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Next generation after SLN® and NLC® – the “chaotic” smartLipids®

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In 1991 the solid lipid nanoparticles (SLN®) [1] were developed as alternative to liposomes, nanoemulsions and polymeric nanoparticles, in 1999 the second generation followed, the so called nanostructured lipid carriers (NLC®) [2, 3]. Now in 2014 the third generation was developed, the smartLipids® [4], possessing advantages compared to the first 2 generations.

All these lipid particles possess a lipidic particle matrix being solid at body temperature. In the SLN this matrix consists of a solid lipid, typically a single solid lipid. Disadvantage was limitation in drug loading due to the formation of highly ordered ? modification. Especially during storage a less ordered SLN particle matrix structure could re-order with time, i.e. forming increasing fraction of ? modification leading to drug expulsion and formation of drug crystals outside the SLN particle (e.g. in the water phase of gels and creams). Consequently in the next generation NLC a nanostructuring of the particle matrix was the aim, i.e. by mixing chemically (spatially) very different lipids, typically 1 solid lipid and 1 liquid lipid (oil). This created more imperfections in the lipid matrix, increasing drug loading and reducing drug expulsion during storage. However, in most NLC still a polymorphic transition occurred during storage.

Consequently the third generation of smarter lipids was developed. In these smartLipids® a “chaos” in the particle matrix is generated by blending about 10 different solid or solid and liquid lipids. Such a chaotic mixture is not able to form a densely packed structure any more, the particle matrix possesses a large or dominant fraction of ? and ?′modifications, no or limited ? modification. These particles possess the following advantages [5] compared to SLN® and NLC®:

- increased drug loading (e.g. 1% vitamin A in SLN®, 5% in NLC® and >15% in smartLipids®),
- no or little effect of surfactant on matrix structure, i.e. higher flexibility in choosing surfactants,
- no (or very limited) polymorphic transitions during storage and thus
- firmer drug inclusion on storage, no drug expulsion, long shelf life.

Based on this, the smartLipids® possess clear advantages for producing dermal formulations in cosmetics and pharma, but also for e.g. oral delivery. However, not each randomly taken mixture creates this chaotic structure, still a lipid selection based on certain structural

principles needs to be performed, followed by a screening to confirm the optimal %age of each lipid.

[1] S. Lucks, R. Müller, European patent EP 0 695 497 (1996)
[2] R.H. Müller et al., European patent EP 1 176 949 (2014)
[3] R.H. Müller et al, US patent US 8,663,692 B1 (2014)
[4] Müller, R. H., Ruick, R., Keck, C. M., smartLipids - the next generation of lipid nanoparticles by optimized design of particle matrix, PT.27, DPhG-Jahrestagung, Frankfurt, 24.-26. September 2014
[5] R. Ruick, PhD thesis Freie Universität Berlin, in preparation