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Anti-oxidative and skin protective effects of drug nanocrystals

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Drug nanocrystals are particles of an active reduced in size to the nanometer range. Due to their small size they possess many special nano properties compared to drug crystals in the micrometer range. Examples are increased dissolution velocity dc/dt, increased saturation solubility cs, and consequently an increased concentration gradient at membranes (e.g. skin), leading to enhanced penetration/permeation. Therefore, nanocrystals are a smart delivery system for poorly soluble pharmaceutical and cosmetic actives.

Dermal application of antioxidants is frequently used to scavenge free radicals in the skin and thus to protect the skin from damages caused by such free radicals. Antioxidants are therefore not only important in anti-aging, but also, in prevention of skin cancer. However, many antioxidants, especially secondary plant metabolites such as flavonoids, are poorly soluble and thus showing no or insufficient penetration into the skin. To assess the penetration enhancing effect, nanocrystals of the poorly water soluble flavonoids (Rutin and Hesperidin) were produced. In a human study, their antioxidant capacity was compared to a water soluble Rutin derivative (rutin with attached glucose). To assess the increase in “bioactivity” in the skin, not concentrations of the active were measured but the pharmacological effect. i.e. the achieved antioxidative activity (protection against UV light, increase in sun protection factor SPF). In addition, the skin protective effect was assessed in vivo by comparing biopsies of healthy, non-irradiated skin with those irradiated with UV light (non-treated, damaged) and irradiated skin treated before with drug nanocrystals.

The in vivo experiments showed up to a 1,000 fold higher activity of the nanocrystals compared to the water soluble rutin derivative (2 fold increase in SPF at 1/500 lower dissolved concentration of active). The skin damaging effect caused by UV was shown by a significant change in the morphology of the Langerhans cells in the biopsy of the irradiated, non-treated skin. The damaging effect was avoided when the skin was treated with nanocrystals prior to the UV irradiation.

In conclusion, nanocrystals can be used as a principal formulation strategy to improve the dermal activity of poorly soluble compounds. The activity increase found let to the development of cosmetic products with rutin nanocrystals (Juvena, line JUVEDICAL) and

hesperidin nanocrystals (la prairie, platinum rare). The same principle can be applied to poorly soluble drugs to increase their dermal activity.