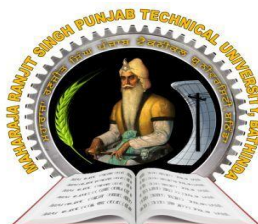


**INTENSIFYING SOLUBILITY AND BIOAVAILABILITY
OF ARTEETHER THROUGH MOLECULAR
ENCAPSULATION BASED ORAL DRUG
DELIVERY SYSTEM**

**A
THESIS
SUBMITTED TO**



MAHARAJA RANJIT SINGH PUNJAB TECHNICAL UNIVERSITY

BATHINDA (PUNJAB)

**IN FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF**

DOCTOR IN PHILOSOPHY

IN

PHARMACY

By

Neha

Registration No. 17211FPE06

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BATHINDA (PUNJAB)**

2023

CANDIDATE'S DECLARATION

I hereby certify that the work which is being presented in the thesis, entitled **“Intensifying Solubility and Bioavailability of Arteether through Molecular Encapsulation based Oral Drug Delivery System”** in fulfillment of the requirements of the award of the degree of Doctor of Philosophy in **Faculty of Pharmacy** and submitted in **Maharaja Ranjit Singh Punjab Technical University, Bathinda** is an authentic record of my own work carried out during a period from Jan, 2018 to July, 2022 under the supervision of Dr. Ashish Baldi, Professor, Department of Pharmaceutical Sciences & Technology, Maharaja Ranjit Singh, Punjab Technical University, Bathinda, Punjab, India.

The matter embodied in this thesis has not been submitted by me for the award of any other degree of this or any other University/Institute.

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This is to certify that the above statement made by the candidate is correct to the best of our knowledge.

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The Ph.D. Viva-Voice examination of Ms. Neha, Research Scholar, has been held on _____.

Signature of Supervisor

Signature of External Examiner

DEDICATED

TO

MY FATHER-IN-LAW

Dr. Charanjit Singh Nabha

ACKNOWLEDGMENT

The acknowledgment of my thesis starts with sincere thanks to my father-in-law, Dr. Charanjit Singh Nabha, whom I refer to as "the man with a positive outlook." Talking about tension with him is as if it were nothing. Ph.D. cannot function without a positive attitude, thus I consider him to be the most important aspect of this degree.

There are no words to express my gratitude to my father, Mr. Gaje Singh Bajwa, for his daily listening to my Ph.D. journey. My nighttime dosage of sleep is his regular evening calls and questions about the day. It is the realisation of his dream. Next, I owe many thanks to my mother-in-law and my birth mother for their support to make me a passionate woman you both are amazing. Special thanks to my mother-in-law for taking care of Nehreet when I was compiling my thesis you really deserve special appreciation. I am grateful to my spouse, Dr. Preet Amol Singh, for his celebratory spirit on such a difficult day. He is the only person who has seen my each day of Ph.D. journey. His determination to accomplish the assignment in any case encouraged me much. Preet has been my closest friend and fantastic companion, loving, supporting, encouraging, entertaining, and helping me go through this difficult moment most positively. Thank you so much, Dr. Sahab. I'd want to express my affection for my daughter Nehreet Kaur. When I enter a home and you greet me with "Mumma," I forget everything, good or bad!! I adore that moment!!

My supervisor, Prof. Ashish Baldi, and his hard work are well regarded after a journey of no project with all researchers completely supported. He has motivated me to become an independent researcher and has shown me the value of critical thinking. He also showed what a brilliant and hardworking researcher can do. His struggles pushed this project to completion. This work was created under his supervision and with his conception.

I send my love to my mother for her anxiety about how you would handle everything!! She comprehends how I handled the baby and the Ph.D. I thank my birth family and in-laws' family for their support during my Ph.D.

I'd like to thank my mentors, Prof. N.K. Jain, Prof. Indu Pal Kaur, Prof. Neelu Sood and Dr. Jitender Madan, for giving me hands-on experience with the topic. I am a great fan of yours all!! Thank you for perfecting me in wet lab and calculations.

