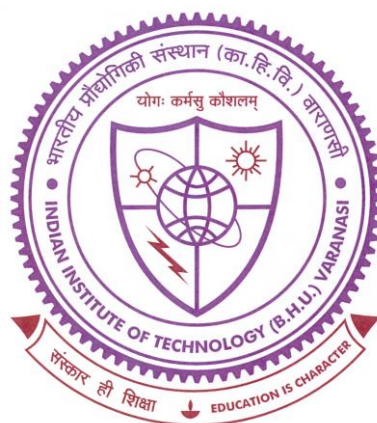


Quality Control studies and Ethnopharmacological evaluation of *Natsiatum herpeticum* Buch.-Ham. ex Arn.



Thesis submitted in partial fulfilment for the
Award of Degree

Doctor of Philosophy

By

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I, Ms. Sangeeta Hazarika, certify that the work embodied in this thesis is my own bonafide work and carried out by me under the supervision of Prof. Siva Hemalatha from July 2017-July 2023, at the Department of Pharmaceutical Engineering & Technology, Indian Institute of Technology (BHU), Varanasi. The matter embodied in this thesis has not been submitted for the award of any other degree/diploma. I declare that I have faithfully acknowledged and given credits to the research workers wherever their works have been cited in my work in this thesis. I further declare that I have not wilfully copied any other's work, paragraphs, text, data, results, etc. reported in journals, books, magazines, reports dissertations, theses, etc., or available at websites and have not included them in this thesis and have not cited as my own work.

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ABBREVIATIONS

AAS	: Atomic Absorption Spectroscopy
ALP	: Alkaline phosphatase
ALT	: Alanine transaminase
AMR	: Antimicrobial resistance
ANOVA	: Analysis of Variance
AST	: Aspartate aminotransferase
BLAST	: Basic Local Alignment Search Tool
CBOL	: Consortium for the Barcode of Life
CPCSEA	: Committee for the Purpose of Control and Supervision of Experiments on Animals
DHFR	: Dihydrofolate reductase
DMNC	: Density of Maximum Neighbourhood Component
DNA	: Deoxyribonucleic acid
dNTPs	: Deoxynucleoside triphosphates
EPC	: Edge Percolated Component
FDR	: False Discovery Rate
GHS	: Globally Harmonized System
GO	: Gene Ontology
IC ₅₀	: Inhibitory Concentration 50
IRAK4	: Interleukin-1 receptor-associated kinase 4
KEGG	: Kyoto Encyclopaedia of Genes and Genomes
LC-MS	: Liquid Chromatography-Mass Spectrometry
LC-MS-MS	: Liquid Chromatography Tandem Mass Spectrometry
LD ₅₀	: Lethal Dose 50

MBC	: Minimum Bactericidal Concentration
MCC	: Maximal Clique Centrality
MD	: Molecular Dynamics
MHA	: Mueller-Hinton agar
MHB	: Mueller-Hinton broth
MIC	: Minimum Inhibitory Concentration
MM-GBSA	: Molecular Mechanics Generalized Born Model and Solvent Accessibility
MNC	: Multinetwork Clustering
NCBI	: National Center for Biotechnology Information
NIH	: National Institutes of Health
OECD	: Organisation for Economic Co-operation and Development
PBP	: Penicillin binding protein
PCR	: Polymerase Chain Reaction
PPI	: Protein-protein interaction
QToF	: Quadrupole Time-of-Flight
QToF-MS	: Quadrupole Time-of-Flight Mass Spectrometer
rGy	: Radius of Gyration
RMSD	: Root Mean Square Deviation
RMSF	: Root Mean Square Fluctuation
SDG	: Sustainable Development Goals
TNF	: Tumour necrosis factor
TRAF6	: Tumour necrosis factor receptor-associated factor 6
UV	: Ultraviolet
WHO	: World Health Organization

PREFACE

Natural resources, particularly plants, have long been used as a source of therapeutics, and over the past centuries, many valuable drugs have been created from these resources. They have been the source of privileged scaffolds for half of all medicinal compounds that are produced synthetically due to their complex structural spaces and physicochemical properties. Emerging risks to human health necessitate a concerted effort to find both preventive and therapeutic approaches, with natural products at the centre of initiatives to develop novel treatments and lower disease transmission and associated mortality. *Natsiatum herpeticum* Buch.-Ham. ex Arn., a least-explored plant, is being considered a wild edible plant by some ethnic groups. In spite of several previous publications suggesting its ethnopharmacological use by different tribes, no documentation or scientific approaches have been made hitherto to validate its ethnopharmacological claims. The research work presented in the thesis addresses four objectives. The first objective of the study is to validate the pharmacognostical quality control assessment of *N. herpeticum* in accordance with standard guidelines. The second objective is to determine the toxicity profile of the plant. The third objective includes the qualitative screening of the aqueous plant extract and network pharmacology-based prediction of the antibacterial and anti-inflammatory potential of the detected compounds. The fourth objective deals with the experimental validation of the pharmacological activity of the aqueous extract of *N. herpeticum* using in silico-in vitro-in vivo approach.

The work embodied in this thesis has been organised into the following chapters:

Chapter 1. This chapter introduces the significance of natural products in drug discovery and development and discusses the significance of modern tools in natural product research. Further, the available ethnopharmacological claims on *N. herpeticum* have been described.

Chapter 2. This chapter deals with the literature available on *N. herpeticum*. It further summarises the application of different methodologies in natural product research.

Chapter 3. This chapter includes the rationale, objectives, and plan of work.

Chapter 4. In this chapter, a description of the methodologies employed in the research work has been provided.

Chapter 5. This chapter includes the findings of the quality control assessment, toxicity studies, network pharmacology-based prediction, and pharmacological evaluations.

Chapter 6. This chapter discusses the major findings of the study and their implications. Further, it describes the current limitations of the study.

Chapter 7. This chapter summarises the key points of the findings from the study and presents future prospective.

Apart from this, the references and appendix, including the additional supplementary data supporting the main findings, have been included.