List of Tables & Figures

Tables		Page No.
Table 1:	Composition of high fat diet	35
Table 2:	List of primers for real time PCR	45

Figures		Page No.
Figure 1:	Types of liver diseases	2
Figure 2:	Reversible and non-reversible stages of nonalcoholic fatty	3
	liver disease (NAFLD)	
Figure 3:	Continent-wise prevalence of NAFLD in the year 2019	4
Figure 4:	Association of metabolic syndrome components with	6
	nonalcoholic steatohepatitis (NASH)	
Figure 5:	The "two-hit" hypothesis in the progression of	7
	Nonalcoholic fatty liver disease (NAFLD) to Nonalcoholic	
	steatohepatitis (NASH)	
Figure 6:	The Liver-gut-brain axis	8
Figure 7:	The liver-brain crosstalk in the condition of lifestyle	10
	disorder	
Figure 8:	Types of Biological rhythms	13
Figure 9:	Circadian rhythms in daily physiological functions	14
Figure 10:	Molecular mechanism of circadian clock	15
Figure 11:	Circadian clock mediated control and coordination of	17
	metabolic functions of liver	
Figure 12:	Chronodisruption mediated perturbations in psychiatric and	21
	metabolic pathologies	
Figure 13:	Alterations in neuro-behavior due to psychosocial and	22
	physiological stress	
Figure 14:	Protective role of melatonin on various organs	23
Figure M1:	Schematic representation of normal and altered	33
	photoperiodic regime to induce chronodisruption	

Figure 1.1:	Flow chart of experimental protocol followed for	50
	validation of experimentally induced Nonalcoholic	
	steatohepatitis	
Figure 1.2:	Viscera showing adipocity build up in experimental mice	55
Figure 1.3:	Body and liver weight in mice subjected to (H) diet and/or	56
	(CD) induced photoperiodic manipulation	
Figure 1.4:	Visceral adipose tissue weight and body circumference in	57
	experimental mice	
Figure 1.5:	Food and water intake in experimental groups	58
Figure 1.6:	Melatonin treatment improves liver function in H and/or	59
	CD subjected mice	
Figure 1.7:	Melatonin treatment improves serum lipid profile in H	60
	and/or CD subjected mice	
Figure 1.8a:	Histological examination of liver done by H&E staining of	61
	H and/or CD exposed group showing improvement in	
	melatonin treatment (100X)	
Figure 1.8b:	Histological examination of liver done by H&E staining of	62
	H and/or CD exposed group showing improvement in	
	melatonin treatment (400X)	
Figure 1.9:	Effects of H and/or CD subjected mice on serum protein	63
	concentrations	
Figure 1.10:	CD and/or H diet alters the expression of hepatic core	64
	circadian clock genes as evidenced by their mRNA profiles	
Figure 1.11:	Altered serum melatonin rhythmicity in mice subjected to	65
	CD and/or H diet	
Figure 1.12:	CD and/or H diet alters the expression of hepatic lipid	66
	regulatory genes as evidenced by their mRNA profiles	
Figure 2.1:	Schematic representation of experimental protocol	76
	followed for inflammatory changes in liver and brain	
	following induction of NASH	
Figure 2.2:	Alterations in circulating inflammatory cytokines in mice	79

	subjected to (H) diet and/or subjected to CD	
Figure 2.3:	Effect of melatonin on genes regulating inflammation	80
	(TNF- α , IL-1 β , IL-6 and MCP-1) in (H) and/or CD	
	exposed mice liver	
Figure 2.4:	Altered mRNA of pro-inflammatory (NFkB, IL-12 and IL-	81
	17) and anti-inflammatory (IL-4 & IL-10) marker genes in	
	mice subjected to (H) and/or CD	
Figure 2.5:	Heat map analysis of pro- and anti-inflammatory gene	82
	expression in the liver	
Figure 2.6:	Effect of melatonin on genes regulating inflammation	83
	(TNF- α , IL-1 β , IL-6 and MCP-1) in (H) and/or CD	
	exposed mice hippocampus	
Figure 2.7:	Altered mRNA expression of (CREB, IBA-1, NF-KB, IL-	84
	12 and IL-17) in hippocampus of mice subjected to CD	
	and/or (H) diet	
Figure 2.8:	Effect of melatonin on anti-inflammatory marker (IL-4 &	85
	IL-10) genes in hippocampus of subjected to CD and/or	
	(H) diet	
Figure 2.9:	Heat map analysis of pro- and anti-inflammatory gene	86
	expression in the hippocampus	
Figure 2.10:	Altered serum corticosterone levels in mice subjected to	87
	CD and/or H diet	
Figure 3.1:	Experimental design for 16s rRNA metagenomic analysis	96
	of gut microbiota	
Figure 3.2:	The percentage relative abundance of identified gut	99
	microbiota in mice subjected to (CD) and exogenous	
	melatonin treated (CDM) group	
Figure 3.3:	The percentage relative abundance of identified gut	100
	microbiota in mice subjected to (H) and exogenous	
	melatonin treated (HM) group	
Figure 3.4:	The percentage relative abundance of identified gut	101
	microbiota in mice subjected to (HCD) and exogenous	

