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It is further certified that the student has fulfilled all the requirements of Comprehensive Examination, Candidacy and SOTA for the award of Ph.D. Degree.

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I, **Mr. Puneet K Samaiya**, 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. Sairam Krishnamurthy** and co-supervision of **Dr. Ashok Kumar** for a period of about **3 years 9 months from July, 2013 to April, 2017** at the **Department of Pharmaceutics, Indian Institute of Technology and Department of Pediatrics (Banaras Hindu University), Varanasi.** The matter embodied in this Ph.D. thesis has not been submitted for the award of any other degree/diploma.

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Date: 24/04/2017

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ACRONYMS

ADHD	Attention Deficit Hyperactivity Disorder
PND	Post Natal Day
GABA	Gamma-Aminobutyric acid
NMDA	N-methyl-D-aspartate
EAA	Excitatory Amino Acid
DISC	Death-Inducing Signaling Complex
OMM	Outer Mitochondrial Membrane
IMS	mitochondrial intermembrane space
SMAC	Second Mitochondrial Derived Activator Of Caspases
DIABLO	Diablo IAP-Binding Mitochondrial Protein
Bcl-2 family	B-cell lymphoma-2
ATP	Adenosine triphosphate
ETC	Electron Transport Chain
MMP	Mitochondrial Membrane Potential
ROS	Reactive Oxygen Species
TMRM	Tetramethylrhodamine Methyl Ester
PN	Peroxynitrite
DNA	Deoxyribonucleic Acid
MPT	Mitochondrial Permeability Transition
ANT	Adenine Nucleotide Translocator
VDAC	Voltage-Dependent Anion Channel
APAF1	Apoptotic Protease-Activating Factor-1
2, 4-DNP	2,4 Dinitrophenol
NO	Nitric oxide
MtNOS	Mitochondrial Nitric Oxide Synthase
BSA	Bovine Serum Albumin
EGTA	Ethylene Glycol Bis(2-Aminoethyl Ether)Tetraacetic Acid
HEPES	4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid
ADP	Adenosine Diphosphate
FCCP	Carbonyl Cyanide 4-(Trifluoromethoxy) Phenylhydrazone

CBF	Cerebral Blood flow
RCR	Respiratory Control Ratio
SOD	Superoxide Dismutase
MDA	Malondialdehyde
LPO	Lipid Peroxidation
NBT	Nitroblue Tetrazolium
PMS	Phenazine Methosulphate
SDS-PAGE	Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis
PVDF	Polyvinylidene Fluoride Membranes
FITC	Fluorescein Isothiocyanate
PI	Propidium Iodide
HPA axis	Hypothalamic–Pituitary–Adrenal Axis

PREFACE

The research work of the thesis entitled "Evaluation of some mitochondrial modulators in the treatment of neonatal anoxia" is based on the identification of a novel mitochondrial-targeted mechanism through which the cortical neuronal cell death progresses in developing brain can be prevented. Moreover, by preserving the mitochondrial function on certain time points may be helpful in improving neurobehavioral outcomes in newborns. The whole work has compiled into eight chapters: **Chapter 1** introduces the topic and its importance. **Chapter 2** investigates the temporal dynamics of mitochondrial bioenergetics after anoxia in rat pups (neonates). **Chapter 3** evaluates mitochondrial dysfunction linked progression of insult and transition of cell death after anoxia. **Chapter 4** investigates the clinical basis of mitochondrial-linked apoptotic markers in the cerebrospinal fluid of anoxic neonates. **Chapter 5** investigates the role of 2,4 dinitrophenol (2,4 DNP) on anoxia-induced mitochondrial dysfunction linked insult progression. **Chapter 6** investigates the role of tempol on anoxia-induced mitochondrial dysfunction induced insult progression. **Chapter 7** describes the combined effect of mitochondrial modulators (2,4 DNP and tempol) for any synergistic or additive effect in the treatment of anoxia-induced synaptic and non-synaptic mitochondrial dysfunction and neurobehavioral alterations from day-21 up to day-150. **Chapter 8** summarizes the study with its important outcomes. It also discusses the future perspective of the work and its potential benefits for science and humanity.