

Novel delivery system smartPearls – efficient delivery system for antioxidants in anti-pollution

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Since a few years, the hot topic in cosmetics and dermal delivery is anti-pollution formulations to protect skin against pollution in the environment. Anti-pollution products are the new mega trend in cosmetics, promising billions of annual sales [1]. The anti-pollution strategy consists of 2 approaches, a mechanical one (= restoration of the protective lipid barrier on the skin) and a molecular one (delivery of protective molecules, mainly antioxidants). The mechanical barrier can protect e.g. against fine dust but not against damaging radiation (e.g. IR, blue light – photo aging [2]). Radiation penetrates undistorted into skin. Thus, skin damaging can only be neutralized on molecular level. Broadly used therefore are antioxidants [3] like rutin.

However, most of the antioxidants being effective on the molecular level are very poorly soluble in both water and lipophilic media (e.g. oils). A simple but very effective strategy is the increase in their saturation solubility c_s . This increases the concentration gradient between the dermal formulation and the skin (c_s - c_{skin}), thus, increasing the passive diffusive flux of the antioxidant molecules into the skin. One successful approach was the use of nanocrystals, possessing an increased c_s due to their nano-dimensional size.

However, the consumer is getting more and more reluctant towards nano, very pronounced in food products, but the same trend is predicted in cosmetics. Companies do not want to have the addendum <nano> in the INCI list of their products any more. A smart solution is the use of amorphous antioxidants. The c_s in the amorphous state is even higher than in the nanocrystalline state. Thus, amorphous is superior to nano. However, the problem by now was the instability of the amorphous state, i.e. re-crystallization in the dermal products – excluding their use. However, the stability problem was elegantly solved by the development of the delivery system smartPearls [4].

The smartPearls are porous silica micrometer particles, no nanoparticles. The active is loaded in the amorphous state inside the pores (2-50 nm pore size). Both large surface area and small diameters of the pores hinders the active to re-crystallize [5]. Rutin smartPearls were already developed with amorphous stability over 1.5 years. However, rutin was loaded in several steps, repeating the addition of rutin DMSO solution and evaporation of DMSO multiply. This process is not favorable for industrial large-scale production. Aim was to optimize the production of rutin



smartPearls, make it industrially friendly – the prerequisite for final market products.

For loading the pores of smartPearls, a novel “immersion evaporation” method was successfully employed. Briefly, the empty silica particles were immersed in ethanolic rutin solution, and subsequently the ethanol was evaporated. Via light microscopy and differential scanning calorimetry (DSC) amorphous state and its long-term preservation were investigated.

Extent of increase in saturation solubility c_s was determined compared to standard raw drug powder. Saturation solubility was determined in situ by UV/VIS measurement using Sirius® inform in water (pH 5-6). Tyndall-Rayleigh scattering from silica is automatically corrected by this device, and thus not interfere with the signal from dissolved rutin. By rutin smartPearls, saturation solubility of 129 µg/ml was reached, being almost 3-times higher than the raw drug powder (46 µg/ml). Important is also the enormous increase of the dissolution rate. Dissolved rutin that have penetrated skin will be immediately replaced in the formulation by new rutin molecules dissolving fast from the smartPearls. Thus, a continuous flow into the skin can be maintained.

In summary: smartPearls are a superior delivery system to nanocrystals. With the development of the more industry-friendly production process, the pre-requisite for introduction into market products has been fulfilled – shown exemplarily for rutin. The smartPearls can be used to deliver generally antioxidants within an anti-pollution strategy.

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