



CERTIFICATE

This is to certify that the thesis entitled "Pharmacological evaluation of some herbs in experimentally induced Rheumatoid Arthritis along with cardiovascular complications" submitted by Ms. Trupti Dubey for the award of degree of Doctor of Philosophy in Pharmacy to Faculty of Pharmacy, The Maharaja Sayajirao University of Baroda, Vadodara has been carried out under my guidance. The matter compiled in this thesis has not been submitted earlier for the award of any other degree.

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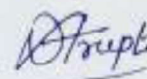
DECLARATION

I, *Trupti Dubey* undersigned, hereby declare that the thesis topic "**Pharmacological evaluation of some herbs in experimentally induced Rheumatoid Arthritis along with cardiovascular complications**" which is submitted herewith to The Maharaja Sayajirao University of Baroda, Vadodara for the award of degree of **Doctor of Philosophy in Pharmacy** is the result of work done by me at Faculty of Pharmacy, The Maharaja Sayajirao University of Baroda, under the guidance of **Dr. Kirti V. Patel** Associate Professor, Pharmacology, Faculty of Pharmacy, The Maharaja Sayajirao University of Baroda.

I further declare that the results of this work have not been previously submitted for any degree or fellowship.

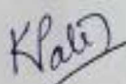
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This is to certify that the following enlisted publications (list of publications are attached herewith) belong to Ph.D. student Ms. Trupti Dubey who wishes to submit thesis entitled "Pharmacological evaluation of some herbs in experimentally induced Rheumatoid Arthritis along with cardiovascular complications" herewith to The Maharaja Sayajirao University of Baroda, Vadodra for the award of Ph.D. in Pharmacy.

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
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CERTIFICATE FOR ANTI PLAGIARISM

This is to certify that the Ph.D. thesis entitled "**Pharmacological evaluation of some herbs in experimentally induced Rheumatoid Arthritis along with cardiovascular complications**" submitted by **Ms. Trupti Dubey** has been checked for anti Plagiarism test by Drillbit Software provided by The Maharaja Sayajirao University of Baroda, Vadodara. After checking only 6% of similarity was found which is below the allowed plagiarism notify by the University Grant Commission. This research work has been carried out by **Ms. Trupti Dubey** under my Supervision at Faculty of Pharmacy, The Maharaja Sayajirao University of Baroda, Vadodara.


