Evaluation of alternative methods for the preparation of nanoemulsions

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

Project description

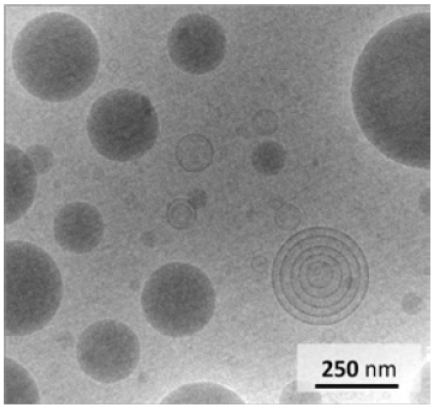

Figure 1: Electronmicroscopic image of nanoemulsion (Lipofundin prepared by high-pressure homogenization).

Colloidal lipid formulations such as liposomes and nanoemulsions can be used for solubilization of poorly water-soluble drugs, e.g. to enable intravenous administration [1]. Moreover, due to the disturbed endothelia in diseased tissues such as tumor tissues, nanoparticles can passively accumulate in these tissues (enhanced permeation and retention (EPR) effect, [2]) providing the possibility of passive drug targeting. Due to the increased demand on cholesterol in tumor tissues and thus increased uptake of low density lipoprotein (LDL), LDL-like formulations have gained high interest for tumor targeting [3]. However, preparation of such LDL-like formulations is often rather complicate and difficult to scale-up.

High-pressure homogenization is a well-established method for the preparation of nanoemulsions and other lipid nanoparticle dispersions [4] and the commercially availble parenteral nanoemulsions (e.g. Lipofundin, Diprivan) are manufactured in large scale by high-pressure homogenization. However, high-pressure homogenization may not always be applicable, for example when only small amounts shall be processed or when the formualtions contains very sensible components. Alternative low-energy preparation methods may be advantegeous for processing of only small amounts or for the production of dispersions containing sensitive components.

Several alternative methods such as solvent-shifting (nanoprecipitation [5]), premix membrane emulsification [6], microemulsion templates [7] or dual centrifugation [8] have been described in the literature. All these methods have their own advantages and limitations and the aim of the projects is to evaluate their efficiency concerning disperseion quality (e.g. size and size distribution, homogeneity of formed colloidal structures) as well as stability of the obtained nanoemulsions in more detail and with special regard to LDL-like formulations.

References

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

[2] T. Lammers, F. Kiessling, W.E. Hennink, G. Storm. Drug targeting to tumors: Principles, pitfalls and (pre-) clinical progress. J. Control. Rel. 161 (2012) 175-187.

[3] P.C.N. Rensen, R.L.A. de Vrueh, J. Kuiper, M.K. Bijsterbosch, E.A.L. Biessen, T.J.C. van Berkel. Recombinant lipoproteins: Lipoprotein-like particles for drug targeting. Adv. Drug Del. Rev. 47 (2001) 251-276.

[4] J. Kuntsche, K. Westesen, M. Drechsler, M.H.J. Koch, H. Bunjes. Supercooled smectic nanoparticles: A potential novel carrier system for poorly soluble drugs. Pharm. Res. 21 (2004) 1834-1843.

[5] I.V. Zhigaltsev, N. Belliveau, I. Hafez, A.K.K. Leung, J. Huft, C. Hansen, P.R. Cullis. Bottom-up design and synthesis of limit size lipid nanoparticle systems with aqueous and triglyceride cores using millisecond microfluidic mixing. Langmuir 28 (2012) 3633-3640.

[6] S. Gehrmann, H. Bunjes. Preparation of lipid nanoemulsions by premix membrane emulsification with disposable materials. Int. J. Pharm. 511 (2016) 741-744.

[7] J.M. Koziara, J.J. Oh, W.S. Akers, S.P. Ferraris, R.J. Mumper. Blood compatibility of cetyl alcohol/polysorbate-based nanoparticles. Pharm. Res. 22 (2005) 1821-1828.

[8] F. Tenambergen, C.H. Maruiama, K. Mäder. Dual asymmetric centrifugation as an alternative preparation method for parenteral fat emulsions in preformulation development. Int. J. Pharm. 447 (2013) 31-37.