Exploring Shear-sensitive Liposomes

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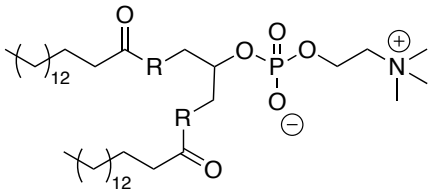
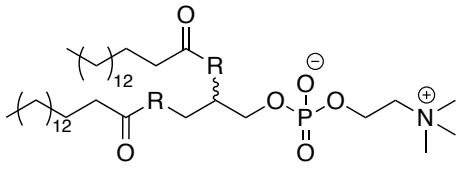
Liposomes of the artificial phospholipid Pad-PC-Pad (pictured below) show a surprisingly low complement activation related pseudo allergy response,[1] they are of lenticular shape and shear-sensitive.[1,2] These facetted liposomes release their cargo, when they are exposed to mechanical forces, whereas if they are at rest the embedded content remains inside the liposomes.[2] This mechano-sensitive behavior of the liposomes could be used as a novel trigger in targeted drug delivery.[3] Shear-stress differences in blocked arteries could then trigger the release of e.g. a vasodilator from liposomes for the acute treatment of myocardial infarction patients.



Pad-PC-Pad R = NH
Pes-PC-Pes R = O



Pad-Pad-PC R = NH
DPPC R = O

In order to understand the formation of facets and the mechano-sensitive behavior of Pad-PC-Pad vesicles, a library of phospholipids with and without hydrogen bond forming linkers, different tail lengths and with the natural 1,2-substitution pattern as well as the artificial 1,3-substitution pattern at the backbone were synthesized. Furthermore, release data were determined in order to understand which parameters in the lipids influence their mechano-sensitivity. From our observations, one can conclude that lipids with intramolecular hydrogen bonding form facetted d-formed[4] or cubic vesicles, whereas the ones without the ability to form hydrogen bonds present spherical liposomes. From the investigated lipids, Pad-PC-Pad is the most promising candidate for targeted drug delivery induced by shear-stress due to its high release under mechanical stress and its high stability over time.

[1] S. Bunga, M. Buscema, S. Matviykiv, *et al.*, *Nanomed. NBM*, **2016**, *12 (3)*, 845.
[2] M. N. Holme, I. A. Fedotenko, D. Abegg *et al.*, *Nature Nanotechnol.* **2012**, *7*, 536.
[3] D. Mellal, A. Zumbuehl, *J Mater. Chem. B* **2014**, *2*, 247.
[4] R. Tanasescu, M. A. Lanz, D. Mueller, *et al.*, *Langmuir*, **2016**, *32 (19)*, 4896.