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# SmartCrystals® – development of commercial concentrates for cosmetic industry

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SmartCrystals are a technology for efficient penetration enhancement of poorly soluble cosmetic and pharma actives [1]. Using this technology, molecules which are not active at all or much too low in activity can be made sufficiently bioavailable, e.g. anti-oxidants such as rutin. The trick is to reduce the insoluble micrometer crystals in size to the nanodimension (< 1000 nm = SmartCrystals) by a combination of bead milling and high pressure homogenization. By entering the nanodimension, the saturation solubility  $C_s$  increases strongly (e.g. factor of 10-100), and thus the diffusive flux from the dermal formulation with SmartCrystals into the skin. For example, the anti-oxidant activity of rutin could be increased in-vivo by a factor of 1,000 (human study).

To use this technology in products, SmartCrystals need to be available for purchase by companies. Apart from being IP-protected, the production process is too complex and thus too costly to be established for products in one cosmetic company. A number of years ago, large scale production was established for formulations using highly accepted pharmaceutical stabilizers (e.g. Tween 80, Poloxamer 188, even being i.v. injectable). However, nowadays in cosmetics PEG containing molecules are not preferred any more – one looks for skin-friendly, PEG-free alternatives. Thus a study was performed, screening of 10 different stabilizers with preferred application onto the skin, e.g. alkyl polyglycosides such as Plantacare®. A few stabilizers were identified which stabilized the produced crystals in a size range of about 400 nm, e.g. Plantacare® 810 UP, 1200 Up and Eumulgin® SG. From the short term stability by now (increase in size below 4% over 1 month) a long-term stability as SmartCrystal suspension of at least 1 year can be predicted (data by now).

The size of the SmartCrystals can be adjusted by the input of milling energy and milling time. In general, the size is in the submicron range, that means distinctly above 100 nm. The crystals are no nanoparticles (EU, US definition), but possess the properties of nanoparticles (e.g. saturation solubility increase adhesiveness onto the skin).

Rutin formulations are planned to be launched as SmartCrystal concentrates (5% active) in April this year. They can be simply admixed to any cosmetic product in the last step of production with a dilution factor of typically 50. The rutin concentrates will be available in the original composition (used in the human study) but also with other novel stabilizers. Also tailor-made products are possible with exclusive molecules of the customer.

[1] Petersen, R. (2015). U.S. Patent No. 9,114,077. Washington, DC: U.S. Patent and Trademark Office.

