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Dermal formulations with rutin nanocrystals & peptide-loaded liposomes - mechanisms & in vivo performance

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Drugs soluble in water or lipophilic media can be incorporated into liposomes, the novel delivery system nanocrystals is suitable for formulating poorly soluble actives. From this a combination of both delivery systems is able to deliver each cosmetic or pharmaceutical active mixture to the skin – independent on its solubility. This combination was firstly realized on the market in cosmetic products (e.g. intense lifting eye serum, Dr. JK Cosmeceuticals).

Primary penetration enhancing physical mechanisms are occlusion for liposomes, penetration into the skin can only occur when using liposomes with special composition (transfersomes [1]). Nanocrystals are crystals in the nano dimension (typically 300-600 nm) which create an increase in saturation solubility for poorly soluble compounds. This leads to an increased concentration gradient between dermal formulation and skin, thus increasing passive diffusion. Active penetrated from the cream/gel into the skin is instantly replaced by new active dissolving from the nanocrystal depot, thus maintaining a constant high concentration gradient.

A formulation (intense lifting eye serum, Dr. JK Cosmeceuticals) was developed containing liposomes loaded with Argireline (acetyl hexapeptide-3) and Eyeseryl (acetyl tetrapeptide-5) and rutin nanocrystals. It was designed to improve the skin appearance and wrinkle profile around the eyes. The formulation was characterized in vitro regarding size characteristics (photon correlation spectroscopy, laser diffractometry), rheological behavior, and in vitro occlusion.

To assess in principle the in vivo skin effects in the eye region, this liposome-rutin combination [2] was investigated in a human study, male (8) and female (7) volunteers. The skin appearance was quantified using a VISIA Scan system (Canfield Imaging Systems, Fairfield, New Jersey), the skin profile (roughness) was quantified using the PRIMOS system, (GF Messtechnik GmbH, Teltow, Germany). Hyperpigmented area on the skin decreased significantly ($p<0.05$) in male and female groups after four weeks of treatment. Skin vascular structure was improved in the female groups ($p<0.05$). Thus the skin color was improved

because melanin and hemoglobin are the main skin colorants. Interestingly, skin roughness was more reduced in the female group after eight weeks of treatment. The roughness parameters decreased significantly ($p<0.05$), being most pronounced for the roughness parameter Rmax. There was a clear correlation between the decrease in roughness parameter Ra with the consumption of the product, highlighting the importance of application compliance to the skin effect.

References:
[1] Jain, S., et al., Drug Dev Ind Pharm, 2003. 29(9): p. 1013-26.
[2] Sinambela P., et al., Proceeding #900, Int. Symp. Control. Rel. Bioact. Mater. 40, Honolulu/Hawaii, 21-24 July 2013.