

Table of contents

Sr. No.	Title	Page No.
Abstract		
Chapter 1 Introduction		
1.	Lifestyle Disorders	4
1.1	The pancreas and insulin	4
1.1.1	Mechanism of Insulin secretion	5
1.1.2	Insulin signalling pathway	5
1.2	Epidemiology of Diabetes Mellitus	7
1.2.1	Symptoms, classification, diagnosis and pathogenesis of Diabetes Mellitus	7
1.3.1	Type 1 Diabetes	8
1.3.2	Type 2 Diabetes	9
1.3.2.1	Mechanism involved in Type 2 Diabetes	10
1.3.2.2	Role of adipose tissue and liver in type 2 diabetes	12
1.4	Role of genetic factors in type 2 diabetes	14
1.5	Role of resistin in type 2 diabetes	15
1.5.1	Genetic variants of resistin	17
1.6	Role of omentin-1 in type 2 diabetes	17
1.6.1	Genetic variants of Omentin-1	18
1.7	Role of Vaspin in Type 2 Diabetes	19
1.7.1	Genetic variants of Vaspin	20
1.8	β -cell Regeneration	21
1.9	β -cell dysfunction/ death	23
1.10	Strategies to combat Diabetes Mellitus	24
1.10.1	Contemporary therapies having the power of β -cell regeneration	26
1.11	Diet: acting as a switch to regulate Type 2 Diabetes	26
1.12	γ -Aminobutyric Acid (GABA): Potential β -cell regeneration molecule	27
	References	31
Objectives		
Chapter 2 To study the role of Resistin in Type 2 Diabetes		
2.1	Introduction	41
2.2	Material and Methods	42
2.2.1	Study subjects	42
2.2.2	Anthropometric parameters, Lipid profiling and DNA extraction	42
2.2.3	Genotyping of <i>resistin</i> gene polymorphisms	43
2.2.4	Determination of plasma resistin protein levels	44
2.2.6	Statistical analyses	44
2.3	Results: Baseline Characteristics	44
2.3.1	Genetic analysis of the <i>resistin</i> polymorphisms	45
2.3.2	Haplotype analysis of the <i>resistin</i> polymorphisms	47
2.3.3	Linkage Disequilibrium analysis of the <i>resistin</i> polymorphisms	47

2.3.4	The association of the <i>resistin</i> polymorphisms with the metabolic profile	48
2.3.5	Plasma resistin protein levels and their association with <i>resistin</i> polymorphisms and metabolic profile	48
2.4	Discussion	49
	References	52
Chapter 3 To study the role of Omentin-1 in Type 2 Diabetes		
3.1	Introduction	59
3.2	Materials and Methods	60
3.2.1	Study subjects	60
3.2.2	Anthropometric parameters, Lipid profiling and DNA extraction	60
3.2.3	Genotyping of <i>Omentin-1</i> gene polymorphisms	60
3.2.4	Determination of the transcript levels	61
3.2.5	Determination of plasma omentin-1 protein levels	62
3.2.6	Statistical analyses	62
3.3	Results: Baseline Characteristics	62
3.3.1	Genetic analysis of the <i>omentin-1</i> polymorphisms	63
3.3.2	Haplotype analysis of the <i>omentin-1</i> polymorphisms	64
3.3.3	Linkage disequilibrium analysis of the <i>omentin-1</i> polymorphisms	65
3.3.4	The analysis of the association of the <i>omentin-1</i> polymorphisms with the metabolic profile	65
3.3.5	<i>Omentin-1</i> transcript levels and their association with <i>omentin-1</i> polymorphisms, and a correlation with the metabolic profile	66
3.3.6	Plasma omentin-1 protein levels and their association with <i>omentin-1</i> polymorphisms and metabolic profile	67
3.4	Discussion	67
	References	70
Chapter 4 To study the role of Vaspin in Type 2 Diabetes		
4.1	Introduction	76
4.2	Materials and Methods	77
4.2.1	Study subjects	77
4.2.2	Anthropometric parameters, Lipid profiling and DNA extraction	77
4.2.3	Genotyping of the polymorphisms	77
4.2.4	Determination of the transcript levels	78
4.2.5	Determination of plasma vaspin protein levels	79
4.2.6	Statistical analyses	79
4.3	Results: Baseline Characteristics	80
4.3.1	Genetic analysis of the <i>vaspin</i> polymorphisms	80
4.3.2	Haplotype analysis of the <i>vaspin</i> polymorphisms	82
4.3.3	Linkage Disequilibrium analysis of the <i>vaspin</i> polymorphisms	82
4.3.4	The analysis of the association of the <i>vaspin</i> polymorphisms with the metabolic profile	83
4.3.5	<i>Vaspin</i> transcript levels and their association with <i>vaspin</i> polymorphisms, and a correlation with metabolic profile	83

4.3.6	Plasma vaspin protein levels and their association with <i>vaspin</i> polymorphisms and metabolic profile	84
4.4	Discussion	85
	References	87
<i>Chapter 5 To investigate the effect of GABA, CR and combination treatment on pancreatic β-cell proliferation in HFD + STZ induced experimental mouse model</i>		
5.1	Introduction	93
5.2	Animals and experimental strategy	94
5.2.1	Animals	94
5.2.2	Development of T2D mouse model	94
5.2.3	Treatment	94
5.2.4	Metabolic and Biochemical Parameters	95
5.2.4.1	Metabolic profiling	95
5.2.4.2	Intraperitoneal Glucose Tolerance Test (IPGTT) and Intraperitoneal Insulin Sensitivity Test (IPIST)	96
5.2.4.3	Assessment of Insulin and C-peptide levels	96
5.2.5	Gene expression profiling	96
5.2.6	Estimation of Oxygen Consumption Rate (OCR)	97
5.2.7	Pancreatic tissue preparation, Immunohistochemistry (IHC), Assessment of β -cell regeneration and apoptosis	98
5.2.8	Statistical analyses	99
5.3	Results: HFD+STZ induced T2D mouse model establishment	99
5.3.1	Metabolic and Biochemical Assessment	100
5.3.1.1	Metabolic profiling	100
5.3.1.2	Lipid profiling	100
5.3.1.3	Glucose Tolerance and Insulin Sensitivity	101
5.3.1.4	Insulin and C-peptide levels	102
5.3.2	Gene expression profiles	102
5.3.3	Oxygen consumption rate	105
5.3.4	Pancreatic β -cell regeneration and apoptosis	105
5.4	Discussion	109
	References	113
<i>Conclusions</i>		
<i>Appendix</i>		
<i>Publications and presentations</i>		
<i>PhD Synopsis report</i>		