From Nanovesicles to Fibers: A Hybrid Electrospun Membrane for Enhanced Ketoprofen Skin delivery

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Ketoprofen is a widely used non-steroidal anti-inflammatory drug (NSAID) for pain management, but its oral administration is limited by low bioavailability and systemic side effects. Topical formulations have been developed as alternatives; however, skin penetration remains a major challenge, and main penetration enhancement strategies may lead to irritation.
In this study, we designed a novel hybrid membrane by incorporating ketoprofen-loaded lipid nanovesicles into electrospun polyethylene oxide (PEO) nanofibers, aiming to improve skin permeation while reducing irritation risks. Nanovesicles were prepared by ethanol injection, with the optimized formulation showing a mean diameter of below 100 nm, narrow size distribution, and ~65% drug entrapment efficiency. Addition of 3.5% w/v PEO yielded the best colloidal stability, viscosity, and conductivity, enabling the fabrication of a stable and homogeneous nanofiber mat by electrospinning.
Characterization by SEM/EDX revealed randomly oriented fibers with uniform vesicle distribution (Fig.1). DSC, TGA, and Raman analyses confirmed suitable interactions between PEO and the nanovesicles. In vitro release experiments demonstrated a sustained biphasic release profile from the hybrid membrane compared to free nanovesicles. In vitro studies using human stratum corneum epidermis (SCE) confirmed superior drug permeation than commercial ketoprofen gel.
Finally, in vivo evaluation in healthy volunteers demonstrated both safety and improved efficacy in a methyl-nicotinate-induced erythema model, showing a stronger anti-inflammatory effect than conventional gel-dosage form.
These findings suggested that the proposed hybrid nanofiber-based system represents a promising, easy-to-handle, and fast-converting gel formulation with enhanced performance over conventional topical ketoprofen products.

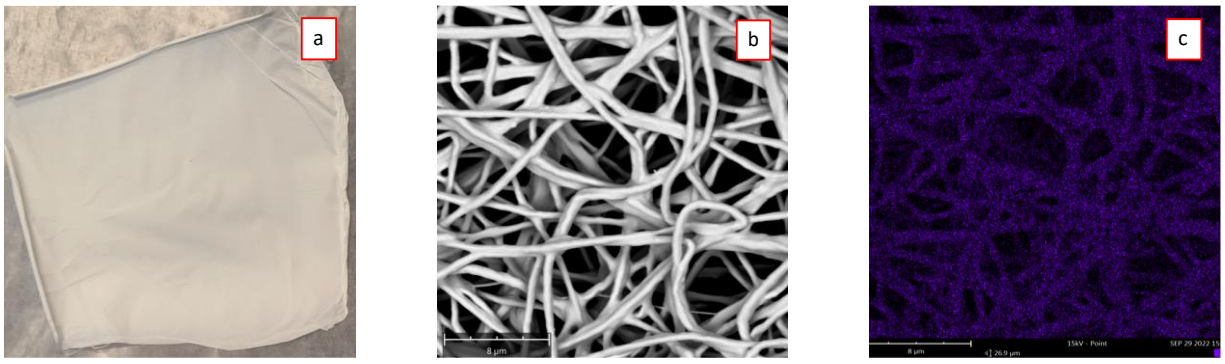

Figure 1. a) Macroscopic hybrid fibers mat; b) SEM photogram c) Phosphorous atoms distribution within electrospun fibers.