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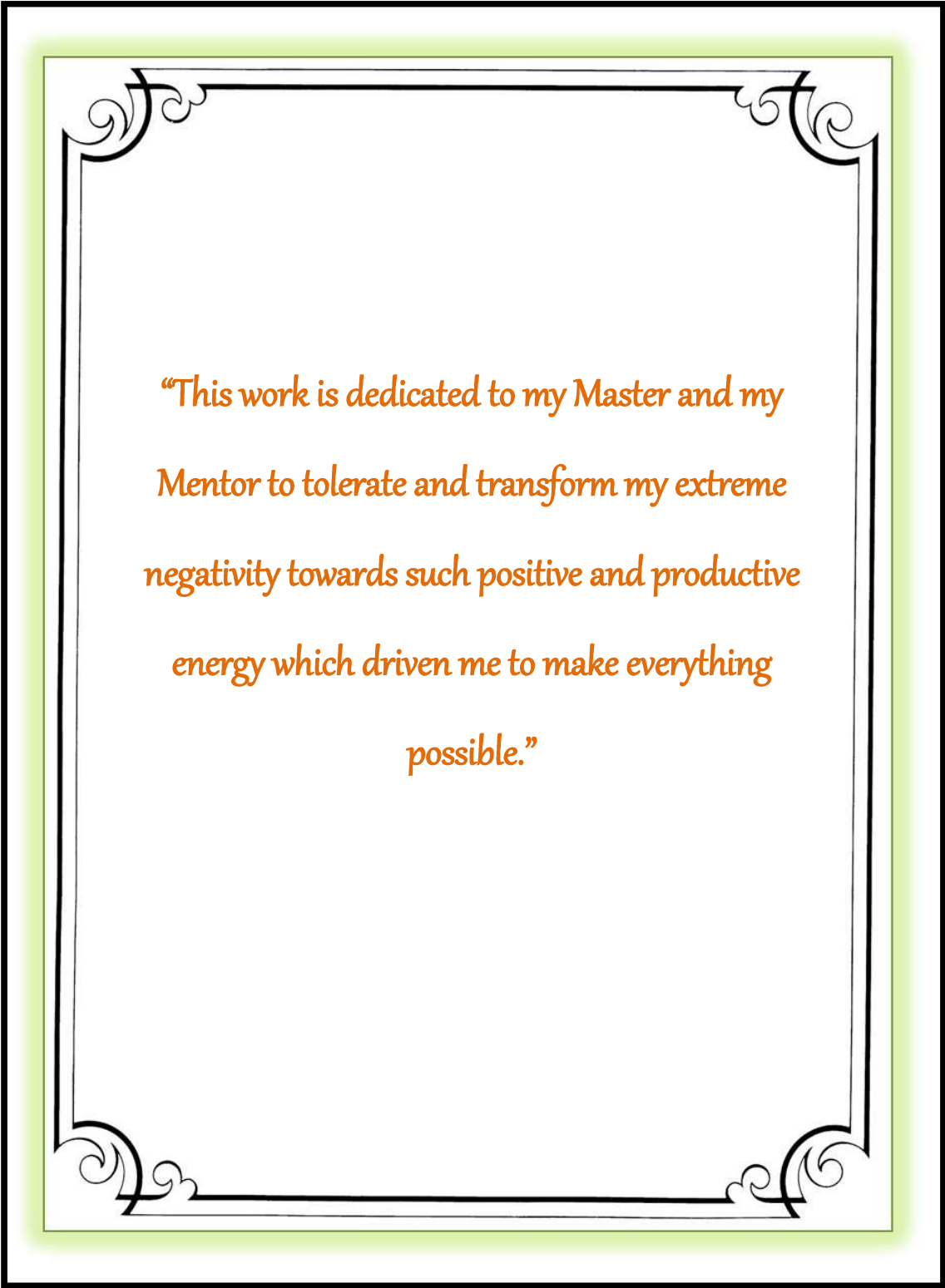
IAEC Approval of Animal Studies

Animal husbandry, handling and treatments were performed as per the CPCSEA guidelines. Animals were provided pelleted diet and water *ad libitum* in normal groups and High Fat Diet was prepared and given to animals during study period. They were housed in polypropylene cages with corn cobs as bedding material at $22 \pm 2^{\circ}\text{C}$ temperature and 50-75% relative humidity under 12hr light/dark cycle. Animals were monitored daily for any sign of distress and mortality. All the mentioned studies were approved by the Institutional Animal Ethics Committee (IAEC), Pharmacy Dept, Faculty of Pharmacy, The M. S. University of Baroda *vide* the protocol number mentioned below:

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*“This work is dedicated to my Master and my
Mentor to tolerate and transform my extreme
negativity towards such positive and productive
energy which driven me to make everything
possible.”*

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“First, Last and always, I want to acknowledge the source of everything that is life--and of life itself”

