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TURBISCAN: Accelerating Formulation Success for Lipid Nanoparticles (LNP)

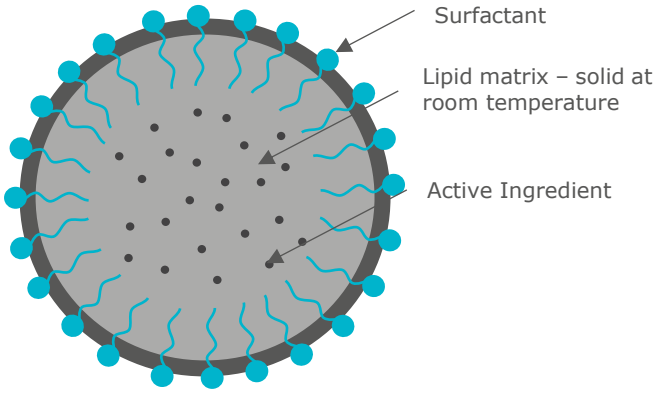
CONTEXT

The development of efficient drug delivery systems remains a key challenge in the pharmaceutical, nutraceutical, and cosmetic industries. **Solid Lipid Nanoparticles** (SLN or LNP) present a promising carrier platform, combining high biocompatibility, protection against drug degradation, and tunable release kinetics. However, current formulation evaluation and optimization processes are hampered by the complexity of dispersion behaviours, scale-up challenges, and the need for rapid, quantitative, and non-destructive assessment methods. Accelerating LNP development and screening requires techniques that can simultaneously provide insight into particle formation, stability, aggregation, and drug loading efficacy with minimal manual intervention.

SOLID LIPID NANOPARTICLES

Lipid Nanoparticles (LNP) are advanced delivery carriers, can be seen as lipid nano-droplets solidified, developed to overcome stability and efficacy limitations of conventional emulsions. Their unique structure and properties provide key benefits:

- Easier redispersion by limit physical destabilization by promoting agglomeration instead of coalescence and minimizing Ostwald ripening due to lipid solidification.
- Active protection: the solid lipid core offers effective protection of encapsulated lipophilic drugs against oxidation.
- Targeting: LNP allow for functionalization with target-specific ligands, making them suitable for applications such as targeted therapy.



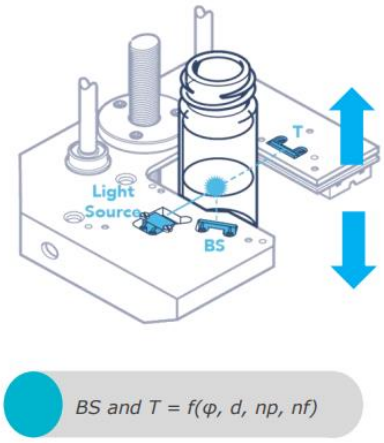
However, formulating stable LNP dispersions remains challenging due to the need for high-energy production methods or solvents, the

tendency of particles to agglomerate, and the difficulty in selecting optimal surfactant systems to ensure both stability and scalability.

To address these formulation challenges, this study utilizes the TURBISCAN to rapidly identify the optimal surfactant and co-surfactant combinations for stable LNP dispersions. Curcumin and β-carotene active ingredients were studied as valuable additive in food and nutraceutical industries.

TURBISCAN: HOW IT WORKS

TURBISCAN technology, based on Static Multiple Light Scattering, consists on sending a light source (880 nm) on a sample and acquiring backscattered (*BS*) and transmitted (*T*) signal all over the height of a sample. By repeating this measurement over time at an adapted frequency, the instrument enables to monitor physical stability. The signal is directly linked to the particle concentration (φ) and size (d) according to the Mie theory:



The measurement of the *BS* and *T* can be performed either in scanning mode, to provide homogeneity and stability measurement, or with very high frequency for fast time-resolved and online measurement. The measurements are done without any dilution & on the native sample.

STABILIZER SCREENING

Identifying an effective surfactant system is a critical stage in LNP formulation, as it directly influences particle size, dispersion stability. In this study, two primary surfactants were selected: Sodium Dodecyl Sulphate (SDS) and Cetyltrimethylammonium Bromide (CTAB), chosen for their strong electrostatic and repulsion interfacial activity promoting a negative surface charge for SDS and a positive one for CTAB.

