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Research Article

Experimental Design Supported Liposomal Aztreonam Delivery: *In Vitro* Studies

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Abstract

Purpose: The present study focuses on a systemic approach to develop liposomal aztreonam as a promising dosage form for inhalation therapy in the treatment of pneumonia and explores the *in-vitro* antimicrobial and cell uptake efficacy.

Methods: Liposomes were prepared by ethanol injection method using the lipids - soya phosphatidylcholine (SP) and cholesterol (CH). A central composite design (CCD) was employed to optimize the lipid composition to evaluate the effect on vesicle size, zeta potential and entrapment efficiency of the formulation. A numerical and graphical optimization was carried out to predict the optimized blend. The optimized formulation was characterized for vesicle size, surface charge, encapsulation, surface morphology, differential scanning calorimetry (DSC), powder X Ray Diffraction (PXRD), thermogravimetric analysis (TGA), *in vitro* diffusion, accelerated stability studies, antimicrobial studies on *Pseudomonas aeruginosa* NCIM 2200 and *in vitro* cell uptake studies.

Results: The optimized formulation was found to have a particle size of 144 nm, a surface charge of -35 mV, with satisfactory drug entrapment. The surface morphology study proved the formation of nanosized vesicles. The drug release from liposomal matrix was biphasic in nature. The solid-state study revealed the reason for good encapsulation of drug. The moisture retention capacity was found to be minimum. The anti-microbial study revealed the potential antibacterial activity of the optimized formulation over the pure drug. The formulation was found to be safe on the epithelial cells and showed a marked increase in cellular uptake of aztreonam in a lipid carrier.

Conclusion: It can be concluded that the optimized liposomal aztreonam could be considered as a promising approach for the delivery of aztreonam through inhalation.

Introduction

Lung disease in infants and elderly people has been recognized to be the greatest reason for morbidity and mortality.[1] Chronic infection in lungs leads to acute exacerbations and affects the functioning of the lungs. *Pseudomonas aeruginosa*, a gram-negative bacterium is considered as the most important pathogen in infections.[2] It is an opportunistic bacterium that colonizes in the bronchopulmonary tract and forms a thick biofilm owing to its fast growth.[3] Antimicrobial resistance has also been reported to the class of antibiotics known as carbapenems.[4] The low permeability of the bacterial outer membrane, efflux mechanisms and the synthesis and secretion of various enzymes by the bacteria made antibacterial agents difficult to permeate through the cell membrane of the bacteria. Hence the development of bacterial resistance is quite frequent.[5]

A review of literature showed that antibiotic loaded liposomes had better activity against *P. aeruginosa* compared to its free drug.[6] Microorganisms responsible for pneumonia exhibit a high intrinsic resistance because of its outer membrane which restricts low permeation to antimicrobials. Liposomal formulations are found to be effective to fuse with the outer membrane of bacteria and thus can penetrate easily through the cell wall or biofilm produced by them. Further such liposomal formulations are found to be effective in mucus penetration, bypassing pulmonary clearance. Liposomes also help to maintain a steady state drug concentration to inhibit biofilm growth. This quality is attributed to its release profile which happens in two phases, with a preliminary launch followed by sustained release of the drug.[7]

Rudokas et al[8] reviewed on pulmonary delivery of liposomal anti-cancer drugs through nebulization therapy and their effect of composition and liposome size on therapeutic outcomes. They elaborated on the success of liposomes as an inhalable carrier for the treatment of other lung diseases. Shirley[9] studied on liposomal inhalation

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