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On the structure and function of lipid nanoparticles for delivery of bioactive molecules

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Non-lamellar lipid aqueous phases, such as reverse cubic or hexagonal phases, have increasingly been used to entrap biomolecules. We here discuss encapsulation of two key types of enzymes of different sizes, namely Aspartic protease (34 KDa), Beta-galactosidase (460 KDa) as well as heme proteins of importance for e.g. food iron supply. Although the curvature of the lipid aqueous interfaces in these phases determines the size of the aqueous cavities and hence the space given to the enzyme, the interaction between the enzyme and the lipid layer is an important factor that controls the efficiency of the encapsulation. We used mixtures of acylglycerides and acyldiglycerides, which can form highly swollen sponge phases (L3), with aqueous pores up to 13 nm of diameter and with the help of the dispersing agent polysorbate 80 (P80) they form well defined nanoparticles in excess water.Size exclusion chromatography show efficient encapsulation of both enzymes, yet they retained their enzymatic activity over months, surpassing the storage stability of pure enzymes in solution. The reason for this can be understood in terms penetration of the enzymes into the formed lipid bilayer as shown by Raman spectroscopy and neutron reflectometry on supported lipid bilayer of same composition. This has been confirmed by neutron spin echo and molecular dynamics simulations.

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