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## Development of amphotericin B-double loaded liposomes using Design of Experiment (DoE)

N Basaran Mutlu Agardan and Nevin Çelebi  
Gazi University, Turkey

Systemic invasive fungal infections are the leading causes of mortality and morbidity among immunocompromised patients such as, cancer patients undergoing chemotherapy, AIDS patients and recipients of solid organ transplants. Amphotericin B (AmB), a polyene group antibiotic is a common choice for life-threatening systemic fungal infections and parasitic diseases due to its broad spectrum of activity. AmB is a BCS class IV drug with low solubility and low permeability properties. Although amphotericin B is a very potent agent, clinical use is limited due to its narrow therapeutic index and side effects. Cyclodextrins (CDs) are a group of pharmaceutical excipients containing a lipophilic central cavity and a hydrophilic outer surface. In aqueous solutions, they have the ability to form inclusion complexes with many drugs by taking up a drug molecule/some lipophilic moiety of the drug molecule into their central cavity. The inclusion complexes are very successful at increasing the solubility of low-soluble drugs. The main goal of a drug delivery system is to enhance the therapeutic index and reduce side effects of encapsulated drug. Liposomes are the macro/nano sized vesicular drug delivery systems with well-established advantages. The aim of this study was firstly, preparation and characterization of inclusion complexes of AmB with CDs. Secondly, formulation development of AmB double loaded liposomes by loading AmB-CD inclusion complex to the inner hydrophilic compartment, and hydrophobic AmB to the outer phospholipid membrane. For this purpose, solubility studies were carried out by using three CD derivatives ( $\alpha$ -CD, HP- $\beta$ -CD and sulfobutyl ether  $\beta$ -CD).  $\alpha$ -CD was found to be the most enhancing derivative of AmB solubility. AmB-  $\alpha$ -CD complexes were prepared and characterized by DSC, FTIR, X-ray diffraction measurements. Design of experiment (DoE) is planned to assist the formulation of AmB and AmB-  $\alpha$ -CD double loaded liposomes in order to obtain more comprehensive and comparable results.

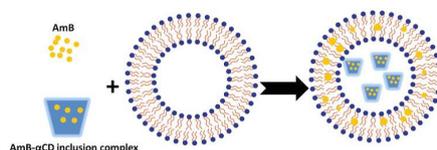


Figure 1: Schematic illustration of AmB double loaded liposomes

### Recent Publications

1. Pattni B S, Chupin V V and Torchilin V P (2015) New developments in liposomal drug delivery. *Chemical Reviews* 115(19):10938–10966.
2. Mutlu Ağardan N B, Değim Z, Yılmaz Ş, Altıntaş and Topal T (2015) The effectiveness of raloxifene-loaded liposomes and cochleates in breast cancer therapy. *AAPS PharmSciTech* 1–10.
3. Maestrelli F, González-Rodríguez M L, Rabasco A M, Ghelardini C and Mura P (2010) New “drug-in cyclodextrin-in” deformable liposomes” formulations to improve the therapeutic efficacy of local anaesthetics. *International Journal of Pharmaceutics* 395(1):222–231.
4. Malaekheh-Nikouei B and Davies N (2009) Double loading of cyclosporine A in liposomes using cyclodextrin complexes. *PDA Journal of Pharmaceutical Science and Technology* 63(2):139–148.
5. Nucci M and Perfect J R (2008) When primary antifungal therapy fails. *Clinical Infectious Diseases* 46(9):1426–1433

### Biography

N Basaran Mutlu Agardan graduated from Gazi University Faculty of Pharmacy, and obtained there her PhD from the Department of Pharmaceutical Technology. She then gained a scholarship from the Scientific and Technological Research Council of Turkey and completed her Post-doctoral research studies at the Center for Pharmaceutical Biotechnology and Nanomedicine, Northeastern University, Boston. Her area of research focuses on the smart drug delivery systems, liposomes, drug/gene delivery in cancer and oral absorption enhancement.

bmutlu@gazi.edu.tr