Thesis Title Physicochemical Properties of Amphotericin B Liposome Prepared by Reverse-Phase Evaporation Method

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ABSTRACT

Liposomes are used as drug delivery systems due to their advantages, for example , biocompatibility , low toxicity , drug stability enhancement or ability to trap a variety of drugs. Amphotericin B is a broad spectrum antifungal agent, and is drug of choice for the treatment of serious fungal infections despite its harmful side effects. Liposomal amphotericin B formulation will decrease the toxicity to the host, leading to more effectiveness. It has been studied in a variety of *in vitro* and *in vivo* infections, there have been few studies of its physicochemical properties.

Liposomal amphotericin B prepared using a reverse-phase evaporation method was studied to investigate the effect of varying the amount of amphotericin B,the amount of total lipid and the molar ratio of phosphatidylcholine to cholesterol on its physicochemical properties , which were

studied using scanning electron microscopy , transmission electron microscopy , a submicron particle size analyzer and differential scanning calorimetry ; entrapment efficiency was assessed.

Suitable conditions for preparation of the liposomes were a ratio of diethyl ether to normal saline solution 3:1 (by volume), sonication time 5 minutes at 7 °C and evaporation of diethyl ether at 25 °C : these gave a homogenous liposome suspension. Microscopic analysis showed that the prepared liposomes were spheroids , with unilamellar , oligolamellar or multilamellar structure. The entrapment efficiency depended on the amount of amphotericin B added during the preparation of liposomes. The formulation which contained amphotericin B 2.0 mol% of total lipid led to the highest percentage of drug entrapped. An increase in total lipid content affected the trapping efficiency of liposomes. Total lipid 250 μmol was the best preparation when prepared using diethyl ether 15 ml and aqueous phase 5 ml. Cholesterol content affected the encapsulation efficiency and the particle size of the liposomal amphotericin B. The preparation which provided the highest drug entrapment efficiency and the largest particles was that prepared with 1:1 molar ratio of phosphatidylcholine to cholesterol , which entrapped approximately 95 % and gave liposomes between 1307 and 1451 nm in diameter. Differential scanning calorimetry showed the interaction of amphotericin B and phosphatidylcholine , or phosphatidylcholine/cholesterol , in an amorphous state or molecular solid dispersion , both in the physical mixture and in liposomes.