I am thankful to Prof. Bhavesh Kevadia (Head), Virus Theranostics Laboratory at the University of Nebraska in the United States for his consistent encouragement to publish publications in high-impact journals.

You can't function without seniors, and whatever a senior says, you have to trust it. I value my seniors from the time I am an undergraduate. I am grateful to my seniors, Dr. Randeep Kaur, Dr. Amandeep Kaur, Dr. Mandeep Singh, Dr. Keerti Jain, and Dr. Virender sir, for providing me with the literature, software, and an overview of each

experiment. Thank you so much for taking my late-night calls and ensuring that I understood every calculation.

Juniors are like your children in terms of love and affection. Nupur, Shipra, Sristy, Pallavi, Trisha, Shagun, Devesh, Shubam, Dheeraj, Mohit, Ashish, Sumant, Akshay, Manisha, and Pratiksha are among my juniors. Thank you for accomplishing each job I have given you and for participating in the celebrations with each milestone throughout the Ph.D.

I am grateful to Prof. (Dr.) Buta Singh Sidhu's inspirational leadership (Vice Chancellor, Maharaja Ranjit Singh Punjab Technical University, Bathinda). I would also want to thank Dr. Rahul Deshmukh, Late Dr. Uttam Mandal, and Dr. Amit Bhatia HOD, Department of Pharmaceutical Sciences and Technology, MRSPTU for their constant support during my Ph.D. journey. I applaud the registrar sir Dr. Gurinder Pal Singh's constant encouragement and well-wishes. I admire Jagdev Sir and Maninder Sir's assistance with official documents during my Ph.D.

I would like to express my sincere thanks to Dr. Puran Singh, Head, CSIR- CCMB, Hyderabad, and Ms. Amisha for the ex-vivo antimalarial activity. I am thankful to Brooks Lab Ltd. Scientist Mr. Manjit Katoch sir for providing me arteether as gift sample. Finally, I'd want to convey my affection for my experimental rabbits.

I thank Ms. Rachna Baldi for her support during execution of my research work.

The Financial assistance in the form of fellowship by the Indian Council of Medical Research and Council of Scientific and Industrial Research, New Delhi are gratefully acknowledged.

Lastly I thank Post Doc Fellows of University of Turin, Italy for teaching me lab skills.

-Neha

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LIST OF ABBREVIATIONS

Abbreviation	Full Form
%F	Percentage Friability
%T	Percentage Transmittance
Σ	Sum
$\mu\text{g/mL}$	Microgram Per Millilitre
2D	2-Dimensional
3D	3-Dimensional
A	Absorbance
ACN	Acetonitrile
ANOVA	Analysis of Variance
API	Active Pharmaceutical Ingredients
ART	α , β -Arteether
ART -SLNs	α , β -Arteether Loaded Solid Lipid Nanoparticles
ART-CD	α , β -Arteether-Cyclodextrin Complex
ATP	Analytical Target Profile
AUC	Area Under Curve
BBD	Box-Behnken Design
BCS	Biopharmaceutical Classification System
$^{\circ}\text{C}$	Degree Celsius
CAA	Critical Analyte Attribute
CAP	Cellulose Acetate Phthalate
CAT	Cellulose Acetate Trimellitate
CCD	Central Composite Design
CD	Cyclodextrin
cm	Centimetres
CMA	Critical Material Attributes
C_{max}	Maximum Concentration
CMPs	Critical Method Parameters
COVID	Corona Virus Disease
CCSEA	Committee for Control and Supervision of Experiments on Animals
CPP	Critical Process Parameters

