

Identification and Biological Evaluation of Small Molecules as Sirtuin Inhibitor against Breast Cancer



Thesis submitted in partial fulfilment for the
Award of the Degree

DOCTOR OF PHILOSOPHY

By

KOJJA VENKATESWARLU

Department of Pharmaceutical Engineering and Technology
Indian Institute of Technology
(Banaras Hindu University)
Varanasi- 221005
INDIA

Roll No: 19161015

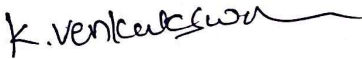
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I, **Kojja Venkateswarlu**, certify that the work embodied in this Ph.D. thesis is my own bona fide work and carried out by me under the supervision of **Dr. Prasanta Kumar Nayak** from July, 2019 to June, 2025 at the **Department of Pharmaceutical Engineering & Technology, Indian Institute of Technology (Banaras Hindu University), Varanasi**. The matter embodied in this Ph.D. thesis has not been submitted for the award of any other degree/diploma. I declare that I have faithfully acknowledged and given credit 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 the journals, books, magazines, reports, dissertations, theses, etc., or available on websites and have not included them in this Ph.D. thesis and have not cited as my own work.

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Kojja Venkateswarlu

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Dr. Prasanta Kumar Nayak
(Supervisor)
सहायक अध्यापक / Assistant Professor
भेषजकीय अभियांत्रिकी एवं प्रौद्योगिकी विभाग /
Department of Pharmaceutical Engineering & Technology
भारतीय प्रौद्योगिकी संस्थान / INDIAN INSTITUTE OF TECHNOLOGY
(बनारस हिन्दू विश्वविद्यालय) / (BANARAS HINDU UNIVERSITY)
वाराणसी-२२१००५ / Varanasi-221005
E-mail: pknayak.phe@iitbhu.ac.in


विभागाध्यक्ष / Head
भेषजकीय अभियांत्रिकी एवं प्रौद्योगिकी विभाग /
Department of Pharmaceutical Engineering & Technology
भारतीय प्रौद्योगिकी संस्थान / INDIAN INSTITUTE OF TECHNOLOGY
(बनारस हिन्दू विश्वविद्यालय) / (BANARAS HINDU UNIVERSITY)
वाराणसी-२२१००५ / Varanasi-221005

Department of Pharmaceutical Engineering & Technology
Indian Institute of Technology
(Banaras Hindu University)
Varanasi-221005



CERTIFICATE

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Dr. Prasanta Kumar Nayak
(Supervisor)

डा० प्रसान्त कुमार नायक / Dr. Prasanta Kumar Nayak
सहायक आचार्य / Assistant Professor
शैवजकीय अभियांत्रिकी एवं प्रौद्योगिकी विभाग /
Department of Pharmaceutical Engineering & Technology
भारतीय प्रौद्योगिकी संस्थान / INDIAN INSTITUTE OF TECHNOLOGY
(बनारस हिन्दू विश्वविद्यालय) / (BANARAS HINDU UNIVERSITY)
वाचणसी-२२१००५ / Varanasi-221005
E-mail: pknayak.phe@iitbhu.ac.in

Date: 02-09-2007

Place: IIT (BHU), Varanasi



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Date:

Place: IIT (BHU), Varanasi

K. Venkateswarlu

Kojja. Venkateswarlu

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List of Abbreviations

Abbreviations	Full Forms
BC	Breast Cancer
PE	Phytoestrogen
COU	Coumestrol
MCF-7	Michigan Cancer Foundation-7
MDA-MB-231	M D Anderson - Metastatic Breast – 231
SIRT	Sirtuin
AVO	Acidic vesicular organelles
NAD ⁺	Nicotinamide adenine dinucleotide
DMEM	Dulbecco's Modified Eagle Medium
PDB	Protein Data Bank
ROS	Reactive oxygen species
ERs	Estrogen receptors
DCFDA	Dichlorodihydrofluroscein diacetate
MTT	(3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide)
HDAC	Histone deacetylases
PAGE	Poly acrylamide gel electrophoresis
RMSD	Root mean square deviation
PVDF	Polyvinylidene difluoride
WB	Western blotting
Bcl-2	B-cell lymphoma
RT	Retention time
PCA	Principal Component Analysis
GC-MS	Gas Chromatography-Mass Spectrometry
IC ₅₀	Inhibitory Concentration
HMDB	Human Metabolome Database
MD simulations	Molecular dynamic simulations
RCSB	Research Collaboratory for Structural Bioinformatics
HER	Human Epidermal Growth Factor Receptor
TNBC	Triple-negative breast cancer
DMSO	Dimethyl Sulfoxide
ADME	Absorption, distribution, metabolism, and excretion
MSTFA	N-methyl-N-trimethylsilyl-trifluoroacetamide
NIST	National Institute of Standards and Technology
MSEA	Metabolite Set Enrichment Analysis
TIC	Total ion chromatograms
LC3	Light chain 3
SRB	Sulforhodamine B
PBS	Phosphate Buffered Saline
TBST	Tris Buffered Saline Tween-20
7ab	1-((6-chlorobenzo[d]thiazol-2-ylamino)(3,4-dichlorophenyl)methyl)naphthalen-2-ol
7ba	1-((6-chlorobenzo[d]thiazol-2-ylamino)(4-bromophenyl)methyl)naphthalen-2-ol

List of Symbols

Symbols	Meaning
α	Alpha
β	Beta
$^{\circ}\text{C}$	Degree Celsius
mg	Mili gram
μg	Micro gram
μM	Micro Mole
mmol	Mili Mole
mL	Mili Liter
μL	Micro Liter
h	Hour
%	Percentage
\geq	More than or equal
$<$	Less than
$>$	More than
\pm	Plus, or minus