



Synthesis of a Novel Drug Delivery System for the Treatment of Invasive Pulmonary Aspergillosis

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Introduction

Liposomes are created when phospholipids are exposed to an excess amount of water, which causes them to arrange in a bilayer structure encapsulating an aqueous core. Liposomes can form mono and multiple lamellar bilayers, called unilamellar and multilamellar liposomes, respectively. Cholesterol is usually added to liposome formulations to facilitate liposome formation or to stabilize them against aggregation. Because of their unique encapsulation trait, liposomes have been extensively studied for their promise as an effective drug delivery system.

Motivation

Invasive pulmonary aspergillosis is a lung infection caused by the fungus aspergillosis. It is the leading cause of death in immunocompromised patients, especially those undergoing chemotherapy or bone marrow transplant. Early detection and treatment with antifungal therapy to the site of infection before the tissue is further compromised is important in improving the clinical outcome of the patient. Because of this, there is a need for a highly specific liposomal drug delivery system to be efficient carrier of poorly soluble or non-targeted drugs with high efficacy. Thus, we propose to synthesize and characterize a stealth targeted liposome as an effective carrier for amphotericin B.

Formulation

Liposomes were formulated using the phospholipids 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC), 1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine (DPPE), and the steroid cholesterol in different ratio formulations using a rotary evaporator. The mixture was afterwards hydrated with phosphate buffer. A centrifugation step was used to isolate the viable liposomes from the formulation mixture. Sonication was carried out to reduce liposome aggregation and particle size. Characterization of the formulated liposomes was performed by means of transmission electron microscopy (TEM), dynamic light scattering (DLS), and fluorescence microscopy (FM).

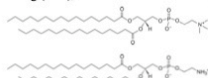


Fig 1. Schematic representation of a liposome for drug delivery (1)

1. www.wjgpub.com

Results

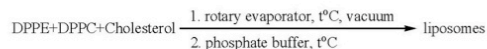


Table 1. Formulation ratios and physical characterization

Formulation ratio	Average diameter size (nm) by	
	TEM	FM/DLS
A 7.4:1:1		1510 ± 113
B 9.37:1:1.25		1290 ± 100
C 7.5:1:1.25	145	165
D 9:1:3	14.16 ± 1.02	
E 9.28:1:1	259.22	

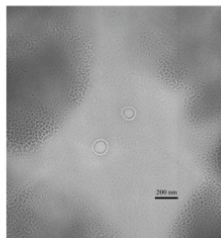


Fig 2. TEM image of liposomes using formulation ratio C as presented in Table 1 (average size diameter 145 nm, 1.5 hours sonication).

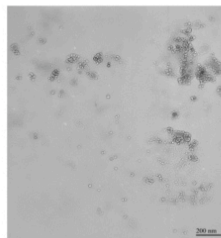


Fig 3. TEM image of liposomes using formulation ratio D as presented in Table 1 (average diameter 14 nm, 1 hour sonication).

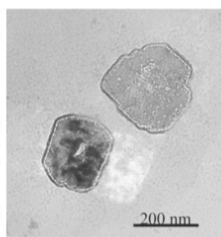


Fig 4. TEM image of liposomes using formulation ratio E as presented in Table 1 (average diameter 259 nm, 2 hours sonication).

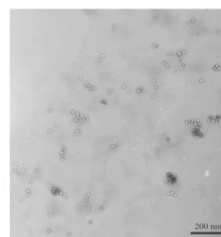


Fig 5. TEM image of liposomes using formulation ratio D as presented in Table 1 (average diameter 14 nm, 1.5 hours sonication).

Results

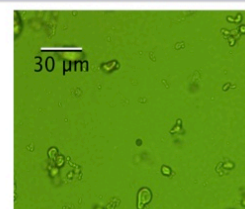


Fig 6. FM image of liposomes using formulation ratio A as presented in Table 1 (average size diameter 1510 nm, 30 minutes sonication).

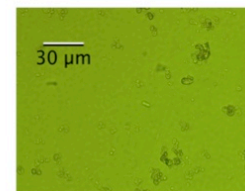


Fig 7. FM image of liposomes using formulation ratio B as presented in Table 1 (average size diameter 1290 nm, no sonication).

Conclusions

- After running several trials with different formulation ratios and physical characterization, it was observed that the formulation ratio 7.5 : 1 : 1.25 is the optimum ratio having the targeted particle size.
- Optimization of the liposome formulation along with measurement of the relevant physical properties are currently under progress.
- Our future objective will be the incorporation of a cyclic peptide, synthesized in our lab, in the formulation ratio, as well as drug-liposome preparation followed by animal model studies.

Acknowledgments

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