

DOCTORAL THESIS

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

Huang, Wenhua

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

Huang Wenhua

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Principal Supervisor: Dr. Yang Zhijun

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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 $41.51 \pm 2.22\%$ 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.

TABLE OF CONTENTS

DECLARATION.....	i
ABSTRACT.....	ii
ACKNOWLEDGEMENTS.....	iv
TABLE OF CONTENTS.....	vi
LIST OF TABLES.....	xii
LIST OF FIGURES.....	xiv
LIST OF ABBREVIATIONS.....	xvii
CHAPTER 1 INTRODUCTION.....	1
1.1 Brief Review of Asthma.....	2
1.1.1 The Background of Asthma.....	2
1.1.2 The Pathophysiology of Asthma.....	3
1.1.3 The Treatment of Asthma.....	6
1.2 The Selected Model Drug of Salbutamol and Salbutamol Sulfate.....	13
1.2.1 The Background of Salbutamol and Salbutamol Sulfate.....	13
1.2.2 Clinical Use of Salbutamol and Salbutamol Sulfate.....	16
1.3 Brief Review of Semipermeable Coated Tablet.....	17
1.3.1 Properties of the Tablets.....	17
1.3.2 Coating of Tablets.....	19
1.3.3 Semipermeable Membrane.....	20
1.3.4 Active Osmotic Agent.....	22

1.4 Brief Review of Liposomes.....	26
1.4.1 Background of Liposomes.....	26
1.4.2 Type of Liposomes.....	27
1.4.3 Composition and Characteristics of Liposomes.....	29
1.4.4 Preparation of Liposomes.....	30
1.4.5 Mechanism of Transportation Through Liposomes.....	35
1.4.6 Prospects of Liposomes.....	35
1.5 Brief Review of Liposomal Dry Powder Inhalers.....	36
1.5.1 The Background of Inhalers.....	36
1.5.2 Preparation of Liposomal Dry Powder Inhalers.....	42
1.5.3 Inhaler Device of Liposomal Dry powder Inhalers.....	45
1.5.4 Properties of Liposomal Dry Powder Inhalers.....	46
1.5.4.1 Flowability.....	46
1.5.4.2 Scanning Electron Microscopy Photomicrograph and Image Analysis.....	47
1.5.4.3 <i>In vitro</i> lung deposition studies.....	47
1.5.5 Advantages of Liposomal Dry Powder Inhalers.....	47
1.6 Aims of the Research and Structure of the Thesis.....	48
1.6.1 Aims of the Research.....	48
1.6.2 Structure of the Thesis.....	50
CHAPTER 2 THE TIMING OF COMPLEX FACTORS ON SBS RELEASE IN SEMIPERMEABLE-COATED TABLETS.....	51

2.1 Introduction.....	52
2.2 Experimental Part.....	55
2.2.1 Materials.....	55
2.2.2 Preparation of the Core Tablet.....	55
2.2.3 Coating of Swelling Agent and Membrane.....	56
2.2.4 <i>In vitro</i> Release Test of SBS and Osmogent.....	59
2.2.5 Swelling Properties and The Change of Tablet Weight.....	67
2.2.6 Photograph by Dissecting Microscope.....	67
2.2.7 Viscosity and Solubility Determination.....	67
2.2.8 Osmotic Pressure Measurement.....	68
2.3 Results & Discussion.....	69
2.3.1 The Release of SBS from the Semipermeable-coated Tablets.....	69
2.3.2 Physicochemical Properties of SBS and Excipients.....	73
2.3.3 <i>In vitro</i> Osmogent Release.....	75
2.3.4 Swelling Behaviors.....	79
2.3.5 The Timing of Factors on the SBS Release.....	84
2.4 Conclusions.....	85
CHAPTER 3 THE PREPARATION AND CHARACTERISTIC OF SALBUTAMOL SULFATE LIPOSOMES.....	87
3.1 Introduction.....	88
3.2 Experimental Part.....	90

