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smartPearls® – a new dermal micro-delivery system for poorly soluble drugs by amorphization

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The poor solubility of many cosmetic actives and drugs limits their dermal bioavailability, e.g. cyclosporin. A physical strategy is to increase the solubility of such actives, i.e. increasing the concentration gradient to the skin and thus passive diffusional flux. Examples are solubilization with surfactants, microemulsions or co-solvents, but all having several disadvantages (e.g. skin irritation, drug precipitation on skin after solvent evaporation resulting in poor penetration). The alternative is to increase the solubility by changing the crystalline state of the drug, i.e. using higher soluble polymorphs or amorphous drug. The common problem of both approaches is the physical instability, which often prohibits use in commercial products. The smartPearls® technology allows to easily generate the amorphous state and keeps it long-term stable in dermal formulations such as gels and creams. All excipients are GMP materials and regulatorily approved for dermal use, i.e. usable in pharmacy prescription and commercial products.

The delivery technology has been transferred from the oral administration route to dermal application. How does the technology work? Drug is loaded into the mesopores of porous materials, e.g. µm-sized silica particles already used in dermal formulations (e.g. Syloid, company Grace). Loading is performed by soaking the pores with organic solution of the drug, and subsequently evaporating the solvent. The drug precipitates, but due to the small dimension of the pores it cannot form crystals, it stays amorphous. Amorphous stability of these powders was shown over more than 4 years [2]. Solvent-free loading of the silica particles is also possible. For dermal application, the powders are simply admixed to the water phase of gels or creams.

The performance of the system was studied using cyclosporin as model drug, being of interest e.g. for psoriasis treatment. Cyclosporin was loaded onto Syloid SP53D-11920, and then particles incorporated into hydroxypropyl cellulose (HPC) gel. The particles proved to be stable in the formulation during storage. As comparative formulations gels were prepared with amorphous µm-sized cyclosporin powder, and amorphous cyclosporin nanoparticles. Skin penetration was studied in the pig ear skin model, using tape stripping. Despite that a) all the formulations contained amorphous cyclosporin, and b) the reference gels contained higher

drug concentration (5% cyclosporin µm-sized powder, 5% cyclosporin nanoparticles versus only 1% cyclosporin in smartPearls®), the penetration from the smartPearls® was superior. The effect was especially visible when normalizing the penetration profiles (µg drug penetrated/% drug content in formulation). Apart from the penetration, highly essential is the physical stability of the amorphous cyclosporin in the smartPearls®, pre-requisite for a product for the benefit of patients.

The smartPearls® technology can also be used in cosmetics and consumer care products. Considering the increasing reluctance of consumers about nanotechnology, it is important on the long term that smartPearls® are no nanoparticles according to EU definition, they are a microparticulate delivery systems, typical sizes from a few µm to about 50 µm.

References:
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