How phospholipids stabilize macro and nanoemulsions?

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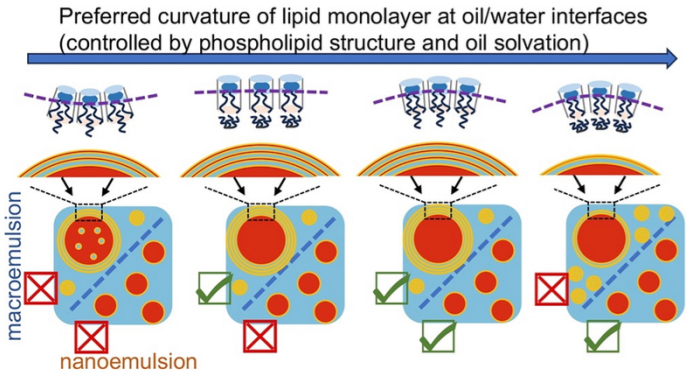
Delivering an emulsion intravenously for nutrition or drug delivery requires droplets to remain metastable at the sub-micronic scale in high ionic strength conditions. There is a large interfacial area to cover with a surfactant monolayer in these nanoemulsions and the amphiphilic species must be non-toxic. Phospholipids are thus industrially used to meet these constraints. However, their low preferred curvature, which sensitively depends on molecular structures and interactions, is not favorable for stabilizing emulsion droplets. We have investigated this problem to find a rationale for choosing formulation conditions leading to metastable emulsions, based on a fine understanding of interfacial properties and structure.
Four phase diagrams were established for ternary aqueous systems containing either DOPC or POPC as the phospholipid and hexadecane or miglyol 812 as the oil. Droplet interfaces were probed using small-angle neutron scattering and the amount of adsorbed lipid was determined using separation and Raman spectroscopy. The metastability of both nano and macro emulsions was systematically assessed over weeks using light scattering.
We show that a lipid monolayer stabilizes nanoemulsion droplets and display excellent metastability if the preferred curvature is positive and large enough, even without any added charges or at high ionic strengths. In contrast, macroemulsion droplets are stabilized with a lipid multilayer, which should possess a positive preferred curvature but also a good enough interfacial anchorage, which is lost upon increasing the preferred curvature. Overall, we provide a mechanistic description through which we can understand the impact of molecular changes in the formulation on emulsion metastability, through the analysis of the lipid film preferred curvature, layering, and interfacial anchorage. These results demonstrate how a virtuous circle can be established between fundamental soft matter approaches and industrial applications in complex formulations.

Keywords:
Parenteral, Emulsion, Self-assembly, Curvature, Metastability



Interplay between spontaneous curvature of the phospholipid monolayer and emulsion metastability

References:

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