


DECLARATION

I declared that the thesis entitled “**Formulation and Development of a Novel herbal drug delivery system with special emphasize on Phytosome incorporating bioactive compounds of flowering buds of *Mesua ferrea* Linn. and Evaluation of its therapeutic potential on Atopic dermatitis**” has been prepared by me under the guidance of **Dr. Bapi Ray Sarkar**, Associate Professor, Department of Pharmaceutical Technology, University of North Bengal.



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It is certified that the work contained in the thesis titled "**Formulation and Development of a Novel herbal drug delivery system with special emphasize on Phytosome incorporating bioactive compounds of flowering buds of *Mesua ferrea* Linn. and Evaluation of its therapeutic potential on Atopic dermatitis**", by **Jugal Sutradhar**, has been carried out under my supervision and his work has not been submitted elsewhere for the requirements for the degree of DOCTOR OF PHILOSOPHY (Ph.D.) in PHARMACY,

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April, 2024

Submission Information

Author Name	Jugal Sutradhar
Title	FORMULATION AND DEVELOPMENT OF A NOVEL HERBAL DRUG DELIVERY SYSTEM WITH SPECIAL EMPHASIZE ON PHYTOSOME INCORPORATING BIOACTIVE COMPOUNDS OF FLOWERING BUDS OF MESUA FERREA LINN. AND EVALUATION OF ITS THERAPEUTIC POTENTIAL ON ATOPIC DERMATITI
Paper/Submission ID	1608518
Submitted by	nbuplg@nbu.ac.in
Submission Date	2024-04-05 16:00:39
Total Pages	94
Document type	Thesis

Result Information

Similarity **2 %**



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ACKNOWLEDGMENT

For every work we do, we receive immense support from some great souls and helping hand persons who are always eager to accompany us in all our endeavours.

I would like to thank my supervisor, Dr. Bapi Ray Sarkar, for giving me this opportunity to work on projects. During my time in the University of North Bengal at Department of Pharmaceutical Technology, I received guidance from him and his enormous support for my research work.

I sincerely thank the University of North Bengal for the instrumental support, and other facilities to complete my research. The entire teaching staff was very much in charge of giving us the best available options. Every mistake of mine was just corrected with a smile by their truthful guidance. With their support, this accomplishment will be achieved.

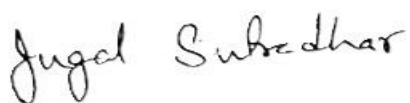
My deepest thanks go to Dr. Alakh Niranjana Sahu, and Mr. Debadatta Mohapatra (Ph.D. Research scholar) at the Department of Pharmaceutical, Indian Institute of Technology BHU, Varanasi, Dr. Nirupam Das, from the Assam University, Silchar.

I thank my parents, Mr. Dinabandhu Sutradhar and Mrs. Shova Sutradhar, my dearest family members, my wife, Mrs. Indrani Pramanik Sutradhar, and my son, Ayush Sutradhar. The author appreciates the help and cooperation of Mrs. Simran Giri, Mrs. Gouhar, Mis. Priya, Mr. Ganesh Dey, Dr. Manish Kumar Gupta, Dr. Ravi Bhushan Singh, and Mr. Ramesh. Without their support, this long journey would have been arduous.

In my research work, I give special thanks to Kali Da, Mallyaban, Bivas, and Debashri that have been helping in instrumental, Labs and also cooperating with me.

Special thanks to Prof. (Dr.) Pranab Ghosh, Director Research, NBU for his valuable suggestions during the project. I owe to the source of information that is needed for my research work, like a large number of books, monographs, articles, computer websites, etc.

At last, I offer my gratitude to God, without whose blessing it would not have been possible for me to achieve the heights of this project.



