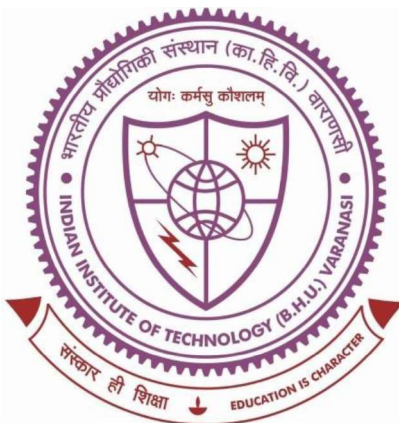


# Glucocerebrosidase Chaperone as a Treatment Strategy for Parkinson's disease



Thesis submitted in partial fulfilment for the  
Award of Degree

**Doctor of Philosophy**

By

***Pratigya Tripathi***

DEPARTMENT OF PHARMACEUTICAL ENGINEERING &  
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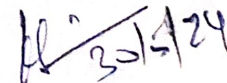
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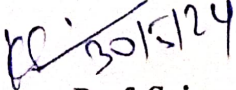
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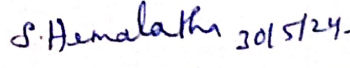
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### **List of Abbreviations**

ACN	: Acetonitrile
ADMET	: Absorption, distribution, metabolism, excretion, and toxicity
ALA	: Alanine
ALA	: Alanine
ALP	: Alkaline phosphatase
ALT	: Alanine aminotransferase
AMB	: Ambroxol
ARG	: Arginine
ARG	: Arginine
ASN	: Asparagine
ASP	: Ischemic reperfusion
AST	: Aspartate aminotransferase
AUC	: Area under the curve
b.w	: Body weight
BBB	: Blood-brain barrier
BE	: Binding energy
BLAST	: Basic Local Alignment Search Tool
BN	: Binucleated nucleus
BP	: Bound protein
CAL	: Calculated
CD	: Circular dichroism
cDNA	: complementary DNA
CHOP	: C/EBP Homologous Protein
CK-MB	: Creatine kinase myocardial band
C <sub>max</sub>	: Maximum plasma concentration
CNS	: Central Nervous system
CON	: Concentrations

---

CRE	: Creatinine
CSF	: Cerebrospinal fluid
CV	: Cardio vascular
CYP450	: Cytochromes P450
CYS	: Cysteine
DA	: Dopamine
DBS	: Deep brain stimulation
DCF	: Dichlorodihydrofluorescein
DCFH-DA	: Dichlorodihydrofluorescein diacetate
DCT	: Distal convoluted tubule
DMEM	: Dulbecco's Modified Eagle Medium
DMSO	: Dimethyl sulfoxide
DNA	: Deoxy-ribonucleic acid
DPX	: Dibutylphthalate Polystyrene Xylene
ELISA	: Enzyme linked immunosorbant assay
ER	: Endoplasmic reticulum
ERAD	: Endoplasmic reticulum associated degradation
ERS	: Endoplasmic reticulum stress
ETDA	: Ethylenediaminetetraacetic acid
FBS	: Fetal bovine serum
FDA	: Food and Drug Administration
FT-IR	: Fourier transform infra-red spectroscopy
G	: Gram
GADD153	: DNA damage-inducible gene 153
GAPDH	: Glyceraldehyde 3-phosphate dehydrogenase
GC	: Glucocerebrosides
GCase	: Glucocerebrosidase
GEF	: Glucocerebrosidase enriched fractions
GH	: Glycoside hydrolase
GlcCer	: Glucosylceramide