3.2.1 Materials.....	90
3.2.2 Preparation of Liposomes	91
3.2.2.1 Film Dispersion Method... ..	91
3.2.2.2 Vesicular Phospholipid Gels (VPGs) Method.....	92
3.2.3 The Measurement of Liposomes Size and Zeta Potential.....	92
3.2.4 Determination of Drug Encapsulation Efficiency in Liposomes.....	92
3.2.5 Transmission Electron Microscope Observation of Liposomes.....	93
3.2.6 <i>In Vitro</i> Release of Liposomes.....	94
3.3 Results & Discussion.....	96
3.3.1 Vesicle Size, Zeta Potential and Encapsulation Efficiency of Liposomes... ..	96
3.3.1.1 Liposomes Prepared by Film Dispersion Method.....	96
3.3.1.2 Liposomes Prepared by Vesicular Phospholipid Gels Method.....	102
3.3.2 The TEM Pictures of Liposomes.....	105
3.3.2.1 Liposomes Prepared by Film Dispersion Method.....	105
3.3.2.2 Liposomes Prepared by Vesicular Phospholipid Gels Method.....	106
3.3.3 <i>In Vitro</i> Release of Liposomes	108
3.3.3.1 Liposomes Prepared by Film Dispersion Method.....	108
3.3.3.2 Liposomes Prepared by Vesicular Phospholipid Gels Method.....	111
3.4 Conclusions.....	112
CHAPTER 4 DEVELOPMENT OF LIPOSOMAL SALBUTAMOL SULFATE DRY POWDER INHALER FORMULATION.....	114

4.1 Introduction.....	115
4.2 Experimental Part.....	116
4.2.1 Materials.....	116
4.2.2 Preparation and Dilution of Vesicular Phospholipid Gels.....	117
4.2.3 Lyophilization of Liposomes.....	117
4.2.4 Development of Liposomal Dry Powder Inhaler Formulations.....	118
4.2.5 Determination of SBS Encapsulation Efficiency in Liposomes.....	119
4.2.6 Determination of Fine Particle Fraction.....	120
4.2.7 Determination of Angle of Repose.....	121
4.2.8 Determination of Particle Size of Liposomes.....	121
4.2.9 Scanning Electron Microscopy (SEM).....	121
4.2.10 <i>In Vitro</i> Release of Liposomes.....	122
4.3 Results & Discussions.....	123
4.3.1 Selection of Cryoprotectants.....	123
4.3.2 <i>In Vitro</i> Release.....	126
4.3.3 Development of Liposomal Dry Powder Inhaler Formulations.....	127
4.4 Conclusions.....	133
CHAPTER 5 PRELIMINARY PHARMACOKINETIC AND PHARMACODYNAMICS STUDY OF VPGS LIPOSOMES OF SBS.....	134
5.1 Introduction.....	135
5.2 Materials and Methods.....	136

5.2.1 Chemicals.....	136
5.2.2 Animals.....	136
5.2.3 Preparation of VPGs and Liposomes.....	137
5.2.4 <i>In vitro</i> Release of SBS.....	138
5.2.5 Transport of SBS across Pulmonary Membrane.....	139
5.2.6 Pharmacokinetic Study.....	141
5.2.7 Pharmacodynamics Study.....	144
5.3 Results & Discussions.....	145
5.3.1 Effect of Lactose Hydration on Drug Encapsulation Efficiency.....	145
5.3.2 <i>In vitro</i> Release Rate of SBS from Liposomes.....	146
5.3.3 Suspension of Pulmonary Transport Rate of SBS by Liposomes.....	148
5.3.4 Pharmacokinetic Parameters of SBS in Liposomes and SBS Solution.....	151
5.3.5 Anti-asthmatic Effect of SBS Liposomes in Comparison with Other Preparations.....	155
5.4 Conclusions.....	157
CHAPTER 6 SUMMARY AND PROSPECTIVE OF THE RESEARCH.....	158
6.1. Summary and Conclusions of the Research.....	159
6.2. Prospective for Further Research.....	163
REFERENCES.....	165
PUBLICATIONS.....	179
CURRICULUM VITAE.....	180