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The fate of therapeutic nanoparticles in a model biological medium: interactions with serum albumin

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In the field of nanomedicine, nanostructured nanoparticles (NPs) made of self-assembling prodrugs emerged in the recent years. In particular, the squalenoylation concept has been applied to several therapeutic agents with promising results.[1,2] These nanoparticles allow a high encapsulation rate of the active principle, the protection from quick degradation, and a good control of the targeting and release. Beyond the high potential of these NPs, there is still a need for a better understanding of their evolution in biological media. The colloidal stability of the NPs, their interaction with proteins and the impact of their internal nanostructure on their efficacy are essential questions to go towards a better understanding of the mechanism of their fate in the organism (nanoparticle disassembly, targeting etc…).

We chose to investigate these questions on the particular case of Squalene-Adenosine (SQAd) nanoparticles,[3] whose neuroprotective effect has already been demonstrated in murine models and model biological media.[4] From the combination of multiple techniques (neutron and x-ray scattering, cryogenic transmission electron microscopy, circular dichroism, fluorescence spectroscopy, isothermal titration calorimetry and DFT calculations) we have investigated the interactions between the SQAd NPs and the serum albumin, one of the main proteic components of blood plasma. We show that albumin affects the colloidal stability of the nanoparticles but also partially disassembles the nanoparticles by forming SQAd-albumin complexes. Albumin should thus play a crucial role in the transport of the prodrug, while the nanoparticles would act as a circulating reservoir in the blood stream.[5]

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