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SOLVING THE SUSTAINABLE BEAUTY EQUATION

"Beyond Delivery: Redefining Liposomes as Active Modulators through Large-Scale Transcriptomic Profiling"

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Abstract

Objective: In cosmetic applications, liposomes have been extensively studied as penetration enhancers and carriers. However, their potential to actively modulate skin gene expression and cooperate with active ingredients at the molecular level has not been systematically investigated. This study employed large-scale time-course transcriptomic analysis to elucidate liposomes' intrinsic biological activities and their cooperative interactions with niacinamide.

Methods: *Ex vivo* human skin explants (female, age 51) were treated with empty phosphatidylcholine liposomes, niacinamide, and niacinamide-loaded liposomes for 24h and 48h. Bulk RNA Barcoding sequencing (BRB-seq) enabled multiplexed transcriptomic profiling across 20,000+ genes. Differential expression analysis, principal component analysis (PCA), and functional enrichment analysis were performed for comprehensive data analysis.

Results: PCA showed the first two principal components (PC1: 56.77%, PC2: 26.41%) explained 83% of variance. PC1 separated time-dependent responses, while PC2 demonstrated clear treatment-specific clustering at 24h, establishing distinct biological activities among treatments. At 24h, empty liposomes showed differential expression in 538 genes compared to control, niacinamide 402 genes, and niacinamide-loaded liposomes 683 genes. Functional enrichment revealed empty liposomes activated transcriptional programs, tight junction remodeling, cell migration pathways, and keratin downregulation. Niacinamide-loaded liposomes uniquely expressed 241 genes not found with either component alone, enriched in translational machinery. By 48h, 95% of responses resolved, converging to barrier-strengthening proteins and antimicrobial peptides.

Conclusion: This study demonstrates that liposomes possess intrinsic biological activity, redefining them from passive carriers to active modulators. Furthermore, cooperative interactions with niacinamide generated combination-exclusive responses. Large-scale analytical methods enabled comprehensive evaluation of complete formulation functionality beyond individual ingredient characterization. This data-driven approach provides a foundation for the strategic design of advanced dermatological formulations.