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3rd generation technology – BergaCare smartLipids® submicron carrier for improved retinol formulation

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The solid lipid nanoparticles (SLN®) [1] are the first generation, the nanostructured lipid carriers (NLC®) [2, 3] the second generation of "lipid nanoparticles with solid particle matrix". In 2014 the third generation was developed, the smartLipids® [4, 5], being technically a specialized version of the NLC.

Basic difference is the lipid composition for particle production. The SLN consist typically of 1 solid lipid, the NLC of a blend of a 1 solid lipid and 1 liquid lipid (oil).The 3rd generation consists of a "chaotic" mixture of 5-10 lipids, either solid lipids only, or with limited admixture of oils. The chaotic mixture leads to more imperfections in the particle matrix, thus to an increased loading capacity for cosmetic and pharmaceutical actives. Retinol was incorporated into smartLipids® particles. The loading, reported in the literature, with firm incorporation was 1% for SLN, 5% for NLC, but 15% could be incorporated into smartLipids®. In addition, localization in imperfections inside the particle should protect the actives against degrading influences, i.e. increasing the chemical stability.

The complex lipid mixture delays/avoids polymorphic transitions of the lipid particle matrix to more ordered ß modification, which can lead in SLN (and partially in NLC) to expulsion of loaded actives from the particle matrix (in more highly ordered particle matrix is no space anymore for foreign molecules). The smartLipids® approach increases firm inclusion during storage.

The particle size produced is preferable >100 nm and <1,000 nm (= 1 µm), i.e. being in the "submicron range" and legally the particles are no nanoparticles (no declaration according to EU guidelines as "nano" on products). However, due to the size in the nanodimension (< 1,000 nm), these submicron particles possess still special skin beneficial nano-properties, but being legally no nanoproducts. The mean sizes of the bulk populations of the produced retinol smartLipids® was in the range 112 nm to 400 nm (determined by photon correlation spectroscopy - PCS).

Retinol was incorporated into smartLipids prepared from medium to highly chaotic lipid mixtures (i.e. 7 or 8 lipids of different complexity, e.g. mono- to triglyceride content, at simultaneously very different fatty acid chain lengths). To study additionally the influence of

the stabilizer on chemical stability, particles were prepared with different stabilizers, e.g. anti-irritant sodium cocoamphoacetate. The stabilizer affects the stability via its influence on the crystalline structure of the particle matrix (i.e. delay or acceleration of polymorphic transitions, subsequently reduction of imperfections for protective localization of active). Particle suspensions were stored at room temperature and at 40 °C. Stability data were compared with previously published stability data by Jenning [6] and Hommoss [7].

A very pronounced effect of the stabilizer was found, sodium cocoamphoacetate was most protective for retinol. Both high but also the medium chaotic lipid mixture (only solid lipids) had a good stabilizing effect on retinol (e.g. 94-97% both after 3 months at room temperature, 48% (medium) and 70% (highly chaotic mixture) at 40 °C). After 6 months at room temperature the stabilities of retinol in smartLipid mixtures (solid and liquid lipids) were about 88%, clearly higher than [7]. It should be pointed out, that the mixtures did not contain added anti-oxidants (e.g. BHA, BHT etc.), the pure protective effect of the carrier was investigated. The combination of protective effect and long-term firm inclusion into the particle matrix by absence of polymorphic transitions makes the smartLipids® a highly attractive carrier not only for retinol, but generally for chemically labile cosmetic and pharmaceutical actives.

For the final formulation, in addition to the protection by the lipid matrix, antioxidants were added for perfect protection. A study was performed adding different antioxidants, e.g. BHT, Tinogard TT etc., and the formulations were stored for 6 months at stress condition of 40°C. Even under this stress, the best combinations had a remaining retinol content of about 67%. Thus, long term stable retinol in dermal formulations is possible by effective combination of NLC/smartLipids and anti-oxidants.

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