RESEARCH CENTER PHARMACEUTICAL ENGINEERING

Formulation Components' Role in Shaping Continuous Nanocarrier Production through Impingement Jet Mixing

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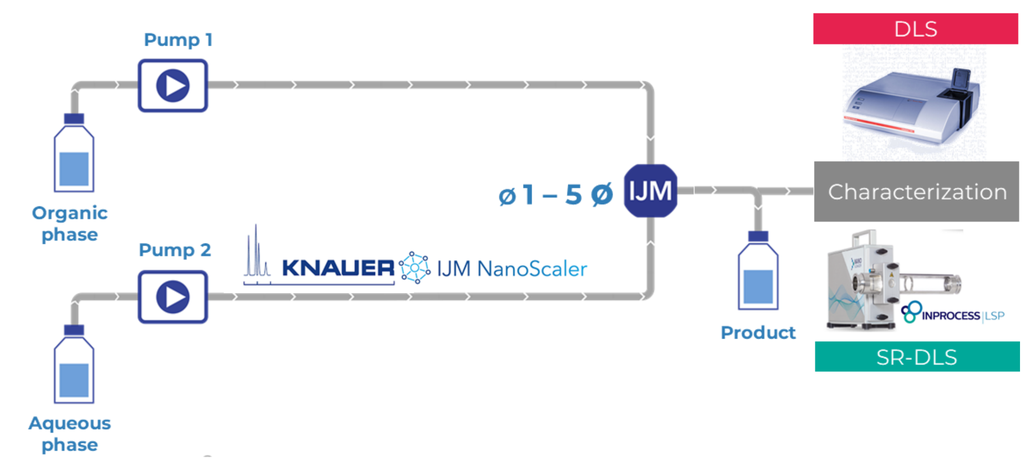
INTRODUCTION

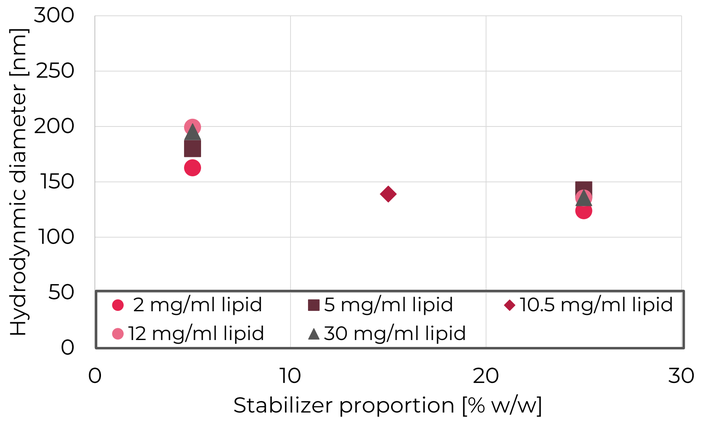
The predominant approach for manufacturing nanocarriers on an industrial scale is batch production [1]. Here, a specific quantity of raw materials undergoes a stepwise transformation from a raw state into a refined dispersion. Once the processing line is complete, the dispersion is filled into dosing units, subjected to quality control, released for use, and the production unit is prepared for the next batch. However, this involves the risk that a batch may not meet the release specifications and has to be discarded, or scalability problems may occur [2,3]. One way to overcome these challenges is to produce nanocarriers in a continuous production line that includes real-time monitoring and in-line quality control. Flash nanoemulsification using impingement jet mixing (IJM) represents a promising bottom-up approach to enable the production of nanocarriers that meet the final product specifications [4]. In addition, spatially resolved dynamic light scattering (SR-DLS) has the unique capability to measure droplet sizes in-line under flow conditions, including very turbid samples [3]. This study focused on optimizing the amount and ratio of various formulation components to tailor lipid-based nanocarriers via IJM considering size measurements.

MATERIALS & METHODS

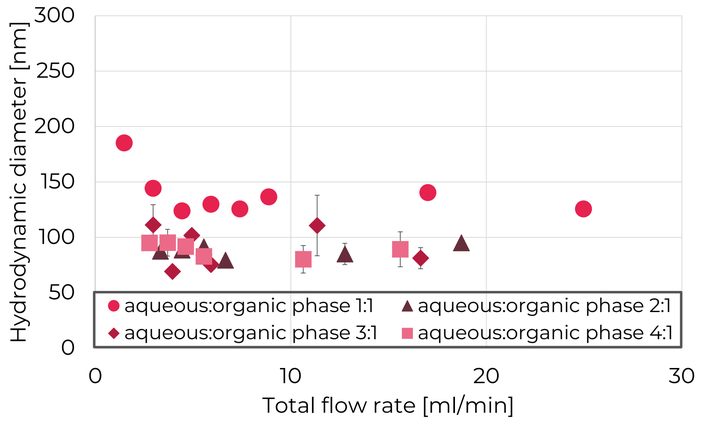


- Organic phase: Labrafac™ lipophile WL 1349 (lipid) in ethanol in various concentrations (2 -30 mg/ml)
- Aqueous phase: Tween® 80 (stabilizer) in water in various concentrations (0.1 – 7.5 mg/ml)
- Investigation of the following parameters:
  - Variation of the flow rates at 1:1 phase ratio using IJM1 and different lipid and stabilizer concentrations
  - Variation of the flow rates at various aqueous to organic phase ratios (1:1 – 4:1)
- Characterization: DLS and SR-DLS

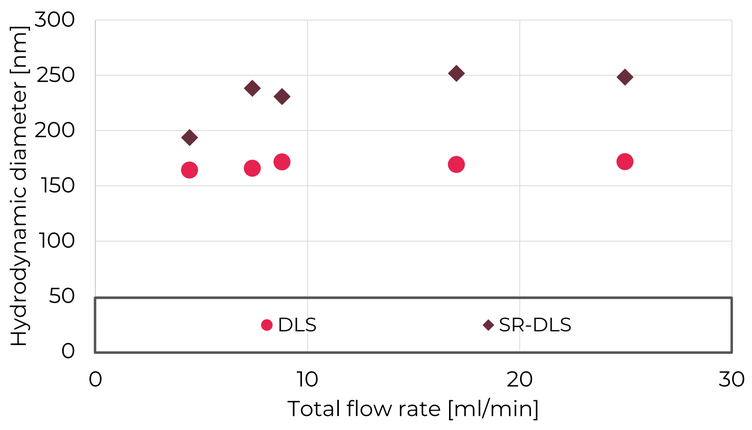
RESULTS



Most pronounced effect of stabilizer proportion on size



Size dependent on total flow rate and ratio of the two phases



Slight size deviations of DLS and SR-DLS due to different light sources

CONCLUSION

This study revealed that the droplet sizes were directly related to the applied stabilizer concentrations, the aqueous to organic phase ratios and the total flow rates. Thereby, comparable results were obtained using DLS and SR-DLS highlighting that undiluted samples can be measured via SR-DLS even in the presence of an organic solvent. This study is therefore a first step toward formulation optimization and targeting of a continuous bottom-up nanomanufacturing line equipped with process analytical technology (PAT) including SR-DLS to facilitate the manufacturing of adequate end products.

References:

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The Research Center Pharmaceutical Engineering (RCPE) is funded within the framework of COMET - Competence Centers for Excellent Technologies by BMK, BMAW, Land Steiermark and. SFG. The COMET program is managed by the FFG.

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