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Date: 22/04/2024

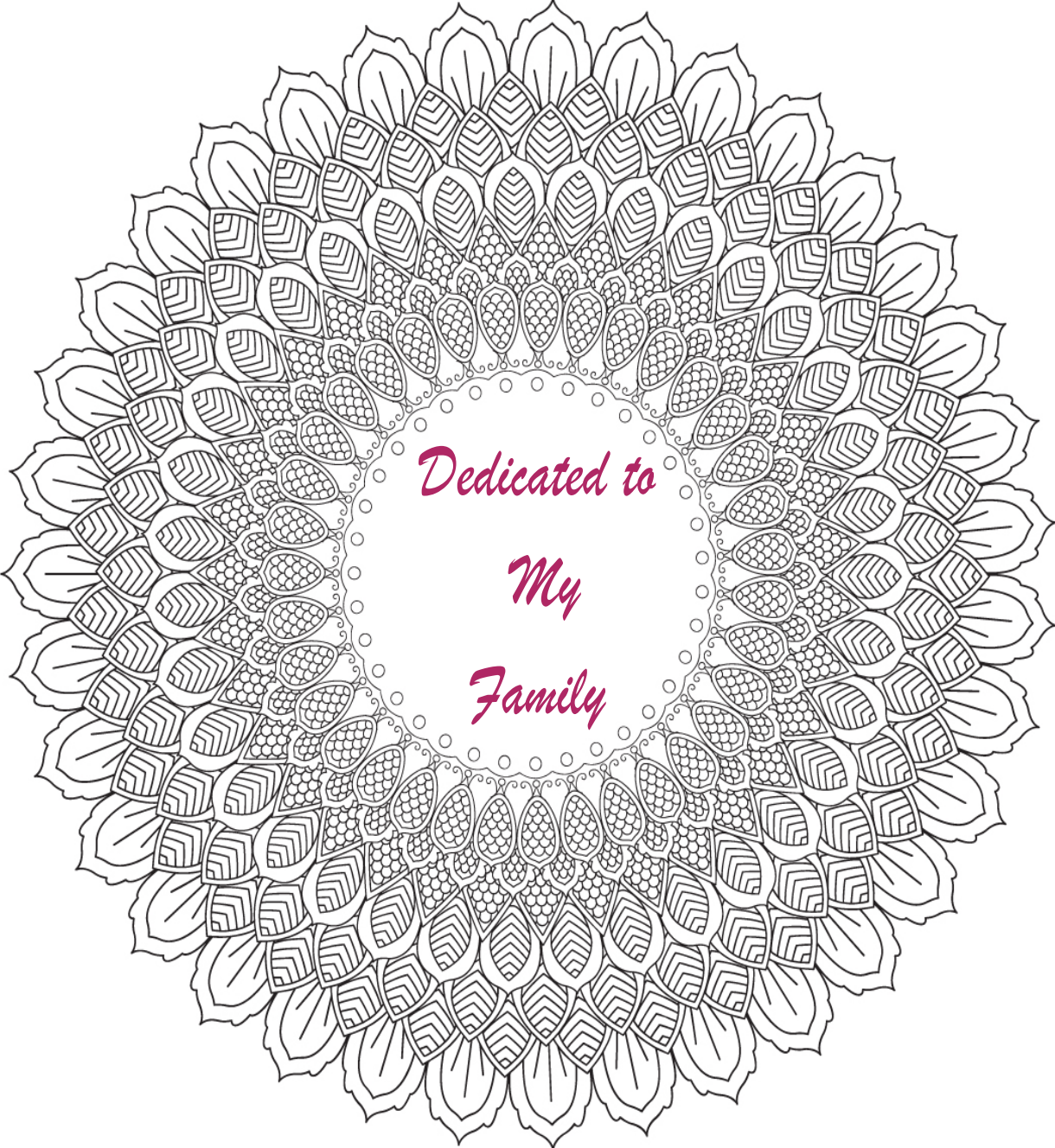
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Dedicated to

My

Family

PREFACE

Herbal medicinal plants have been used recently for different human diseases and are essential for saving lives worldwide; among them, a large evergreen tropical tree, *Mesua ferrea* Linn. is found all across tropical nations. This medicinal plant's flowering buds have been shown to have various activities. One patented technique in phytosome formulation creates an intermolecular bonding between a phytomolecule and one or more phosphatidylcholine molecules. That produces more bioavailability, increasing solubility, and permeability than a simple herbal extract because it increases the capacity to cross bio-membrane and reach blood circulation.

