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smartPearlsTM – novel dermal delivery system for amorphous cosmetic and pharma activess

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Achieving a sufficient penetration and bioactivity of poorly soluble actives is a challenge in formulation technology. A simple but very efficient approach is the increase in saturation solubility Cs, thus increasing the concentration gradient Cs-Cskin between formulation and skin, and subsequently the diffusional pressure. This can be achieved by transforming the active powder into the nanodimension, i.e. producing nanocrystals [1] (e.g. smartCrystals®). Alternatively the active can be transferred from the crystalline to the amorphous state, being even more efficient – but the amorphous state has physical stability problems excluding the dermal use. Ideal would be to combine the solubility enhancing effects of size reduction and amorphous state – this was realized in the smartPearlsTM delivery system [2].

The delivery principle was previously employed for oral delivery [3] (CapsMorph®), and has now been transferred to dermal delivery. The cosmetic or pharma active is caged in the pores (typically 2-100 nm) of meso- or macroporous materials, e.g. silica (Syloid 3D, company Grace). The space restriction prevents re-crystallization, the amorphous state was proven stable up to 5 years [4]. The silica particles are loaded by the impregnation method or spray-drying, and the loaded silica particles simply dispersed in the water phase of gels or creams.

The anti-oxidants rutin and hesperdin as model actives were loaded onto Syloid® SP53D-11920 (SYLOID® 3D). These smartPearlsTM were further studied in a porcine ear skin test to investigate the penetration behavior. The loading of active was 32.0% by using the wetness impregnation method. The amorphous state was verified for 6 months (until now) by x-ray diffraction (XRD). smartPearlsTM were incorporated into a 5% hydroxypropyl cellulose (HPC) gel. The dermal formulations were physically stable by judging from microscopy (absence of silica particle aggregations) and XRD (no crystal peaks appeared).

smartPearlsTM gels with only 1% active were applied to the pig ear tape stripping. Controls were 5% raw drug powder (RDP) gels and 5% nanocrystal (NC) gels. In absolute terms, the smartPearlsTM formulation were slightly superior to nanocrystals, the difference became very clear after normalization of the data to 1% active content. Results were “normalized” dividing the drug amount (µg) per strip by the active concentration (%) in the applied formulation. Both

smartPearlsTM formulations showed clear superiority.

The smartPearlsTM technology stabilizes efficiently the amorphous state in porous materials, shows similar or even better dermal penetration than nanocrystals, is industrially feasible, and thus a promising dermal delivery technology for poorly soluble actives. The particle size of the smartPearls is typically 10-40 µm, thus outside the nano size range and no “nanoparticle” product. This is of increasing importance for the consumer due to the nanotoxicology discussions.

[1] C.M. Keck, Nanocrystals and amorphous nanoparticles and method for production of the same by a low energy process. US patent application 2013/0095198

[2] F. Monsuur, H.H. Höfer, C.M. Keck, US patent application 2014

[3] Q.H. Wei, C.M. Keck, R.H. Müller, CapsMorph® technology for oral delivery – therory, preparation and characterization. Int. J. Pharm. (2015), dx.doi.org/10.1016/ j.ijpharm. 2014.10.068

[4] Müller, R. H., Wei, Q., Keck, C. M., CapsMorph: >4 Years long-term stability of industrially feasible amorphous drug formulations, p. 50, 7th Polish-German Symposium on Pharmaceutical Sciences, Gdansk, 24-25 May 2013