DOCTORAL THESIS

Investigation of semipermeable coated tablet and liposomal dry powder inhaler formulation of salbutamol sulfate

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Date of Award:
2010

Investigation of Semipermeable Coated Tablet and Liposomal Dry Powder Inhaler Formulation of Salbutamol Sulfate

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A thesis submitted in partial fulfillment of the requirements

for the degree of

Doctor of Philosophy

Principal Supervisor: Dr. Yang Zhijun

Hong Kong Baptist University

September 2010

ABSTRACT

Asthma is a chronic disease that affects about 300 million patients' airways in the world. The main objective of my study is to develop the dosage forms which can be controlled released for treating the disease of asthma. Salbutamol (SB) and Salbutamol sulphate (SBS) are selected as the model drugs. First, the bilayer semipermeable film-coated tablets were prepared. The effects of excipients on drug release were investigated. The results showed that the release speed of SBS from the tablets was depended on the complex factors of osmotic pressure, swelling, viscosity and solubility. However, it was hard to control the release speed of SBS within a desirable range and it was hard to control the onset time of inhibiting the asthma with this kind of tablets. To overcome these problems, we develop a formulation of liposomal SBS dry powder inhalers by applying the advantage of liposomes that can act as a sustained release reservoir for drug. Liposomes of high encapsulation efficiency (more than 80% before lyophilization and about 45% after dehydration-rehydration) were prepared by a vesicular phospholipid gel (VPGs) technique. SBS VPGs liposomes were subjected to lyophilization using different kinds of cryoprotectants in various mass ratios. Coarse lactose (63-106 μm) in different mass ratios was used as a carrier. Magnesium stearate (0.5%) was added as a lubricant. The dry liposomal powders were then crushed by ball milling and sieved through a 400-mesh sieve to control the mean particle size at about 10 μm. The effects of different kinds of cryoprotectants and the amount of lactose carrier on the fine particle

fraction (FPF) of SBS (<5 μm) were investigated. The results showed that the developed formulation of liposomal dry powder inhaler was obtained using lactose as a cryoprotectant with a mass ratio of lyophilized powder to carrier lactose at 1:5; 0.5% magnesium stearate was used as a lubricant. The value of FPF for SBS was 41.51 ± 2.22% for this formulation. Sustained release of SBS from the VPGs liposomes was found in the *in vitro* release study. Preliminary *in vivo* study of VPGs liposomes of SBS on guinea pigs showed that, compared with commercial SBS preparation, SBS liposomes exerted an anti-asthmatic effect for more than 9 hours after pulmonary administration. The results offer the promising possibility of localized pulmonary delivery of liposomal SBS.

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