Each primary surfactant was combined with ten different co-surfactants covering a wide range of hydrophilic–lipophilic balance (HLB) values. The objective was to identify optimal combinations that promote complete dispersion during lipid melting, minimize aggregation upon cooling, and maintain long-term stability.

Oil-in-water emulsions were prepared with 10 % v/v palm oil, 1 wt. % primary surfactant, and 0.5 wt. % co-surfactant, under identical processing and controlled cooling conditions to ensure direct performance comparison.

Example of backscattering variation over time

Figure 1 shows the Δ-backscattering profile as a function of sample height for a representative LNP system after synthesis (10 % v/v palm oil, 1 wt % SDS, 0.5 wt % Span), monitored over 7 days at 25 °C. Each scan corresponds to a different measurement time, from the initial scan (blue) to the final scan (red). The systems were sufficiently turbid so that no transmission signal was detected.

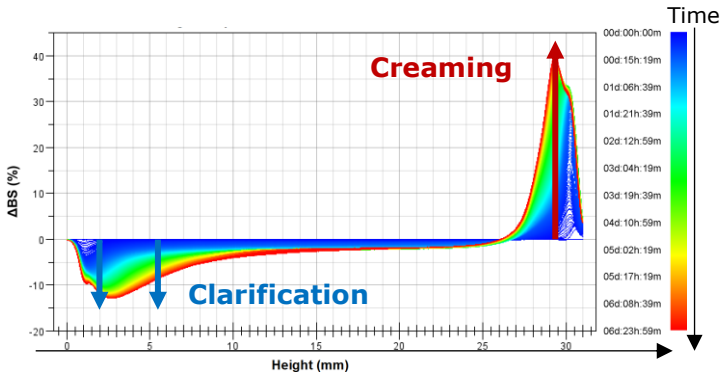


Fig. 1 Delta backscattering in function of sample height (mm) for LNP system with 10v/v% palm oil, 1wt% SDS and 0.5wt% Span

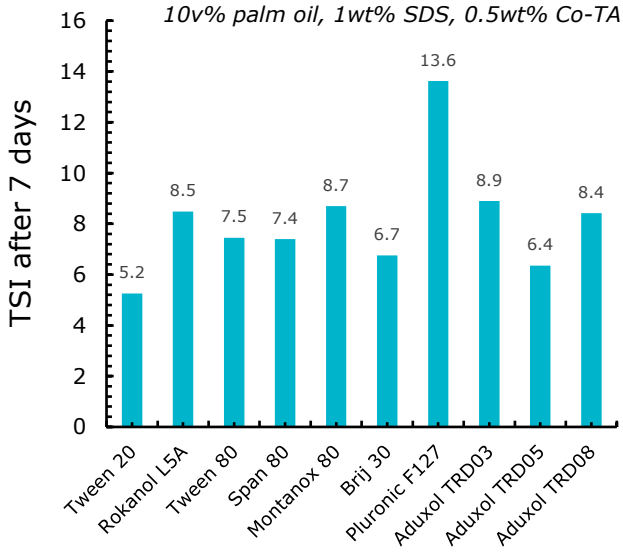
An increase in backscattering was observed at the upper zone of the sample (left side of the graph), corresponding to the upward migration of lipid nanoparticles (creaming). Conversely, the lower region showed a decrease in signal intensity associated with clarification. Notably, the onset of creaming was detected within the first 10 minutes

of analysis, illustrating the high sensitivity of the TURBISCAN to early-stage destabilization.

