Studying shear-stress sensitive liposomes using microfluidics

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INTRODUCTION: Heart diseases are among the top causes of death worldwide [1]: up to 50 % of people struck by heart attack die before arriving at the hospital. A shear-stress sensitive liposome [2] loaded with a vasodilator is a valid tool to overcome the high risk of mortality. To investigate the morphology and the mechanical properties of such promising phospholipid liposome, small angle X-ray scattering (SAXS) technique has been combined with microfluidics.

METHODS: The shear-sensitive artificial liposome 1,3-diamide Pad-PC-Pad has been synthesized [2]. The natural and no shear-stress sensitive 1,2-diester DPPC (Lipoid, Zug, Switzerland) has been used as control. Both lipid formulations were prepared by the thin lipid film hydration method and the extrusion technique [3]. Polycarbonate membranes were used to achieve liposomes of around 100 nm in diameter. The microfluidic devices were built using soft lithography combining poly(di-methylsiloxane) (PDMS), UV-curable adhesive material, and polyimide films [4]. The technique allows for building flexible and reproducible microfluidic channels mimicking diseased blood vessels [5]. SAXS measurements were carried out at the beamline ID02 (ESRF, Grenoble, France) using a photon energy of 12.4 keV and a beam size of 20×60 µm^2. The liposomes were measured both in conventional glass capillaries and in microfluidic devices. Flow simulations were performed to predict the suitable range of shear stress values, where the liposomes properties as to be studied [5].

RESULTS: Figure 1 shows a simplified scheme of the mechano-sensitive liposome based on the phospholipid Pad-PC-Pad. The inner cavity is designed to incorporate a vasodilator such as nitroglycerin (a). Flow simulations of micro-channels (b) are a valuable tool to test a wide range of shear rate values according to those one found in healthy and diseased human coronary arteries [6]. The SAXS data, which are still under evaluation, reflect the structural properties of the liposomes. Potential structural changes due to the applied shear rates can be revealed.

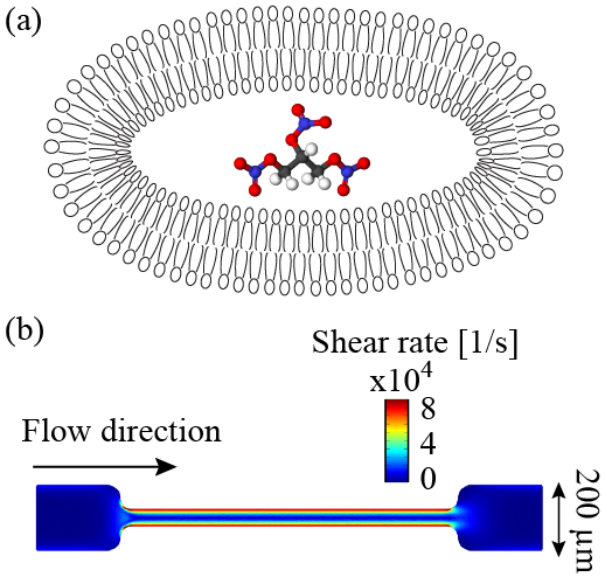

Fig. 1. Pad-PC-Pad mechano-sensitive liposome containing nitroglycerin (a); shear rate profile of a micro-channel setting the flow rate at 1 µL/s (b).

DISCUSSION & CONCLUSIONS: The optimization of the local release of a vasodilator using a phospholipid liposome is not trivial. SAXS combined with microfluidics is a precious tool to determine the structural changes due to the enhanced shear stress, as present in the diseased, stenosed human artery.

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