CQ	Chloroquine
CQA	Critical Quality Attributes
CQR	Chloroquine Resistant
CRT	Chloroquine Resistant Transporter
DF	Degree of Freedom
DLS	Dynamic Light Scattering
DoE	Design of Experiment
DSC	Differential Scanning Calorimetry
EDR	Endpoint Detection and Response
EDTA	Ethylene Diamine Tetraacetic Acid
EE	Entrapment Efficiency
FbD	Formulation by Design
FD	Factorial Design
FDA	Food and Drug Administration
FESEM	Field Emission Scanning Electron Microscopy
FFD	Fractional Factorial Design
FMEA	Failure Mode and Effects Analysis
FPQC	Finished Product Quality Control
FT-IR	Fourier Transform Infrared Spectroscopy
F-value	Fit Value
GI	Gastro Intestinal
gm	Gram
GMP	Good Manufacturing Practices
h	Hour
H	Height
HP-F	High Powder Field
HPLC	High Performance Liquid Chromatography
HPMC	Hydroxy Propyl Methyl Cellulose
HPMCP	Hydroxy Propyl Methylcellulose Phthalate
HPMC-AS	Hydroxypropyl Methylcellulose Acetate Succinate
HP- β -CD	Hydroxy Propyl- β -Cyclodextrin
HR-TEM	High Resolution Transmission Electron Microscopy

<i>i.m.</i>	<i>Intra –muscular</i>
<i>i.v.</i>	<i>Intra-venous</i>
IAEC	Institutional Animal Ethics Committee
ICH	International Conference on Harmonization
IP	Indian Pharmacopoeia
IPA	Isopropyl Alcohol
IPQC	In Process Quality Control
IR	Infrared
KN	Kneading Technique
KV	Kilo Volt
LOD	Limit of Detection
LOQ	Limit of Quantification
Max	Maximum
MA-EA	Methacrylic Acid-co-Ethyl Acrylate
MCC	Microcrystalline Cellulose
MDR	Multi Drug Resistant
min	Minutes
µg	Microgram
mL	Millilitre
mL/min	Millilitre Per Minute
MLRA	Multiple Linear Regression Analysis
MRT	Mean Residence Time
M-β-CD	Methyl- β-Cyclodextrin
NIC	Nicotinamide
NLCs	Nanostructured Lipid Carriers
nm	Nano Meter
ODMT	Oro Dispersible Mini Tablets
OVAT	One Variable at A Time
PAT	Process Analytical Tools
PBPK	Physiological Based Pharmacokinetics
PBS	Phosphate Buffer Solution
PDE	Percentage Drug Entrapped

PDE	Partial Differential Equation
PDI	Polydispersibility Index
PEG	Poly Ethylene Glycol
PFCRT	<i>Plasmodium. falciparum</i> Chloroquine transporter gene
PFMDR1	<i>Plasmodium. falciparum</i> Multi Drug Resistant 1
PGH	Permeability -Glycoprotein Homologue
Poly (MA-EA)	Poly (Methacrylic Acid-Co-Ethyl Acrylate)
PS	Particle Size
P-value	Probability Value
PVAP	Polyvinyl Acetate Phthalate
PVP	Polyvinyl Pyrrolidone
PXRD	Powder X-ray diffraction
QbD	Quality by Design
QN	Quinine
QRM	Quality Risk Management
QTPP	Quality Target Product Profile
r	Radius
R ²	Correlation Coefficient
RAM	Risk Assessment Matrix
RES	Reticulo Endothelial System
RH	Relative Humidity
rpm	Rotation Per Minute
RSD	Relative Standard Deviation
R _t	Retention Time
S	Slope
SB	Sodium Benzoate
SC	Sodium Citrate
SD	Standard Deviation
SE	Standard Error
SEM	Scanning Electron Microscope
SLNs	Solid Lipid Nanoparticles
SMEDDS	Self-Microemulsion Drug Delivery System

SOP	Standard Operating Procedure
S-SMEDDS	Solidified Self-Microemulsion Drug Delivery System
TDC	Total Drug Content
TDW	Triple Distilled Water
TEM	Transmission Electron Microscopy
T _{max}	Time for Drug to Reach Maximum Concentration
USP	United States Pharmacopoeia
UV-VIS	Ultra Violet-Visible
V _d	Volume of Distribution
w/o/w	Water/Oil/Water
w/v	Weight/Volume
WHO	World Health Organization
XRD	X-Ray Diffraction Analysis
ZS	Zeta Sizer
ΔH	Enthalpy Change
ρ_b	Bulk Density
ρ_t	True Density
ρ_{tap}	Tapped Density
θ	Angle of Repose