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Hemolytic Assessment of Geranylgeraniol/ Clindamycin-Loaded Composite Hydrogel

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Abstract

Objectives: This study investigated the hemolytic activity of a geranylgeraniol (GGOH)/ clindamycin (CDM)-loaded composite hydrogel developed as a potential preventive measure for medication-related osteonecrosis of the jaw associated with bisphosphonate (MRONJ-B).

Methods: The surface and structural properties of the drug-loaded hydrogel were characterized using stereomicroscopy, scanning electron microscopy, confocal fluorescence microscopy, and micro-computed tomography. The hemolytic activity of the drug-free (control) and drug-loaded hydrogels was comparatively assessed using three *in vitro* models: washed red blood cells (RBCs), diluted whole blood, and clotted whole blood, to evaluate the impact of the plasma and fibrin matrix on the hemolytic potential of the materials.

Results: The results showed that the drug-loaded hydrogel exhibited an average pore size of 38±24 µm, with a porosity of 84±4.3% and an interconnectivity of 99.9±0.1%. The control hydrogel demonstrated minimal hemolysis (<0.5%) in all test models. While the drug-loaded hydrogel exhibited increased hemolysis (>5%) in both washed RBC and diluted whole blood models, the presence of natural fibrin formation and platelet lysate significantly mitigated the hydrogel's hemolytic activity. Notably, platelet lysate encapsulation provided superior RBC protection compared to natural fibrin within the clotted whole blood model. Histological analysis of the drug-loaded hydrogel in *ex vivo* cultures with clotted whole blood did not reveal significant RBC toxicity.

Conclusions: These findings suggested that the drug-loaded composite hydrogel may be suitable for further *in vivo* investigations of its biocompatibility and efficacy in preventing MRONJ-B.

Keywords: geranylgeraniol, hemolysis, hydrogel, medication-related osteonecrosis of the jaw, platelet lysate