Production and Characterization of Liposome Systems for Pharmaceutical Applications

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Abstract:
Liposomes are increasingly used in medical and scientific applications. In this study, materials and methods used for producing liposomes, methods of characteristizing the liposomes and applications are summarized.

1. Introduction:
Liposomes are spherical closed structures, composed of curved lipid bilayers, which enclose part of the surrounding solvent into their interior. The size of a liposome ranges from some 20 nm up to several micrometers and they may be composed of one or several concentric membranes, each with a thickness of about 4 nm [Bergstrand, 2003]. Liposomes posses unique properties owing to the amphiphilic character of the lipids, which make them suitable for dug delivery. Drug delivery, in its broadest sense, is a rapidly developing and evolving discipline that is represented and practiced in most biomedical research facilities and institutions throughout the world [Anne, 2002]. Liposomes were first produced in England in 1961 by Alec D. Bangham, who was studying phospholipids and blood clotting. It was found that phospholipids combined with water immediately formed a sphere because one end of each molecule was water soluble, while the opposite end is water insoluble. Water-soluble medications added to the water were trapped inside the aggregation of the hydrophobic ends; fat-soluble medications were incorporated into the phospholipid layer [Bergstrand, 2003].

2. Objective:
The overall objective of this study was to review the methods used for producing and characterizing liposomes for drug delivery.

3. Materials and methods:
Liposomes can be produced by a variety of methods including (1) sonication, (2) extrusion, (3) homogenization, (4) swelling, (5) electroformation, (6) inverted emulsion and (7) reverse evaporation method [Bergstrand, 2003]. They are used as biocompatible carriers of drugs, peptides, proteins, plasmic DNA, antisense oligonucleotides or ribozymes, in pharmaceutical, cosmetic, and biochemical applications. The enormous versatility in particle size and in the physical parameters of the lipids affords an attractive potential for constructing tailor made vesicles for a wide range of applications. Efficient drug delivery systems based on liposomes need to posses a large number of special qualities. First, good colloidal, chemical and biological stability is required. The fact that liposomes are non equilibrium structures does not necessarily mean that they are unsuitable for drug delivery. On the contrary, a colloidal stable non-equilibrium structure is less sensitive to external changes than equilibrium structures, such as micelles [Pautot, 2003]. Hence colloidal stable liposomes often work well in pharmaceutical applications.

4. Measurements
In order to determine the size, shape and surface changes on the liposome and to was characterize the solution number of techniques including TEM, Surface Tensio meter, viscometer, zeta analyser, DLS and fluorescence micrograph will be used to characterize the emulsion.

TABLE 1: Production and Characterization of liposomes

	Topic/Reference	Materials / Methods	Measurements	Applications
1	"Production of unilamellar vesicles using an Inverted emulsion" Pautot S. et.al. (2002)	Phospholipids (POPC, POPS), Oil (Dodecane), water / **Inverted emulsion**	Inverted microscope (Leica), Fluorescene Quenching assay, Dynamic light scattering	Used to transport macromolecules through blood stream or through the skin, leading to the widespread use of vesicles in cosmetics and drug delivery
2	"Physicochemical characterization of PEG coated liposomes loaded with Doxorubicin" Polo D. et.al. (1997)	Phospholipids(PC,PG), Layer Stabilizer(PEG),Oil (methanol),water /**Rotary Evaporation**	Surface activity (Langmuir balance), Micro viscosity (Membrane interior probe (DPH), Bilayer fluidity,	Drug administration, Targeting cells, "in vivo" half life improvement
3	"Biophysical aspects of using liposomes as delivery vehicles" Anne S.U. et.al. (2002)	Phospolipids (DMPC, DOTAP), water, oil (propane) / **Homogenizaion**	Fluorescent microscopy, Zeta analyzer, Differential scanning calorimeter (DSL)	Biocompatible carriers of drugs, peptides, proteins, plasmic DNA, antisense oligonucleotides or ribosomes, for pharmaceutical, cosmetic, and biochemical purposes.
4	"Oil in water liposomal emulsions: characterization and potential use in vaccine delivery." Jean M.M. et.al. (1999)	Phospolipids (DMPC, DMPG), Mineral oil, water/**Extrusion**	Fluorescent microscopy, Rotational viscometer	As constituents of oil in water emulsion adjuvants for vaccines

5. Conclusions

Phospholipids are exclusively used for liposome production. Number of methods are used for characterize the liposome.

6. References:

1) Pautot S., Barbara J.F. and Weitz D.Z. "Production of unilamellar vesicles using an inverted emulsion (2003)" *Journal of Langmuir (2003)*, Vol 19, pp 2870-2879

2) Polo D., Haro I., Alsina M.A. and Reig F. "Physicochemical characterization of Poly (ethylene glycol) coated liposomes loaded with Doxorubicin" Journal of Langmuir (1997),Vol 13, pp 3953-3958

3) Anne S.U. "Biophysical aspects of using liposomes as delivery vehicles" *Journal of Bioscience Reports Apr.* (2002) Vol 22, pp 129-149

4) Jean M.M., Gary R.M., Lynn E.S., and Carl R.A. "Oil in water liposomal emulsions: Characterization and potential use in vaccine delivery", *Journal of Pharmaceutical sciences*, Vol 88, No 2 pp 1332-1339.