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List of Abbreviations

Ab	Antibody
ACCP	Anti Cyclic Citrullinated Peptide
ACR	American College of Rheumatology
ANOVA	Analysis of Variance
APC	Antigen Presenting Cells
ARRIVE	Animal Research Reporting of <i>in-vivo</i> Experiments
ASC	Apoptosis Associated Speck like Protein
CARD	Caspase-recruitment domain
CCL	Chemokine Ligands
CD4 ⁺	Cluster of Differentiation
CFA	Complete Freund's Adjuvant
CIA	Collagen Induced Arthritis
COMP	Cartilage Oligomeric Matrix Protein Precursor
COX	Cyclooxygenase
CPAE	<i>Carica papaya</i> Aqueous Extract
CPCSEA	Committee for Control and Supervision of Experiments on Animals
CRP	C- Reactive Proteins
CVD	Cardiovascular Diseases
DAMP	Damage Associated Molecular Patterns
DAS	Disease Activity Index
DMARDs	Disease Modifying Anti Rheumatoid Drugs
DMEM	Dulbecco's Modified Eagle's Medium
DMSO	Dimethyl Sulfoxide
DPPH	2, 2 diphenyl 1 Picrylhydrazyl
DTNB	5, 5' Dithiobis (2-nitrobenzoic Acid)
ECVAM	European Centre for the Validation of Alternative Methods
EDTA	Ethylenediamine tetra acetic acid
ELISA	Enzyme Linked Immunosorbent assay
ESR	Erythrocyte Sedimentation Rate
EULAR	European League against Rheumatism
FBS	Fetal Bovine Serum
FDA	Food and Drug Administration
FIMD	Framework To Identify Models For Disease
GM-CSF	Granulocyte Macrophage Colony Stimulating Factor
GSH	Glutathione
GUT	Gastrointestinal Tract
HDL	High-Density Lipoprotein
HFD	High Fat Diet
HLA-DRB	Human Leukocyte Antigen (HLA) Complex

Hyc	Homocysteine
IAEC	Institutional Animal Ethics Committee
Ig	Immunoglobins
IκB Proteins	inhibitors of NF-κB DNA binding
IL-6	Interleukin-6
iNOS	Inducible nitric oxide synthase
IPA	Iso Propyl Alcohol
JAK	Janus Activated Kinase
LDL	Low Density Lipoprotein
LPS	Lipopolysachcharide
MAP	Mitogen Activated Protein
MCAE	<i>Momordica charantia</i> Aqueous Extract
MCP	Metacarpophalangeal
MHC II	Major Histocompatibility Complex Class II
MMP	Matrix Metalloproteinase
MRI	Magnetic Resonance Imaging
MTP	Metatarsophalangeal
MTT	3(4, 5 Dimethylthiazole 2 yl) 2, 5 diphenyltetrazolium bromide
MTX	Methotrexate
NCCS	National Centre for Cell Science
NF-κB	Nuclear Factor Kappa Light Chain Enhancer Of Activated B Cells
NLR	NOD like Receptors
NLRP	Nucleotide-binding leucine-rich repeat receptor Proteins
NLRP 3	NOD Like Receptor Protein subtype 3
NO	Nitric Oxide
NOD	Nucleotide-binding oligomerization domain
NSAE	<i>Nigella sativa</i> Aqueous Extract
NSAIDs	Non-steroidal anti-inflammatory drugs
<i>p.o.</i>	Per Oral
PAD4	Peptidyl Arginine Deiminase
PAMPs	Pathogen Activated Molecular Patterns
PBS	Phosphate buffered Saline
PGs	Prostaglandins
PIP	Proximal interphalangeal
PTPN	Protein Phosphatase Non Tyrosine Receptor Type Gene
RA	Rheumatoid Arthritis
RANKL	Receptor Activator of Nuclear Factor kappa B Ligands
RCTs	Randomized Controlled Trial
RF	Rheumatoid Factor
ROS	Reactive oxygen species
<i>s.c.</i>	Subcutaneous
SAARDs	Slow Acting Anti Rheumatic Drugs
SEM	Standard Error of Mean

SF	Synovial Fluid
SNH	Symptomatology And Natural History Criteria
SOD	Superoxide Dismutase
Th-Cells	T-Helper Cells
TLR-4	Toll Like Receptor Protein – 4
TNF- α	Tumour Necrosis Factor- alpha
TRAF protein	Tumor necrosis factor receptor–associated factor
WHO	World Health Organization