

Crystal Engineering strategies for the design of tailor-made Curcumin crystals as Pickering stabilizers

Abstract

Emulsions are multiphase systems formed by two immiscible phases, usually water and oil, which are made stable and homogeneous by the addition of a stabilizer, usually an amphiphilic molecular surfactant. Emulsions are widely used systems with applications ranging from food, cosmetics, pharmaceuticals, and agrochemical industries. Due to their intrinsic thermodynamic instability, emulsions naturally tend to destabilization phenomena, like sedimentation, coalescence, and phase separation. Particularly in surfactant-based emulsions, where the interphase is stabilized by a thin molecular layer, mechanical and thermal stresses have a high impact on the formulation stability. In recent years, Pickering emulsions have gained growing interest. They are a particular emulsion system, where the interphase is stabilized by solid particles, anchoring at the droplet surface, making the system homogeneous.

Being the solid particles, the stabilizing element, the control over their properties is crucial.

The work presented here aims to address a central challenge in the design of Pickering formulations, the need for particles with tailored properties. In this context, crystallization techniques combined with a crystal engineering approach

Among the advantages of Pickering formulations, an extensive use of naturally derived materials, such as cellulose, proteins, and fat crystals, was reported. In this work, the use of polyphenol crystals as Pickering stabilizers is investigated, focusing on curcumin as a model compound.

The first part of the work focuses on developing a crystallization strategy based on antisolvent crystallization for the production of curcumin particles with reduced size. An extensive solid-state characterization, including Raman spectroscopy, Powder X-ray diffraction (PXRD), Solid State NMR (SSNMR), and Differential Scanning Calorimetry (DSC) analysis, demonstrates the formation of curcumin metastable form III, which was tested as a Pickering stabilizer for the stabilization of W/O emulsion. The particle size and shape were addressed by Scanning Electron Microscopy (SEM) image analysis, and the wettability was determined by the measurement of the contact angle.

Subsequently, the production of recrystallized curcumin particles in pure polymorphic form I and III will be addressed, where the antisolvent technique is combined with a seeding strategy, to ensure control over a specific polymorph nucleation. The particles, comparable in size and shape, are used to investigate the influence of polymorphism in interphase stabilization, together with the effect of particle concentration and water content.

Lastly, the thus obtained formulations are tested as a delivery system for hydrophilic active ingredients. Methylene Blue was selected as the model compound, and its release kinetics from the

formulations was determined by in-vitro dialysis release studies, with the released MB quantified via UV-Vis spectroscopic technique.

Overall, this thesis demonstrates the strong potential of integrating crystal engineering strategies into the design and production of Pickering particles. It provides a crystallization-based methodology to tailor particle properties and improve the understanding of their role in multiphase systems, offering a basis for the future development of more rational and predictive approaches to Pickering formulation design.