**A Sunless Tan That Works With Your Body: A New Vehicle for Pigmentation Therapy**

Our skin is more than a protective barrier, it is a gateway. We rely on it to protect us, but we also rely on it to absorb the creams and cosmetics many apply every day. Sun exposure remains one of the leading causes of skin ageing and cancer, yet a tanned appearance continues to be aesthetically desirable. For years, sunless tanners containing dihydroxyacetone (DHA) have offered an alternative, though they are prone to uneven application and orange discoloration. Spray formulations raise further concern, as inhaled DHA has been shown to cause respiratory tract and eye irritation in humans. The lack of comprehensive long-term human safety data, combined with demonstrated cellular toxicity in laboratory settings, means that regulatory agencies continue to recommend caution. Alternative tanning methods or acceptance of natural skin tone may be preferable for individuals concerned about potential health risks, especially those with respiratory conditions or sensitivities.

NPP-4 is a peptide designed to stimulate melanin production by targeting melanocytes at the junction between the epidermis (the outermost layer) and dermis (the layer beneath). To reach them, NPP-4 must cross the skin's outermost barrier built to keep foreign substances out. Therefore, the formulation in which NPP-4 is delivered must enhance permeation while maintaining stability and spreadability. When dissolved in $H_2O$ and tested on reconstructed human skin, NPP-4 successfully reached and activated melanocytes. However, NPP-4 was unstable in $H_2O$, and hence Coegin Pharma developed a gel serum that made NPP-4 stable, however skin permeation data are lacking. For consumers, NPP-4 means a safer, more reliable alternative to ultraviolet radiation. For the cosmetic industry, it demonstrates the capability of peptide-based approaches. Using a lab-grown human skin model (MatTek EpiDermFT), NPP-4 showed measurable permeation across the epidermis, dermis, and receptor medium, when formulated in the gel serum and $H_2O$. When excluding the medium, NPP-4 concentrations were significantly higher in the dermis when formulated in the gel serum ($p < 0.05$). Additionally, significantly higher dermal concentrations ($p < 0.05$) under both vehicles suggested deeper permeation, likely driven by NPP-4's small molecular size and the model's elevated permeability.

Methylene blue (MB) was used as a model permeant in Franz diffusion cells, a device that measures how substances move through a barrier. It was applied across synthetic (Strat-M) and porcine skin membranes to evaluate whether these cheaper, more accessible models could serve as alternatives to human skin. MB permeation revealed to be below the limit of detection across both membranes, likely attributed to MB's physiochemical properties. Porcine skin yielded higher flux across most conditions, though this may reflect thermal disruption of the stratum corneum lipid structure from scalding rather than true permeability differences. No statistically significant vehicle effect was detected in either membrane, and inconsistent trends were attributable to high inter-replicate variability, precluding any definitive conclusions on vehicle effects.