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DEVELOPMENT AND PHYSICOCHEMICAL CHARACTERIZATION STUDIES OF NOVEL PHYTOCOMPOUND CO-LOADED LIPOSOMES FOR IMPROVED WOUND HEALING

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Abstract

Chronic wounds are characterized by a prolonged inflammatory phase and healing time, with a high risk of infections and the development of biofilms in the wound beds, making them quite difficult to treat, especially with the growing issue that is antimicrobial resistance. Hence, they pose a significant problem in today's

society, having a heavy influence on the patients' quality of life, and a strong impact on healthcare systems as well. Therefore, novel more effective therapies are urgently needed. In this context, natural compounds can be of use, since overall many plant-derived compounds have demonstrated significant regenerative, anti-inflammatory, antimicrobial, and antioxidant activities, all of which can be relevant for wound management. Additionally, while a single compound can be effective, the combination of more than one molecule with relevant bioactivity can lead to improved therapeutic effects, since multiple aspects of wound healing can be tackled simultaneously, and synergistic effects might be potentially achieved. For this purpose, co-encapsulation into liposomes can be beneficial, since these phospholipid bilayer nanometric vesicles have both hydrophilic and hydrophobic regions, hence enabling the encapsulation of water-soluble compounds in their aqueous core, and lipid-soluble compounds in their lipid membrane.

Hence, our work aimed to develop a novel liposomal formulation co-encapsulating two phytocompounds simultaneously (one hydrophilic compound, and one hydrophobic compound), for topical administration, for improved wound treatment.

The liposomes were prepared using the thin-film hydration method, followed by ultrasonication and extrusion through a small pore membrane (for vesicle size reduction and homogenization). The liposomal vesicles were composed of a lipid 1:lipid 2 80:20 molar ratio. The mean particle size and polydispersity index (PDI) of these liposomes were evaluated using dynamic light scattering, and their zeta potential was measured using electrophoretic light scattering, both using a Zetasizer apparatus. The encapsulation efficiency was determined using a previously developed and validated high-performance liquid chromatography method, after formulation filtration through ultracentrifugation, for the quantification of both phytocompounds.

Results showed that optimized dual phytochemical-loaded liposomes exhibited a mean particle size of 134.08 ± 16.27 nm, consistent with adequacy for topical application (increased permeation and retention), a PDI of 0.21 ± 0.05 (corresponding to a homogeneous particle size distribution), and a zeta potential of -15.57 ± 9.20 mV (consistent with a moderate contribution to the electrostatic stabilization of the nanovesicles). Obtained encapsulation efficiencies of 41.76 ± 5.05% for the hydrophilic compound, and 91.36 ± 0.01% for the hydrophobic compound, suggested that both phytocompounds were effectively encapsulated.

Hence, the physicochemical properties of the developed co-loaded liposomal vesicles indicated a homogeneous and potentially stable nanosystem, with a small particle size, suitable for skin application and potentially facilitating the penetration and co-delivery of the encapsulated compounds into deeper skin layers. These preliminary findings suggest that these liposomes are promising nanocarriers for the co-encapsulation of natural compounds, and further in vitro release studies and bioactivity and safety assays are being conducted to complement these results, so that the potential of these newly developed co-loaded nanoplatforms can be further confirmed.

Keyword:

Co-Delivery, Liposome, Phytocompound, Wound Healing