologous grafts are limited by morbidity and availability. Levan-based hydrogels provide a biodegradable scaffold for localized delivery of bioactive compounds, while insulin-like growth factor 1 (IGF-1) and cannabidiol (CBD) offer complementary osteogenic and anti-inflammatory effects but require encapsulation for stability and efficacy. We therefore developed a levan-based hydrogel containing liposomes co-loaded with IGF-1 and CBD and evaluated it`s *in vitro* potential for oral bone regeneration.

METHODS: Liposomes composed of DSPC with or without DSPE-PEG were prepared by thin-film hydration and loaded with CBD and/or IGF-1 during the hydration step. Liposome size, surface charge, and morphology were characterized using dynamic light scattering (Anton Paar Litesizer 500) and scanning transmission electron microscopy (Verios 5 UC). Enzymatically produced and hydrolyzed levan was crosslinked with BDDE to form hydrogels, into which the prepared liposomes were incorporated. In vitro studies were performed using patient-derived gingival mesenchymal stem cells (GMSCs; ethical approval No. 6-1/12/47). Cell viability and osteogenic differentiation were evaluated.

RESULTS: The hydrodynamic diameter of liposomes decreased upon incorporation of bioactive compounds (Fig. 1; from 1167 ± 83 nm to 307 ± 21 nm). The release of CBD and IGF-1 was monitored over 14 days, reaching 34 ± 2% and 94 ± 1% release of the encapsulated amount, respectively. All levan hydrogel formulations exhibited typical gel-like behaviour within the linear viscoelastic region, with the storage modulus (G′) exceeding the loss modulus (G″). Alizarin Red S staining and alkaline phosphatase (ALP) activity assays of GMSCs cultured with liposomes and hydrogels for 28 days demonstrated significantly higher osteogenic activity compared with the positive control (up to 50 % increase).

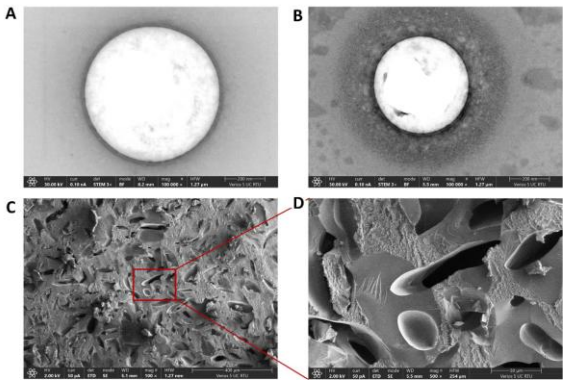

Fig. 1: STEM micrographs of (A) D_CBD/IGF-1 and (B) D-PEG_CBD/IGF-1 liposomes and (C, D) the cross-section and pore structure of swelled and then freeze-dried LH sample.

The increase in ALP activity occurred concurrently with a decrease in cell viability, suggesting a metabolic shift from glycolysis to oxidative phosphorylation as cells matured into osteoblasts during osteogenic differentiation.

DISCUSSION & CONCLUSIONS: CBD release followed the Korsmeyer–Peppas model, consistent with non-Fickian diffusion. The system maintained cell viability and significantly enhanced osteogenic differentiation, demonstrating a synergistic effect of CBD and IGF-1 within the levan hydrogel matrix.

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