Design, Synthesis, and Biological Evaluation of Piperic Acid Template Based Naturally Inspired Novel Multifunctional Molecules for the Treatment of Alzheimer's Disease

Thesis submitted in partial fulfilment for the

Award of Degree

Doctor of Philosophy

By

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I, *"Jitendra Kumar"*, certify that the work embodied in this thesis is my own bonafide work and carried out by me under the supervision of *"Dr. Sunil Kumar Mishra"* from *"January 2016" to "December 2024"*, 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 willfully 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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List of Abbreviations

Abbreviations	Full forms
AD	Alzheimer's disease
ACh	Acetylcholine
*h*ACh	Human acetylcholine
AChE	Acetylcholinesterase
ADME	Absorption, Distribution, Metabolism, and Excretion
AFM	Atomic force microscopy
ATCI	Acetylthiocholine iodide
BTCI	Butyrylthiocholine iodide
BChE	Butyrylcholinesterase
BBB	Blood-Brain Barrier
CAS	Catalytic active site
$CDCl_3$	Deuterated chloroform
DMSO-d_6	Deuterated dimethyl sulfoxide-d_6
DPZ	Donepezil
DTNB	5,5'-dithiobis-2-nitrobenzoic acid
DPPH	2,2-diphenyl-1-picrylhydrazyl
EDCI.HCl	1-[3-(dimethyamino)-propyl]-3-ethylcarbodiimide hydrochloride
PA	Piperic acid
FA	Ferulic acid
HBA	Hydrogen bond acceptor

HBD	Hydrogen bond donor
HRMS	High-resolution mass spectrometry
HOBt	*N*-hydroxybenzotriazole
IC_{50}	Inhibitory concentration is required to kill 50% of the population
MW	Molecular weight
MTT	3- (4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium
PAS	Peripheral anionic site
ROS	Reactive oxygen species
TMS	Tetramethylsilane

List of Symbols

Symbols	Meaning
α	Alpha
β	Beta
δ	Delta
ºC	Degree Celsius
Å	Angstrom
mg	Milligram
μg	Micro gram
μM	Micromole
mmol	Millimole
mL	Milliliter
μL	Microliter
h	Hour
s	Singlet
nm	Nanometer
µm	Micrometer
mm	Millimeter
cm	Centimeter
ppm	Parts per million
rpm	Revolutions per minute
Kcal	Kilocalories

Hz	Hertz
MHz	Megahertz
J	Coupling constant
d	Doublet
t	Triplet
m	Multiplet
dd	Doublet of doublet
m/z	Mass to charge ratio
%	Percent
pH	Potential of hydrogen
≤	Less than or equal
<	Less than
>	More than
±	Plus or minus