Mediterranean *Bituminaria bituminosa* in Ethosomal Systems for Novel Approaches to Skin Healing

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In recent years, skin regeneration has become a key focus in dermatology and biomedical research, with growing attention toward sustainable and biocompatible therapies [1]. Medicinal plants provide an abundant source of bioactive compounds, yet their translation into clinical settings remains challenging due to issues of solubility, stability, and potential toxicity [2].
Bituminaria bituminosa, a Mediterranean leguminous plant traditionally employed for wound healing and inflammation, is characterized by a rich phytochemical profile including flavonoids, furanocoumarins, and pterocarpans [3]. Nevertheless, its potential role in regenerative medicine remains underexplored.
In this work, we applied an aqueous, low-impact extraction process to obtain a phytocomplex (BIT) from *B. bituminosa*. Before extraction, the plant material was genetically authenticated to confirm species identity. The extract was chemically characterized for its total phenolic and flavonoid content, as well as antioxidant activity through DPPH, ABTS, and FRAP assays. It was then evaluated in vitro on human keratinocytes (HaCaT) and dermal fibroblasts (BJ) to assess cell viability, proliferative capacity, migration, and the expression of genes linked to repair pathways. In addition, in a cell-based oxidative stress assay on BJ fibroblasts, BIT attenuated H_2O_2-induced damage, further supporting its antioxidant potential in a biologically relevant context.
Following these encouraging outcomes, BIT was encapsulated into ethosomal vesicles to enhance topical delivery and overcome the intrinsic limitations associated with plant-derived preparations. Ethosomes, deformable lipid carriers enriched with ethanol, are well known to enhance transdermal transport, preserve labile compounds, and reduce cytotoxicity at effective concentrations. BIT-loaded ethosomes were thoroughly characterized in terms of particle size, polydispersity index, surface charge, as well as stability under storage and pH stress conditions.
Overall, the results indicate that *B. bituminosa* extract promotes cellular processes fundamental to skin repair, and that ethosomal encapsulation ensures nanoscale stability and suitability for topical application. This study supports the development of environmentally friendly nanocarriers integrating phytochemicals as innovative therapeutic candidates for skin tissue regeneration.

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