

Probing the Complex Loading-dependent Structural Changes in Ultrahigh Drug-loaded Polymer Micelles by Small-angle Neutron Scattering

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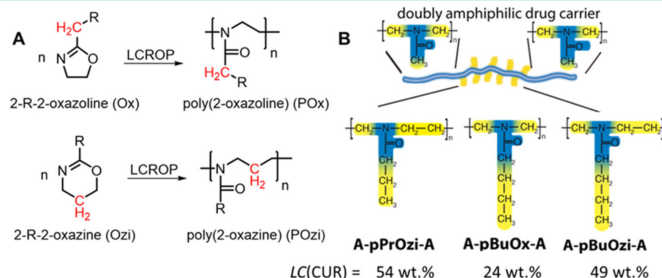
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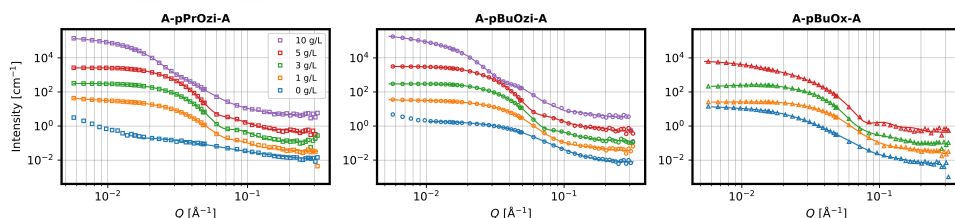
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Curcumin-Formulations based on POx and POzi

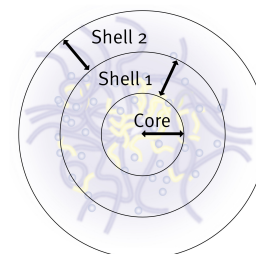
One important challenge in pharmaceutical technology is the formulation of strongly hydrophobic drugs. Amphiphilic block copolymer based on poly(2-oxazolines) and poly(2-oxazines) show excellent potential as solubilizers for drugs like Curcumin (CUR) with high loading capacities (LC) and stabilities of the loaded micelles. To better understand the solubilisation process and the availability of the drug in the organism, it is necessary to learn more about the drug-loaded aggregates. It is commonly assumed that the drug stabilisation process is dominated by the hydrophobic micellar core, but recent studies, like this one, show that the whole polymer including its hydrophilic end groups has to be involved to explain the abnormally high loading capacities.



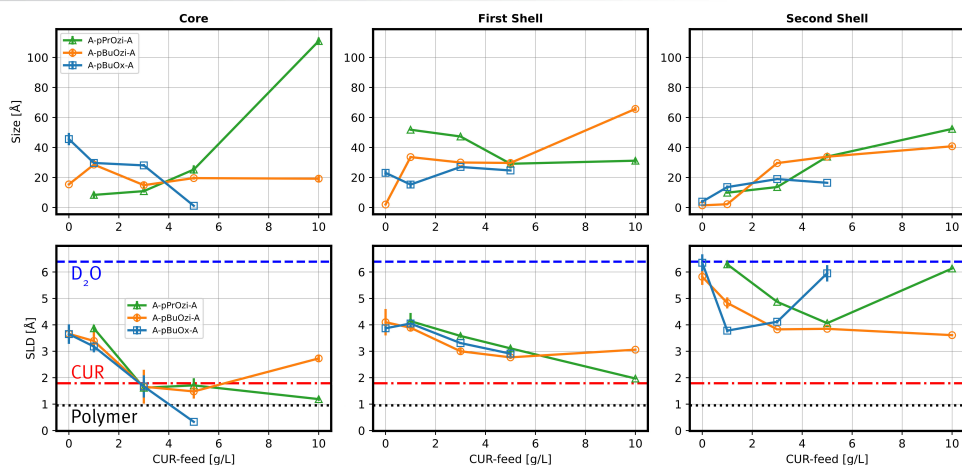
Small-angle Neutron Scattering



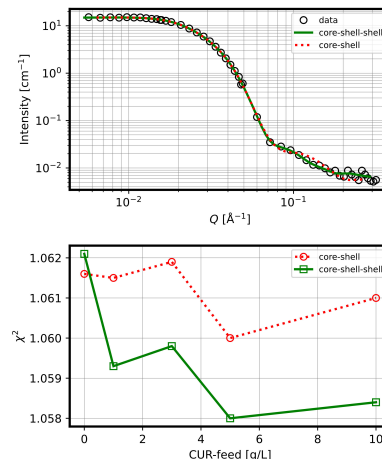
Choice of Fit Model



Fit Results



Comparison of one- and two-shell model:



Drug-Localisation in Micelle

By combining the structural information of the drug-loaded micelles with experimental data on their loading capacities, it was possible to calculate the amount of drug stabilised by the micellar core and more hydrophilic shell. At low CUR concentrations, the core is still capable of taking up everything or large portions of it by its own. But with increasing drug loading, the core uptake reaches a limit and the remaining CUR is stabilized by the hydrophilic end groups. Interestingly, the oxazoline variant (A-pBuOx-A) is unable to surpass loading capacities of 30 wt% before precipitation, while both polymers with an oxazine-based main chain easily reach 50 wt% or more. The middle-blocks seem to determine if the polymer is able to stabilize the drugs, but the interplay between the side chains and the hydrophilic end groups enables ultrahigh loading capacities.

