

# Polymer and Colloid Highlights

Division of Polymers and Colloids

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## Shear Stress as Drug Delivery Trigger

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In Switzerland over 20,000 people die each year from an atherosclerosis-derived cardiovascular disease, accounting for 37% of all deaths. Mortality is highest in the first hour after a heart attack. It is therefore important to have efficient first-line treatments in the emergency vehicle. Currently, an injection of the vasodilator nitroglycerine acts on the entire vasculature, which can lead to a dangerous drop in blood pressure without treating the diseased stenosed vessel responsible for a heart attack or stroke. A preferential release of a vasodilator at the site of a stenosis would greatly improve both the acute treatment by a selective vasodilatation and the subsequent quality of life of the patient.

There is no specific biomarker overexpressed at the site of a stenosis in diseased arteries. Therefore, it is impossible to use a standard biological targeting factor. Under a grant of the Swiss National Science Foundation NRP 62 'Smart Materials', we asked ourselves if it was possible to use the tenfold increase in shear stress between a healthy and a diseased artery as a purely physics-based trigger for targeted drug delivery (Fig. 1).<sup>[1]</sup>

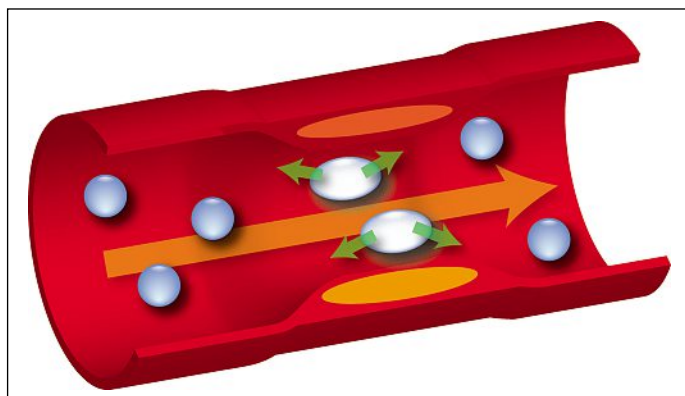


Fig. 1. Concept of using changes in local shear stress as a purely physical trigger for targeted drug delivery to stenosed arteries.

A new type of phospholipid vesicle was introduced: Natural liposomes made from eggPC leak their content spontaneously and will do so even more if they are shaken. Other liposomes

made from 16:0 SM or DPPC do not leak spontaneously or when shaken. However, vesicles from the artificial synthetic 1,3-diamidophospholipid Pad-PC-Pad<sup>[2]</sup> with a lentil-shaped morphology show no spontaneous leaking but can release their content under mechanical stress. This observation qualifies these vesicles as drug delivery vehicles.

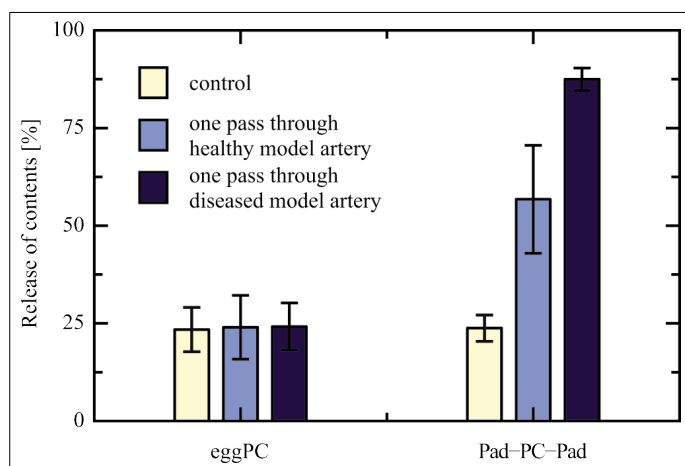


Fig. 2. Proof-of-concept that it is possible to use a mechanosensitive phospholipid vesicle as shear-sensitive drug delivery vehicle. 5(6)-Carboxyfluorescein release from designed artificial phospholipid Pad-PC-Pad vesicles is compared to release from natural eggPC vesicles.

The Pad-PC-Pad vesicles were loaded with the self-quenching fluorescent dye 5(6)-carboxyfluorescein and passed through an artificial cardiovascular system. An extracorporeal heart pump provided appropriate hemodynamic flow and temperature conditions. It was linked to a model of healthy and diseased artery morphology. After one passage through this system, the released carboxyfluorescein was measured and a significant difference between the two systems was found. No effect was measurable with natural phospholipids such as eggPC.

Using the human body's own physics as a drug delivery trigger is a highly attractive concept and might find a wide field of applications. Indeed, recently Korin *et al.* used the same concept in order to target stenosed vasculature with a shear-responsive nanoconstruct.<sup>[3]</sup> The time seems ripe for mechanosensitive drug delivery.

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