Atopic dermatitis is a complex and multifactorial, critical chronic inflammatory skin disease that frequently rises in developing countries and occurs at any age of human life, generally in children but similarly common in adults.

In this research study, the flowering buds of *Mesua ferrea* Linn. were collected and authenticated through conventional taxonomical and DNA barcoding (RBCL). The collected bud powder material and extracts were studied based on the pharmacognostical and phytochemical parameters. The powder sample was extracted through low polar to high polar solvents, and finally, standardized n-hexane extract was selected for the anti-microbial study.

The standardized n-hexane extract, soya lecithin, and cholesterol were mixed with chloroform solvent, and the phytosomes were prepared using the thin film hydration method. The phytosomes were evaluated by the zeta potential, polydispersity index, hydrodynamic vesicle size, entrapment efficiency, loading capacity, yield, and high-resolution transmission electron microscopy. Then, a standardized n-hexane extract-loaded phytosome gel was prepared with different concentrations of Carbopol-934.

Characterizations were performed through the organoleptic properties, pH and homogeneity, syneresis, extrudability, spreadability, viscosity, drug content, the permeability coefficient, drug permeation rate in steady state, enhancement ratio, drug excipient study through FTIR (Fourier transform infrared spectroscopy) study.

Finally, phytosome gel was selected for DNCB-induced atopic dermatitis-like animal model study, and the therapeutic potential was estimated through spleen weight, ear thickness, and blood tests such as WBC, lymphocytes, monocytes, eosinophils, neutrophils, and serum test (IL4, IFN- γ , TNF- α).

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LIST OF ABBREVIATIONS

AD: Atopic dermatitis

T2: Type 2 immunity

DMSO: Dimethyl sulphoxide

DSC: Differential scanning calorimetry

PCS: Photon correlation spectroscopy

DLS: Dynamic light scattering

AFM: Atomic force microscopy

BBB: Blood-brain barrier

TEM: Transmission electron microscopy

SEM: Scanning electron microscopy

HPLC: High-performance chromatography

TLC: Thin-layer chromatography

AMFE: Aqueous *M. citrifolia* Fruit Extract

FTIR: Fourier-transform infrared spectrometry

et al.: And others

g: Gram

h: Hour

mg: Milligram

cm: Centimeter

min: Minute

ml: Milliliter

M.P.: Melting point

ERR α : Estrogen-related receptor alpha

FBMF: Flowering buds of *Mesua ferrea* Linn.

CLSI: Clinical and Laboratory Standards Institute

ppm: Parts per million

MIC: Minimum inhibitory concentrations

RA: Relative humidity

ICH: International Conference on Harmonization

LOQ: Limit of quantification

LOD: Limit of detection

SMf: Standardized n-hexane extract of *Mesua ferrea* Linn. flowering buds

G-0.5: 0.5 % w/v phytosome gel

G-1.0: 1.0 % w/v phytosome gel

G-1.5: 1.5% w/v phytosome gel

G-SMf: SMf-loaded 1.0% w/v gel

G-Placebo: Plain Phytosome-loaded 1.0% w/v gel

TEA: Triethanolamine

ATR- FTIR: Attenuated total reflectance Fourier transform infrared spectroscopy

kp: Permeability coefficient

Q_i : Cumulative amount

OECD: Organization for Economic Co-operation and Development

PII: Primary irritation index

PCR: Polymerase chain reaction

w/v: Weight by volume

SD: Standard deviation

SEM: Standard error of mean

v/v: Volume by volume percentage

RSD: Relative standard deviation

ARRIVE: Animal Research: Reporting of *In-Vivo* Experiments

%: Percentage

⁰C: Degree centigrade

μ: Micro

μg: Microgram

Conc.: Concentration

RA: Relative humidity