	melatonin treated (HCDM) group	
Figure 3.5:	Rarefaction curves of microbial clusters in fecal samples of	102
	different experimental groups	
Figure 3.6:	The species diversity and richness indices of the gut	103
	microbiome in the faecal sample of experimental groups	
Figure 3.7:	Stacked bar chart of relative abundance of the gut	104
	microbiota in faecal samples experimental mice subjected	
	to (H) diet and/or (CD)	
Figure 3.8:	Heat map showing the relative abundances and distribution	105
	of representative 16S rRNA gene tag sequences classified	
	at the genus level	
Figure 3.9:	Corrective changes by melatonin treatment in abundance of	106
	Firmicutes and Bacteroidetes (F/B ratio) of experimental	
	mice subjected to (H) diet and/or (CD)	
Figure 3.10:	Alterations in the abundance of Ruminococcaceae and	107
	Desulfovibrionales in faecal samples of experimental mice	
	subjected to (H) diet and/or (CD)	
Figure 3.11:	Alterations in the relative abundance of genus Alistipes,	108
	Helicobacter and Mucispirillum in faecal samples of	
	experimental mice subjected to (H) diet and/or (CD)	
Figure 3.12:	Positive correlation between the physical characters (body	109
	and liver weight) and F/B ratio	
Figure 3.13:	Correlation between the physical characters (body	110
	circumference and visceral adipose tissue weight)and F/B	
	ratio	
Figure 3.14:	Correlation between the NASH histology (steatosis and	111
	ballooning score) and F/B ratio	
Figure 4.1:	Experimental design for neuro-behavioral analysis in mice	120
	subjected to CD and (H) fed mice	
Figure 4.2:	Locomotor counts (10 min) using infrared actimeter in	125
	diurnal and nocturnal regime	
Figure 4.3:	Head dipping counts in Hole board test in diurnal and	126

	nocturnal regime	
Figure 4.4:	Anxiety-like behavior tested using marble burying in	127
	diurnal and nocturnal experiments	
Figure 4.5:	Total number of marbles buried (n) at different intervals of	128
	10, 20 and 30 minutes in diurnal experiment	
Figure 4.6:	Total number of marbles buried (n) at different intervals of	129
	10, 20 and 30 minutes in nocturnal experiment	
Figure 4.7:	Number of entries in elevated plus maze test in diurnal and	130
	nocturnal regime	
Figure 4.8:	Time spent (s) in elevated plus maze test in diurnal and	131
	nocturnal regime	
Figure 4.9:	Tracking images of mice performance in elevated plus	132
	maze in diurnal and nocturnal regime	
Figure 4.10:	Immobility time in forced swim test in diurnal and	133
	nocturnal regime	
Figure 4.11:	Immobility time in tail suspension test in diurnal and	134
	nocturnal regime	
Figure 4.12:	Sucrose preference test to measure depression and/or	135
	anhedonia behavior in experimental groups	
Figure 4.13:	Time spent (s) and distance travelled (m) in morris water	136
	maze test in diurnal and nocturnal regime	
Figure 4.14:	Number of entries in the platform zone in morris water	137
	maze in diurnal and nocturnal regime	
Figure 4.15:	Tracking images of mice movement in the morris water	138
	maze test during the probe trial	
Figure 5.1:	Experimental protocol followed for hepatic-hippocampal	148
	crosstalk	
Figure 5.2:	Serum bilirubin profile in different experimental groups	152
Figure 5.3:	Altered hepatic mRNA expression of bile acid metabolism	153
	genes	
Figure 5.4:	Altered hepatic mRNA expression of bile acid transporter	154

	genes	
Figure 5.5:	Effect of melatonin on genes regulating BDNF-TrkB	155
	pathway in hippocampus	
Figure 5.6:	Altered hippocampal mRNA expression of neurotrophins	156
Figure 5.7:	Protein expression of BDNF-TrkB pathway	157
Figure 5.8:	Alterations in thyroid hormones in mice subjected to (H)	158
	diet and/or (CD)	