

PREFACE

The thesis research work entitled “Pharmacological intervention in dim light induced changes in circadian rhythm.” assessed the effect of continuous dim light on the rhythmicity of mitochondrial function in the superchiasmatic nuclei (SCN). Further, we evaluated the role of mitochondria in normal circadian rhythm (light dark; LD 12:12 h) and disrupted circadian rhythm (continuous dim light; LL 24:00 h). Further, first time we are showing there is a rhythmic pattern in mitochondrial bioenergetics and mitochondrial DNA in LD condition over the 24-h in along with corticosterone and the rhythmicity was lost in the LL condition. Therefore, we sought to the effect of mitochondrial modulator N-acetylcysteine (NAC) on dim light induced mitochondrial changes in central and peripheral tissue clock. Moreover, we evaluated the NAC effect on different circadian clock genes, endogenous melatonin and hunger hormone leptin and ghrelin which was attenuated at different doses with NAC in mice exposed to dim light. Furthermore, there are several pharmacological agents like metformin that are promising to have a mitochondrial potential or inhibitory effect there is no screening method to test their activity on mitochondria. Hence, we have developed a robust economic *ex-vivo* method for mitochondrial bioenergetics using mitochondrial modulators.

The whole work has been compiled into six chapters: **Chapter 1** introduces the topic and its importance. **Chapter 2** Effect of normal and disrupted circadian rhythm on the mitochondria. **Chapter 3** Effect of N-acetylcysteine on mitochondria dysfunction induced by disrupted circadian rhythm in central clock. **Chapter 4** documents the effect of N-acetylcysteine on mitochondria dysfunction induced by disrupted circadian rhythm in peripheral clock. **Chapter 5** Novel *Ex-vivo* method development for the evaluation of mitochondrial modulators and **Chapter 6** summarizes the entire study with the conclusion and important outcomes.

