Bilayers at the ILL

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pH-induced rearrangements in lipid bilayer causing in drug release from pH-sensitive liposomes

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The development of stimuli-sensitive, particularly pH-sensitive, liposomal nanocontainers for targeted drug delivery is of great value nowadays. The pH-sensitivity of liposomes can be achieved by embedding the pH-switcher into the lipid bilayer, thus the decrease of the pH value would result in release of the entrapped compound.
In this study we examined the pH-dependent kinetics of changes in liposomal membrane containing two types of pH-switchers by SAXS technique combined with the stopped-flow apparatus.
The first type of pH-switcher was the lipid-like compound based on morpholinocyclohexanol. With the acidification of the media the pH-sensitive lipid undergoes the conformational change that results in thinning of the lipid bilayer (creating “defects”) and thus increases the permeability of liposomal membrane. Kinetic release experiments showed that the entrapped compound began to release from the pH-triggerable liposomes just after decreasing the pH value of the media. The notable changes in the SAXS curves appeared at 11 seconds after the pH change from 7.0 to 4.0 and resulted in formation of a peak at q=1.15 nm-1. Over time the peak became more pronounced, what could be attributed to the formation of ordered structure. Only correlation peak was changing with time implying that the vesicular structure of the liposomes was not disrupted in agreement with previous DLS and cryo-TEM results.
The second type of pH-switcher was represented by the derivative of cholesteric acid. The protonation leads to the rotation of the molecule in the lipid bilayer. The initial state of liposomes with switcher of the second type was the same as for the first ones. But the changes in liposomal structure in the second case became to be evident from the 2 second after pH change from 7.0 to 4.0.

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