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Improvement of the Bioavailability of Buspirone Hydrochloride using Intranasal Delivery Systems

By

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A thesis submitted in the partial fulfillment of the requirements for the master degree of Pharmaceutical Sciences (Pharmaceutics)

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2012 Cairo, Egypt

بسم الله الرحمن الرحيم

وأنزلَ الله عليك الكتاب والحكْمةَ وعلمك
ما لم تكُن تعلَم وكَانَ فَضلُ الله عليك عظيما

صدق الله العظيم
سورة النساء اية (3 11)

Acknowledgement

I am deeply thankful to Allah by the grace of which the present work was realized.

I would like to express my best regards and appreciation to ***Prof.Dr. Abd El Hameed Abdallah El-Shamy****, Professor of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Ain Shams University, for his instructive supervision, proving facilities, continuous advice and continuous encouragement.*

I would like to express my deep and sincere gratitude to ***Prof.Dr. Samar Mansour Holayel****, Professor of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Ain Shams University, for suggesting the point, planning the work, her instructive discussion, ultimate advice and her great effort devoted toward the completion of this thesis.*

I am also grateful to ***Dr. Rihab Osman Ahmed****, Lecturer of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Ain Shams University, for her teaching on microemulsion science, valuable advice, support and efforts for this work, careful and exigent reading of the thesis, the critical comments, suggestions and corrections. She has become a mentor and an example for my academic life.*

I would like to thank the members of the department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Ain Shams University.

Dedication

I dedicate this thesis to my dear mother,

brothers, sisters,

and to the soul of my father.

Contents

Chapter I: Preparation and characterization of microemulsion systems for intranasal delivery of buspirone HCl

List of Abbreviations

AB	Absolute bioavailability
AE	Absorption enhancer
AME	Absorptive-mediated transport
ANOVA	Analysis of variance
AUC	Area under the curve
BBB	Blood brain barrier
BCS	Biopharmaceutical classification system
BCSFB	Blood cerebrospinal fluid barrier
BH	Buspirone hydrochloride
BHME	Buspirone hydrochloride microemulsion
BHMME	Buspirone hydrochloride mucoadhesive microemulsion
BHS	Buspirone hydrochloride solution
cAMP	Cyclic-adenosine monophosphate
CD	Cyclodextrin
CD-BHMME	Buspirone hydrochloride mucoadhesive microemulsion containing hydroxypropyl-β-cyclodextrin
CD-MME	Mucoadhesive microemulsion containing hydroxypropyl-β-cyclodextrin
cm	Centimeter
cm^2	Centimeter square
C_{max}	Maximum concentration of drug
CNS	Central nervous system
cp	Centipoise
CPP	Critical packing parameter
CSF	Cerebro-spinal fluid
CTAB	Hexadecyl (cetyl) trimethyl ammonium bromide

CV%	Percent coefficient of variation
^{o} C	Celsius temperature
Da	Dalton
DDAB	Didodcecylammonium bromide
DILT	Diltiazem
DNA	Deoxyribonucleic acid
DTE%	Drug targeting efficiency
DTP%	Nose-to-brain direct transport percentage
ECF	Extracellular fluid
FDA	Food and drug administration
FTIR	Fourier transform infrared spectroscopy
GIT	Gastrointestinal tract
GRAS	Generally regarded as safe
Grp	Group
HLB	Hydrophile-lipophile balance
HP-β-CD	Hydroxypropyl-β-cyclodextrin
HPLC	High performance liquid chromatography
hrs	Hour
IA	Intra-arterial
ICH	International conference on harmonization
IN	Intranasal
IPM	Isopropyl myristate
IS	Internal standard
IV	Intravenous
IVS	Intravenous solution
K	Procedural constant

KDa	Kilo Dalton
kg	Kilogram
Labr	Labrafac lipophile® WL 1349
LOD	Limit of detection
LOQ	Limit of quantitation
µg	Microgram
µl	Microliter
µm	Micrometer
g	Gram
m^2	Meter square
MCC	Mucociliary clearance
ME	Microemulsion
mg	Milligram
min	Minute
ml	Milliliter
mm	Milllimeter
MME	Mucoadhesive microemulsion
MRP	Multi drug resistance associated protein
MRT	Mean residence time
Mw	Molecular weight
NA	Not applicable
ng	Nanogram
nm	Nanometer
O/W	Oil-in-water
PB	Phosphate buffer
PBS	Phosphate buffer saline

PEG	Polyethylene glycol
PG	Propylene glycol
P-gp	P-glycoprotein
PIT	Phase inversion temperature
pKa	Ionization constant
PTS	Peptide transport system
QC	Quality control
R^2	Coefficient of determination
RB	Relative bioavalability
rpm	Round per minute
S_{mix}	Surfactant/cosurfactant mixture
s/n	Signal-to-noise ratio
SD	Standard deviation
SE	Standard error
$t_{1/2}$	Half life
T80	Tween® 80
TEM	Transmission electron microscopy
T_{max}	Time of occurrence for maximum drug concentration
UV	Ultraviolet
W/O	Water-in-oil
w/w	Weight per weight
v/v	Volume per volume

List of Tables