# Investigations on the release and transfer of hydrophobic model compounds from colloidal lipid formulations

Type of project: Bachelor (10 or 15 ECTS) or Master (30 or 45 ECTS)

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Language: Danish or English

Project description

Colloidal lipid formulations (liposomes, lipid nanoparticles, Figure 1) can be used for solubilization of poorly water-soluble drugs, e.g. to enable intravenous administration [1]. Moreover, they may also enable targeted drug delivery as they accumulate passively in diseased tissues, such as tumor tissues, due to the disturbed endothelia (enhanced permeation and retention (EPR) effect). For drug targeting purposes, however, the drug needs to be retained in its carrier long enough to accumulate sufficiently in the tumor tissue. Knowledge about drug release characteristics is thus of uppermost importance for the development of colloidal drug carriers for drug targeting purposes.

After intravenous injection, lipophilic drugs are usually very rapidly released from their carrier (nanoparticle, liposome, etc.) into the physiological sink [2,3]. Two different mechanisms of drug transfer from the carrier to lipophilic acceptor phases (such as lipoproteins) have been suggested in dependence on the physicochemical properties (e.g. water solubility) of the drug [4].

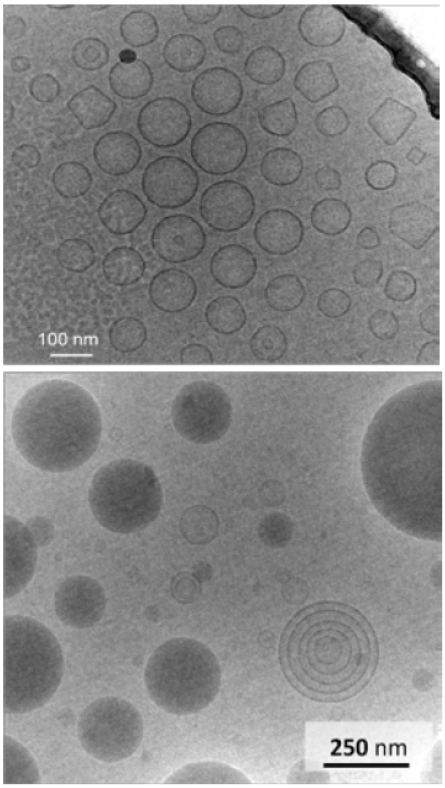


**Figure 1:** Electronmicroscopic images of liposomes (top) and a nanoemulsion (bottom).

The aim of a projects is to get more insight into the mechanism of drug release and transfer of hydrophobic drugs from liposomes and other lipid-based nanoparticles (nanoemulsions, solid lipid nanoparticles) to well-defined acceptor phases (liposomes, micelles) as well as physiological media such as serum. A model drug (pTHPP or mTHPP) with a very similar chemical structure as temoporfin (mTHPC) will mainly be used in addition to other hydrophobic model compounds (e.g. hydrophobic dyes). Temoporfin, a water-insoluble, highly hydrophobic (logP about 9) is a highly potent second-generation photosensitizer and a liposomal formulation is currently in clinical studies to overcome problems associated with the solution formulation Foscan® [5].

Current projects are focusing on elucidation of the recently observed distinct differences in release properties of two structurally very similar porphyrins (figure 2) and on the impact of excess of stabilizer (e.g. poloxamer, polyvinylalcohol) on stability and drug release. The latter project will be in cooperation with the University of Braunschweig (Germany).

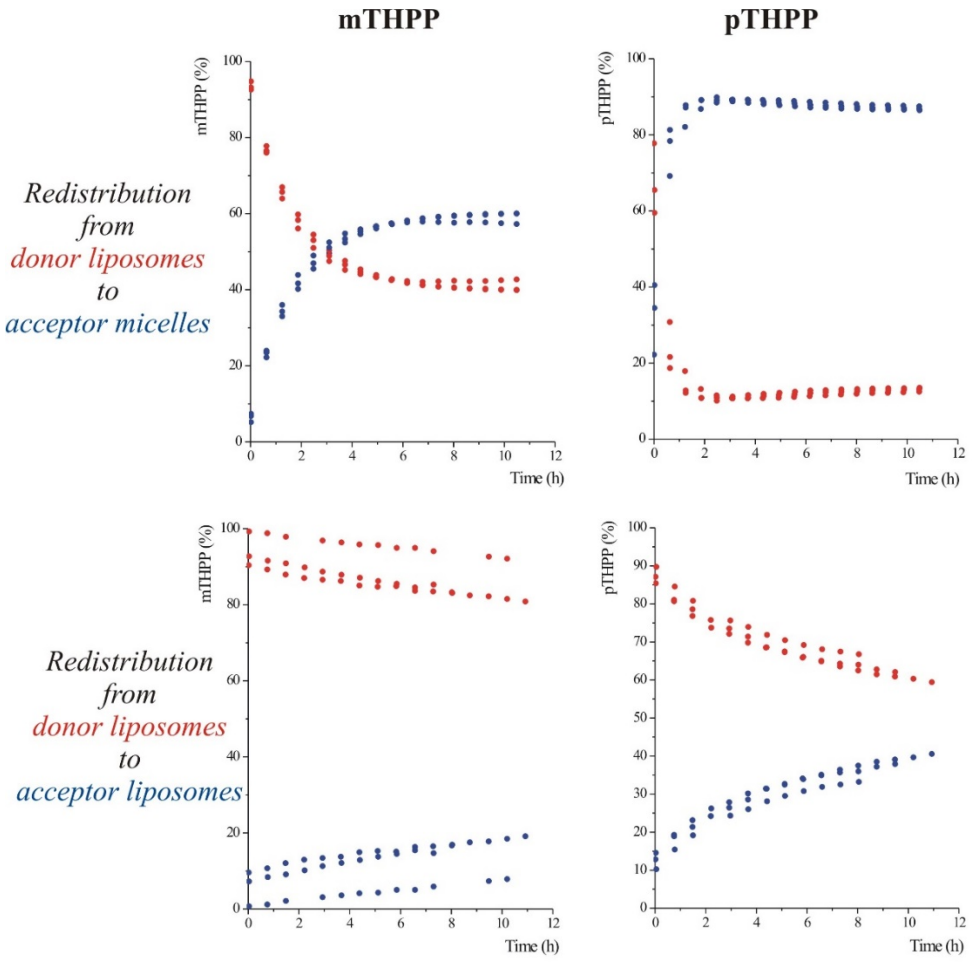


**Figure 2**: Redistribution of mTHPP (left) and pTHPP (right) from liposomes to acceptor micelles (top) or liposomes (bottom). From Master thesis by Kirishana Rajakulendran, SDU 2019.

## References


[1] Bunjes, H. 2010. Lipid nanoparticles for the delivery of poorly water-soluble drugs. J. Pharm. Pharmacol. 62, 1637-1645.

[2] T. Takino, K. Konishi, Y. Takakura, M. Hashida (1994). Long circulating emulsion carrier systems for highly lipophilic drugs. Biol. Pharm. Bull. 17, 121.

[3] A. Fahr, P. van Hoogevest, S. May, N. Bergstrand, M.L.S. Leigh (2005). Transfer of lipophilic drugs between liposomal membranes and biological interfaces: Consequences for drug delivery. Eur. J. Pharm. Sci. 26, 215.

[4] S. Loew, A. Fahr, S. May (2011). Modeling the release kinetics of poorly water-soluble drug molecules from liposomal nanocarriers. J. Drug Del. 2011, Article ID 376548, 10 p.

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