بسم الله الرحمن الرحيم

شبكة المعلومـــات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

﴿ قسم ﴾

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأفلام قد اعدت دون آية تغيرات

يجب أن

تحفظ هذه الأفلام بعيداً عن الغبار

في درجة حرارة من 15 – 20 مئوية ورطوبة نسبية من 20-40 %

To be kept away from dust in dry cool place of
15 – 25c and relative humidity 20-40 %

بالرسالة صفحات

لم ترد بالأصـــل

بعض الوثائق الأصلية تالفة

Formulation and Bioavailability Study on Some Anti-Asthmatic Drugs

A Thesis
Presented by

Randa Tag Abd El-Rehim

Submitted For the Degree of
Doctor of Philosophy
in

Pharmaceutical Sciences
(Pharmaceutics)

Under The Supervision of

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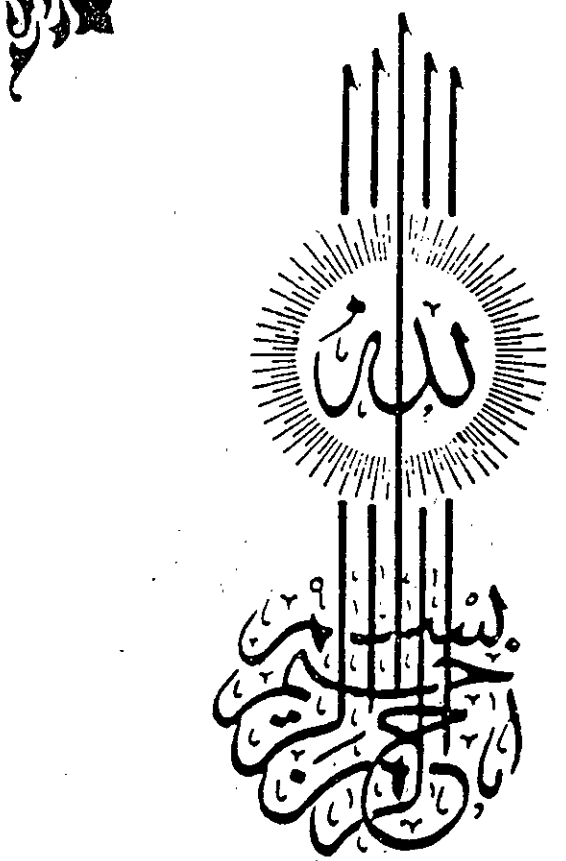
2003

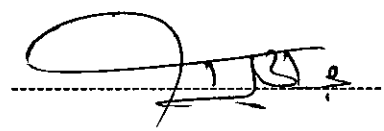


قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا
عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ .

صَدَقَ اللهُ الْعَظِيمُ
البقرة - ٣٢ -

APPROVAL SHEET

Approved by:



أ.د/ محمد رعبد المنعم محمد حمد الله

(Committee in charge)

Date: 23 / 10 / 2003

To My Family

Acknowledgments

I would like to express my deepest gratitude to ***Prof. Dr. Abd El-Halim El- Assasy****, Professor of Pharmaceutics, Faculty of Pharmacy, Cairo University, for his fruitful supervision, patience and generous help throughut my work.*

I am profoundly grateful to ***Dr. Iman Ibrahim Soliman****, Associate Professor of Pharmaceutics, Faculty of Pharmacy, Cairo University, for her great support, encouragement, understanding and devotion.*

I wish also to express my gratitude to all my professors and colleagues in the Department of Pharmaceutics, Cairo University, and every one who helped me to complete this work.

A special debt of love and gratitude is acknowledged to my parents, husband, children and all members of my beloved family for their persistent help, true sympathy, honest prayers and real sacrifices.

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Abstract

ABSTRACT

Diprophylline is a methylxanthines drug used in the treatment of bronchial asthma. The drug has proven therapeutic efficacy, tolerability and safety. The short plasma half-life, ~2 hours, following oral dosing necessitates a three-time a day administration of the drug to maintain peak and trough concentrations within the therapeutic range. Patient compliance is known to be fairly poor with such frequent dosing regimen. Therefore, it was considered desirable to develop controlled-release preparations of diprophylline. Accordingly, the work in this thesis is divided into four chapters, namely, preparation and evaluation of diprophylline microcapsules, preparation and evaluation of sustained release diprophylline tablets and capsules, preparation and evaluation of sustained release diprophylline suppositories and finally bioavailability study of diprophylline from its selected formulations.

Chapter I: Preparation and Evaluation of Diprophylline Microcapsules .

The work in this chapter included the preparation of diprophylline microcapsules using coacervation phase separation by non-solvent technique. Three different polymers, namely cellulose acetate butyrate, ethylcellulose and Eudragit RS100 were used at 1:0.25, 1:0.5,and 1:1 core: coat ratios. The phase separation and subsequent deposition of the polymer solution was achieved by drop wise addition of the coating polymer solution (4%w/v) to the drug suspended in a dispersion medium consisting of 85 g liquid paraffin and containing 0.6 % w/v magnesium stearate. Rigidization of the deposited polymer was achieved by drop wise addition of 30 ml of n- hexane. The prepared microcapsules were

evaluated for their morphology by examination under an optical microscope, mean particle diameters as well as the diameter distribution percentiles using laser diffraction particle size analyzer, yield and drug loading efficiency. An accurately weighed samples of the microcapsules of size ranged from 315-500 μm containing 400 mg of diprophylline were subjected to in-vitro release studies using USP dissolution tester apparatus type I. The kinetic analysis of drug release were determined using the linear regression according to: zero order, first order and also according to simplified Higushi diffusion model. The best-chosen formula of diprophylline microcapsules was shelf stored for 6 and 12 months. Release study has been conducted to study the effect of aging.

On evaluation of the prepared microcapsules, the following was noticed:

1. Cellulose acetate butyrate microcapsules were irregular at the lower ratio of the polymer and became spherical at the higher ratios. Eudragit RS100 microcapsules were characterized being spherical, discrete and free flowing in all the ratios of the polymer tested. Meanwhile ethylcellulose microcapsules were irregular in shape, discrete and free flowing in all the ratios of the polymer tested.
2. The increase in the polymer amount decreased the mean particle size, the yield of the microcapsules as well as the drug loading efficiency.
3. The in-vitro diprophylline release rate retardation was dependent on the type of polymer, as well as core:coat ratio. The percentage amount of drug released from the microcapsules decreased on increasing the polymer amount. The release profiles of drug from its microcapsules is shown to be divided into two distinct phases: An initial curved stage and a terminal linear one in which the drug