Semisolid lipid nanoparticles with thermoresponsive properties: structural and rheological characterization

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One of the main challenges in topical drug delivery is overcoming the skin barrier, particularly the stratum corneum (SC), which prevents transepidermal water loss and limits the penetration of external agents. Lipid-based nanoparticles, such as solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), represent a promising strategy to enhance the delivery of active compounds [1] . Their high affinity for the SC and adhesion to the skin improves penetration and bioavailability, induces an occlusive effect, and enhances skin hydration [2] . However, in topical formulations the efficacy and applicability of the final product is strictly dependent on its rheological properties, and the incorporation of SLNs into conventional dermal formulations can be challenging due to possible incompatibilities and limited SLNs loading [3] . Thus, we developed bulk lipid nanocarrier dispersions with the appropriate semisolid consistency desirable for dermal products and ready for application. This formulation showed thermotropic and thixotropic behavior, with a spontaneous and reversible gel-to-liquid transition from 20°C to 36°C, improving nanosystem spreadability and consequent absorption upon contact with the skin. Small-angle X-ray scattering experiments performed at 20°C and 40°C of both SLNs and NLCs revealed that gelation is associated with the formation of a lamellar liquid crystalline mesophase (Figure 1A). This was confirmed also by the birefringent spherulite structure and Maltese cross patterns revealed by Polarized light microscopy that evidenced the thermotropic nature of the material (Figure 1a insert). Rheological measurements proved the viscoelastic microstructure and thixotropic behavior at both temperatures, with a significant decrease of elasticity at 40°C (Figure 1B). Dynamic Light Scattering measurements on the liquid dispersions showed small and monodisperse population. The addition of a liquid lipid to the core reduced the elastic modulus, likely due to decreased interparticle interactions deriving from lower particle contact and/or differences in particle shape. This may reflect changes in physical state and organization of the lipidic matrix, as suggested by a decrease in the melting point of the lipid core shown by DSC and broadening of SAXS peaks.

Keywords:
drug delivery, lipid nanoparticles, thermoresponsive systems

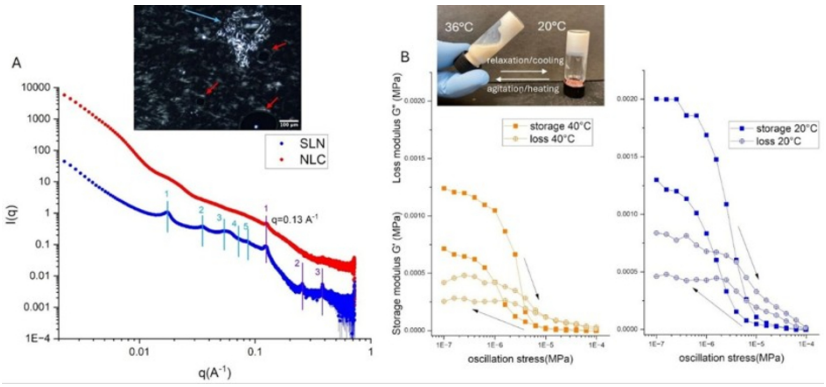

Figure 1: (A) SAXS profile of SLN and NLC liquid crystalline mesophase (inset) polarized optical images showing birefrangent aggregates and Maltese cross patterns. (B) Compex modulus plots at 20°C and 40°C (inset) liquid to solid bulk transition

References:

[1] G. Gabbricci. L. Talarico. I. Clemente. A. Sutinen. C.E. Blanchet. D. Tatini. G. Leone. A. Magnani. Int Jour of Pharm. 688. 126441. 2026
[2] M. Liu. J. Wen. M. Sharma. Curr Pharm Des. 26. 3203–3217. 2020
[3] A. Lippacher. R.H. Muller. K. Mader. Eur. J. Pharm. Biopharm. 58. 561-567. 2004