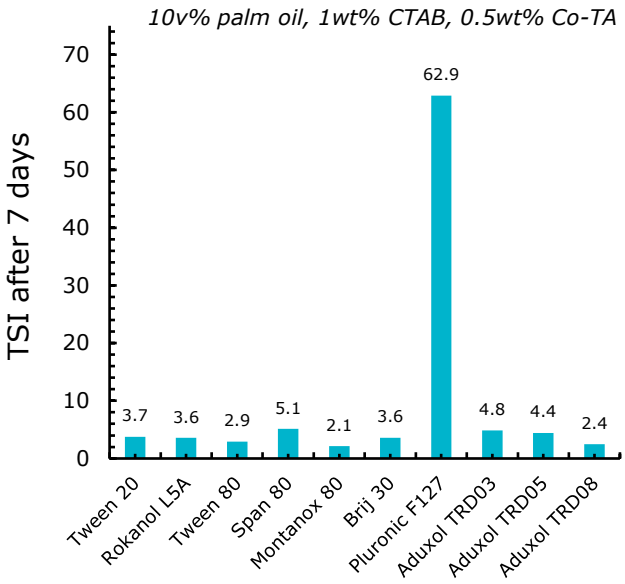
Quantifying destabilization with TSI

Destabilization was quantified using the TURBISCAN Stability Index (**TSI**), which integrates all detected signal variations related to migration phenomena, and particle size changes. At a given ageing time, higher TSI values indicate lower sample stability. A detailed explanation of TSI calculations is available here.

Graphs below present the TSI values after 7 days for both SDS- and CTAB-based systems in combination with the ten co-surfactants tested. The results highlight clear stability differences between surfactant/co-surfactant pairs, allowing rapid identification of the most effective formulations for LNP stabilization.



Graph.1 *TSI after 7 days in function of co-surfactant with SDS surfactant*



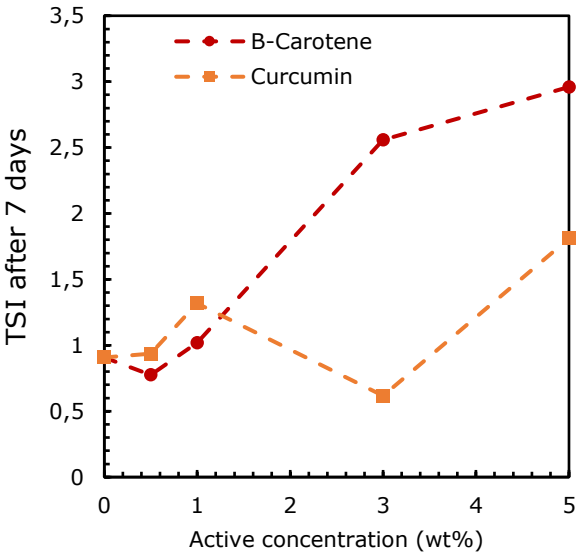
Graph.2 *TSI after 7 days in function of co-surfactant with CTAB surfactant*

From the surfactant screening results, both CTAB- and SDS-based systems formulated with Tween 20 or BRIJ 30 exhibited the lowest TURBISCAN Stability Index (TSI) values, indicating the highest dispersion stability -> More robust formulation.

ACTIVE LOADING EFFICIENCY

For subsequent studies, BRIJ 30 was selected as the co-surfactant of choice due to its consistent performance across both SDS and CTAB. The next objective was to evaluate the robustness of this "ideal" formulation upon addition of active ingredients and under varying loading levels.
Curcumin and β-carotene, selected for their relevance in nutraceutical and food applications, were incorporated at different concentrations into the established LNP composition (10 v/v% palm oil, 1 wt% primary surfactant, 0.5wt% BRIJ 30). Sample preparation and TURBISCAN testing were performed under identical conditions to the surfactant screening phase.

Graph.3 presents the TSI values measured after 7 days as a function of curcumin and β-carotene concentration, highlighting the influence of active ingredient loading on LNP stability.



Graph.3 *TSI after 7 days in function of active ingredient concentration (wt%)*

Based on the ***Graph.3*** obtained from TURBISCAN analysis, we can conclude : The formulation using 1wt% SDS or CTAB and 0.5wt% BRIJ30 can properly encapsulate and remain stable with both **Curcumin** and **β-carotene** even at high concentration. Indeed the TSI remain below 3 after 7 days showing an excellent stability and robustness regarding colloidal and physical stability.

CONCLUSION

TURBISCAN is an indispensable tool for accelerating Solid Lipid Nanoparticle (LNP) development in drug delivery and nutraceutical applications. By providing real-time, non-destructive stability analysis directly on native formulations, it enables rapid identification of optimal surfactant/co-surfactant systems and validates encapsulation performance under high active loading. Early detection of destabilization phenomena saves weeks of conventional testing, streamlining R&D workflows and reducing time-to-market. With its precise, quantitative insights, TURBISCAN empowers researchers to design robust, high-performance delivery systems with confidence.

TURBISCAN RANGE

The world leader in Stability & Dispersibility Analysis