---

GLN	: Glutamate
GLU	: Glutamic acid
GMQE	: Global Model Quality Estimation
H	: Hours
H2O2	: Hydrogen peroxide
Hb	: Haemoglobin
HE	: Hematoxylin-Eosin
hERG	: Human ether-'go-go-related gene
hGCase	: Human glucocerebrosidase
HIA	: Human intestinal absorption
HIS	:Histidine
HPLC	: High performance liquid chromatography
HPLC	: High-performance liquid chromatography
HQC	: High quality control
HRP	: Horseradish peroxidase
I.V	: Intravenous
IAEC	: Institutional Animal Ethic Committee
IC <sub>50</sub>	: Inhibitory concentration
ICH	: International Council for Harmonisation
IDV	: Integrated density value
IS	: Internal standard
IU/mL	: International Units Per Milliliter
K	: Kelvin
KCl	: Potassium chloride
LD <sub>50</sub>	: Lethal dose
LEU	: Leucine
LGA	: Lamarckian Genetic Algorithm
LGA	: Lamarckian genetic algorithm
LLOD	: Lower limit of detection
LLOQ	: Lower limit of quantification

---

LQC	: Low quality control
LSD	: Lysosomal storage disorder
LYS	: Lysine
MDS	: Molecular Dynamic simulation
MET	: Methionine
MIN	: Minuets
mM	: Milimoles
MPTP	: Mitochondrial permeability transition pore (MPTP)
MQC	: Medium quality control
MRT	: Mean residence time
MTT	: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
NACL	: Sodium chloride
NaHCO <sub>3</sub>	: Sodium bicarbonate
NFI	: Normalize fluorescent unit
nM	: Nanometer
NMOLES	: Nanomoles
OCT	: Optimal cutting temperature compound TRITC
OECD	: Organization for Economic Cooperation and Development
<i>p.o</i>	: Per oral
PAGE	: Polyacrylamide gel
PAIN	: Pan Assay Interference Compounds
PBS	: Phosphate buffer saline
PCT	: Proximal convoluted tubule
PD	: Parkinson's disease
PD	: Pharmacodynamics
PDA	: Photodiode array
PDA	: Photo diode
PDB	: Protein data bank
PERK	: Protein kinase R-like endoplasmic reticulum kinase
PHE	: Phenylalanine

---

PK	: Pharmacokinetics
PL	: Protein ligand
PL	: Protein ligand
PLT	: Platelets
PMSF	: Phenylmethylsulfonyl fluoride
PS129	: Phospho- $\alpha$ -syncluin
PT	: Portal tract
PVDF	: Polyvinylidene difluoride
QC	: Quality control
QMEAN	: Qualitative Model Energy ANalysis
QRTPCR	: Quantitative Real-time polymerase chain reaction
RA	: Relative activity
RAMPAGE	: Ramachandran plot
RBC	: Red blood cells
RDV	: Relative density value
R <sub>g</sub>	: Radius of gyration
rGCCase	: Rat glucocerebrosidase
RMSD	: Root mean square deviation
RMSF	: Root mean square fluctuation
ROS	: Reactive Oxygen Species
ROS	: Reactive oxygen species
RPM	: Revolutions per minute
RSD	: Relative standard deviation
SASA	: Solvent accessible area surface
SD	: Standard deviation
SD	: Standard Deviation
SDS	: Sodium dodecyl sulfata
SEL	: Selegiline
SEL	: Selegiline
SER	: Serine

---

SN	: Substantia nigra
SNc	: Substantia nigra pars compacta
SR	: Stabilization ratio
ST	: Striatum
T $\frac{1}{2}$	: Half-life
TBST	: Tris-buffered saline Tween 20
TDA	: Thermal denaturation assay
TDC	: Taurodeoxycholic acid
TH	: Tyrosine hydroxylase
TIM	: Triosephosphate isomerase
TIP3P	: Transferable Intermolecular Potential with 3 Points
T <sub>max</sub>	: Time to reach the maximum plasma concentration
TRP	: Tryptophan
TYR	: Tyramine
UBD	: Unbound protein
UPR	: Unfold protein response
VAL	: Valine
WBC	: White blood cells
$\alpha$ - SYN	: $\alpha$ - synuclein
$\mu$ L	: Microliter
4-MU	: 4-Methylumbelliferone
4-MUG	: 4-Methylumbelliferyl $\beta$ -D-glucopyranoside
6-OHDA	: 6-Hydroxy dopamine
$\text{A}^0$	: Angstrom