INNOVATION

Transdermal Penetration Capabilities of Mesenchymal Stem Cell-Derived Extracellular Vesicles

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TOPICAL THERAPIES OFFER A HIGHLY ATTRACTIVE ROUTE OF ADMINISTRATION that is noninvasive, bypasses first-pass metabolism, and is convenient for patients, which can improve compliance. However, delivering biologics through the skin remains a major challenge. The stratum corneum, the skin's outermost layer, is densely packed with lipids and keratin, forming a robust barrier that blocks most biologic agents.[1]

Mesenchymal stem cell-derived extracellular vesicles (MSC-EVs) offer a promising therapeutic approach to treat several dermatologic and musculoskeletal diseases. These nanoscale messengers, ranging from 30 to 150 nm, are naturally enclosed in a lipid bilayer and carry bioactive molecules such as cytokines, growth factors, and lipids that promote tissue repair and modulate inflammation.[2]

Transdermal Penetration of MSC-EVs

On their own, MSC-EVs have limited transdermal penetration capabilities. Their lipid membranes can briefly loosen the stratum corneum's lipid matrix, allowing small-scale passive diffusion through hair follicles[3] and sweat glands,[4] but only a fraction of vesicles reach deeper layers.[5]

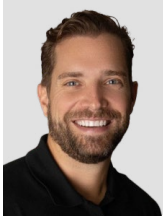
Formulation strategies can improve delivery. Penetration enhancers like dimethyl sulfoxide (DMSO) and camphor are used in FDA-approved topical drugs for arthritis. DMSO is amphiphilic, disrupting lipid packing, altering keratin structure, and increasing hydration to create transient pathways.6 Camphor, a small lipophilic terpenoid, disrupts stratum corneum organization to boost permeability.[7] Another approach is hybridization, where MSC-EVs are coated or fused with synthetic lipid nanoparticles engineered for greater stability and skin penetration.[8]

Once inside the viable epidermis and dermis, MSC-EVs can deliver their bioactive cargo directly to local cells or be transported to deeper musculoskeletal tissues.[9] This ability opens possibilities for noninvasive treatment of joint and tendon injuries, inflammatory arthropathies, and other connective tissue disorders

Future Clinical Outlook

Topical MSC-EV therapies are gaining traction in clinical research. In a phase one trial, a topical MSC-EV formulation for psoriasis was well tolerated.[10] Another study reported reduced melanin production in hyperpigmentation disorders.[12]

Preclinical research is exploring hydrogel embedding and genetic engineering of parent cells to enhance vesicle stability and penetration.[11] These continued advances open the door for effective MSC-EV-based therapies for musculoskeletal diseases without the need for injections or invasive procedures.



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