Cochleate cylinders for drug delivery

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

Project description

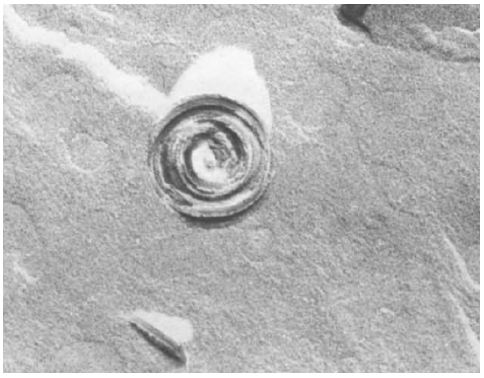

Figure 1: Electronmicroscopic image of a cochleate cylinder (from [1]).

Upon addition of multivalent cations (e.g., calcium ions) to negatively charged phospholipid vesicle suspensions, compact structures with lipid bilayers tightly packed in a spiral arrangement are formed. These structures have first been described by Papahadjopoulos and co-workers in 1975 and – due to their spiral structure – the term "cochleates" has been introduced [1]. Due to the tightly packed lipid structure, cochleates possess a higher stability under harsh conditions such as in the gastro-intestinal tract compared to suspensions of unilamellar vesicles. Moreover, as the formation of cochleates is a reversible process, cochleates generally may provide the possibility of triggered drug release. Although cochleate formulations have already been studied for drug delivery purposes, their formation process and structural features, as well as parameters influencing drug release are still not fully explored. Cochleates have already been investigated as drug delivery system for, e.g., amphotericin B [2] and vaccines [5]. Despite these remarkable results, the potential of cochleates for drug delivery purposes compared to other lipid-based formulations such as liposomes and lipid nanoparticles is still not fully explored.

The projects will focus on cochleates or similar structures (e.g. particles composed of tightly packed lipid bilayers) with respect to drug delivery. Major aims are to better understand the mechanism of cochleate formation as a basis for optimization of the formulations (e.g. structure and size homogeneity), feasibility of cochleate preparation by using natural negatively charged phospholipids as well as lipid mixtures and to comprehensively investigate drug release from cochleate formulations under physiologically relevant conditions. As it has been shown that high salt concentrations can induce the formation of tightly packed multilamellar particles also from neutral phospholipids [4,5], investigations on the effect of salts on the structure formed by neutral phospholipids such as phosphatidylcholine, is of interest.

References

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[3] S. Gould-Fogerite, M. Kheiri, F. Zhang, R.J. Mannino. Cochleate delivery vehicles: Applications in vaccine delivery. J. Liposome Res. 10 (2000) 339-358.

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