

Index

Sr No	Content	Page No.
Chapter 1: Review of Literature		2 - 47
1.1	Introduction	2
1.1.1	The mechanism for regulation of blood glucose	2
1.1.2	Classification of Diabetes mellitus	4
1.1.3	Type 1 Diabetes	4
1.1.4	Type 2 Diabetes	5
1.1.5	Gestational Diabetes	5
1.2	Diagnosis	5
1.3	Pathophysiology of DM	6
1.3.1	Pathophysiology of type 1 diabetes	6
1.3.2	Pathophysiology of type 2 diabetes	8
1.4	Insulin signalling and insulin resistance	9
1.5	Etiological factors leading to T2D	11
1.5.1	Lifestyle	11
1.5.2	Obesity	12
1.5.3	Adipokines	13
1.5.3.1	Adiponectin	13
1.5.4	Genetic alterations	15
1.5.5	Mitochondrial dysfunction	16
1.6	β -cell dysfunction and insulin resistance	18
1.7	β -cell regeneration	20
1.7.1	β -cell proliferation	21
1.7.2	β -cell neogenesis	21
1.7.3	β -cell transdifferentiation	22
1.8	Management of type 2 diabetes	23
1.8.1	L-glutamine	25
1.8.2	Statins	27
1.9	References	29
Objectives		47

Chapter 2: To evaluate the association of ADIPOQ polymorphisms with T2D in Gujarat population and to study the possible genotype-phenotype correlation with plasma adiponectin levels and metabolic parameters. 48-71

2.1	Introduction	49
2.2	Materials and Method	50
2.2.1	Study subjects	50
2.2.2	Blood collection and DNA extraction	50
2.2.3	Screening of <i>ADIPOQ</i> single nucleotide polymorphisms	51

2.2.4	Plasma parameters	53
2.3	Statistical analyses	54
2.4	Results	54
2.4.1	Association of <i>ADIPOQ</i> SNPs with T2D	55
2.4.2	Haplotype and Linkage Disequilibrium Analysis of <i>ADIPOQ</i> SNPs	57
2.4.3	Plasma HMW adiponectin/total adiponectin ratio in T2D patients and controls	59
2.4.4	Association of <i>ADIPOQ</i> SNPs and their genotypes with metabolic parameters and HMW adiponectin/total adiponectin ratio	59
2.4.5	Bioinformatics analyses	61
2.5	Discussion	62
2.6	References	65

Chapter 3: To investigate the therapeutic potential of small molecule enhancers for adiponectin (pitavastatin) and GLP-1 (L-glutamine) secretion in T2D mouse model	72-110
---	--------

3.1	Introduction	73
3.2	Materials and Methods	73
3.2.1	Animals and experimental strategy	73
3.2.2	Metabolic and Biochemical Parameters	76
3.2.2.1	Lipid profiling	76
3.2.2.2	Estimation of plasma insulin and adiponectin levels	76
3.2.3	Assessment of transcript levels	76
3.2.4	Glucoregulatory enzymes activities and liver glycogen content	78
3.2.5	Mitochondrial isolation from skeletal muscle and estimation of oxygen consumption rate (OCR)	78
	Pancreatic tissue preparation, Immunohistochemistry-	
3.2.6	Immunofluorescence (IHC-IF), assessment of β -cell regeneration and apoptosis	78
3.2.7	Western blot analysis	80
3.2.8	Statistical analyses	81
3.3	Results	82
3.3.1	Animals and experimental strategy to develop T2D mouse model	82
3.3.2	Assessment of metabolic and biochemical parameters	83
3.3.2.1	Intraperitoneal glucose tolerance test (IPGTT) and Intraperitoneal insulin sensitivity test (IPIST)	83
3.3.2.2	Lipid profiling	85
3.3.2.3	Plasma insulin and adiponectin levels	86
3.3.3	Gene expression of GLUT2 and glucoregulatory enzymes and their activities in liver	87
3.3.4	Mitochondrial biogenesis markers' transcript levels in skeletal muscle	90
3.3.5	Estimation of oxygen consumption rate (OCR)	91
3.3.6	Western blot analysis	93
3.3.7	Regeneration and apoptosis analysis in pancreatic β -cells	94
3.4	Discussion	96

3.5	References	101
Chapter 4:	Conclusions	108-111
	Appendix	112-114
	List of publications and presentations	115-119
	Ph.D. Thesis synopsis	
