Comparing microfluidic devices and established glass capillaries in laboratory-based X-ray scattering of liposomes as nano-containers for drug delivery

M. Buscema[1], T. Pfohl[2], A. Zumbuehl[3], and B. Müller[1]

[1]Biomaterials Science Center, University of Basel, Basel, Switzerland. [2]Department of Chemistry, University of Basel, Basel, Switzerland. [3]Department of Chemistry, University of Fribourg, Fribourg, Switzerland.

INTRODUCTION: Conventional small angle X-ray scattering (SAXS) is a powerful method to understand the morphology of self-assembled phospholipid nano-containers for targeted drug delivery.[1] SAXS measurements are usually performed in glass capillaries. Here, we show that SAXS-signals obtained from tailored microfluidic devices, made out of a UV-curable adhesive material, poly(di-methylsiloxane) (PDMS) and polystyrene, provide additional information on the structural parameters of liposomes such as shape, size, and bilayer thickness. The flow conditions can be adjusted to study clinically relevant situations.

MATERIAL AND METHODS: We tested two phospholipids, the 1,2-diester DPPC and the 1,3-diamide Pad-PC-Pad. DPPC was from Lipoid (Zug, Switzerland) while Pad-PC-Pad was synthesized as described previously.[2] Both lipids were hydrated with ultrapure water, submitted to freezing and thawing and then to extrusion in order to form unilamellar vesicles 100 nm in diameter[3]. DPPC vesicles suspensions were made at 5, 10, and 14 mg lipid per 1 ml of water and Pad-PC-Pad at 16 mg per 1 ml of water. The liposomes were tested both in glass capillaries and microfluidic devices. Glass capillaries were 1.5 mm in diameter with a wall thickness of 0.01 mm. Microfluidic devices were built using PDMS soft lithography combined with polystyrene film.[4] The device pattern consisted of 150 and 50 µm horizontal channels. SAXS measurements were done on a Bruker Nanostar setup with a microfocus X-ray source (Cu-K_α-radiation, λ=1.54Å). The beam was collimated to a diameter of about 200 µm and the signal was recorded using a 2D HiStar detector (Bruker AXS, Madison, WI, USA). Measurements in glass capillary were carried out under vacuum condition and in microfluidic devices under atmospheric pressure.

RESULTS: Figure 1 shows the *q*-plot of DPPC vesicles obtained from the glass capillary (integration time 1 hour) and from the microfluidic device (integration time 4 hours).

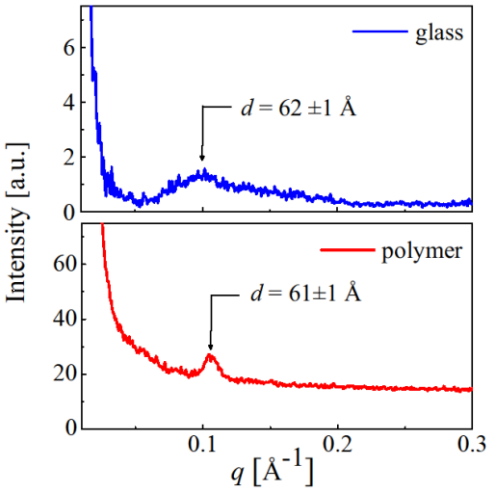

Fig. 1. SAXS signals of DPPC in glass capillary (top panel) and in a microfluidic device (lower panel) with a concentration of 14 mg/ml.

Both graphs exhibit a peak at q = 0.101 Å^{-1} for glass capillary and q = 0.104 Å^{-1} for microfluidic device, which corresponds to the periodicity of the lamellar structure of d = 62±1 Å and d = 61±1 Å respectively, characteristic for DPPC[5]. The signal-to-noise ratio is comparable for the microfluidic device and the glass capillary.

CONCLUSIONS: This SAXS-study confirms that is possible to investigate phospholipids with in-house X-ray facility. Here, tailored polymeric microfluidic devices show comparable results with respect to the established thin-walled glass capillaries.

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