

CONTENTS

Section	Description	Page No.
	Abstract.....	iv-v
	Content.....	ix-xii
	List of Figures.....	xii-xv
	List of Tables.....	xvi
	Abbreviations, notations and nomenclatures.....	xvii-xx
1.	Introduction.....	1-16
2.	Review of Literature.....	17-48
2.1	Gut microbiota.....	19
2.2	Gut microbiota and energy harvest.....	23
2.3	Diabetes and inflammation.....	24
2.4	Gut microbiota and diabetes.....	26
2.5	Diet and gut microbiota.....	27
2.6	SCFAs receptors.....	30
2.7	Regulation of fatty acid metabolism by SCFAs.....	31
2.8	Regulation of glucose metabolism by SCFAs.....	31
2.9	Pattern recognition receptors (PRRs).....	33
2.9.1	Toll like receptors (TLRs).....	34
2.9.2	NOD like receptors (NLRs).....	38
2.10	Gut microbiota modulation for management of metabolic disorder...	41
2.10.1	Modulation with probiotics.....	41
2.10.2	Modulation with prebiotics.....	42
2.10.3	Modulation with antimicrobial agents.....	43
2.11	Classification of antimicrobial agents.....	44
2.11.1	Fluroquinolones.....	45
2.11.2	Oxazolidinones.....	45

2.11.3	Cephalosporins.....	46
2.12	Targeted drug delivery.....	46
2.13	Objectives.....	48
3.	Materials and Methods.....	49-71
3.1	Drugs and consumables.....	51
3.2	Diets and experimental design.....	51
3.2.1	Diet preparation.....	51
3.2.2	Experimental animals.....	52
3.3	Oral glucose tolerance test (OGTT) assay.....	53
3.4	Blood, fecal and tissue sample collection.....	54
3.4.1	Blood biochemical analysis.....	54
3.4.2	FFA and LPS estimation.....	55
3.4.3	Microflora estimation by culturable method.....	55
3.4.4.	Fecal collection and DNA extraction.....	56
3.4.5.	Standard bacterial strains.....	56
3.4.6	Microbial quantification by real-time qPCR.....	57
3.4.7	Bile Salt Hydrolase (BSH) enzyme bacterial quantification.....	58
3.4.8	Determination of SCFAs (metabolites).....	59
3.4.9	Tissue biochemistry.....	60
3.4.9.1	Liver glycogen.....	60
3.4.9.2	Liver total cholesterol.....	60
3.4.9.3	Liver triglycerides.....	60
3.4.10	Gene expression using real time PCR.....	61
3.5	Drugs and polymers.....	63
3.6	Solvents and reagents.....	63
3.7	Fourier transform infrared spectroscopy (FT-IR).....	64
3.8	Formulation of microspheres.....	64
3.9	Physicochemical characterization of microspheres.....	64
3.9.1	Particle size analysis.....	65
3.9.2	Scanning electron microscopy (SEM).....	65

3.9.3	Production yield.....	65
3.9.4	Percentage entrapment efficiency (EE).....	66
3.10	<i>In vitro</i> drug release study.....	66
3.11	Release kinetic modeling.....	67
3.12	<i>In vitro</i> antimicrobial study.....	67
3.13	Animal experimentation.....	68
3.14	The <i>Ex vivo</i> antimicrobial study.....	69
3.15	Histopathological analysis.....	70
3.16	Physiological, biochemical and gene expression analysis.....	70
3.17	Statistical analysis.....	71
<hr/>		
4.	Results and Discussion.....	73-155
<hr/>		
	Objective 1.....	75-106
4.1	Effect on physiological parameters.....	75
4.2	Effect on oral glucose tolerance test (OGTT) assay.....	76
4.3	Effect on blood biochemical parameters.....	78
4.4	Effect on hepatic inflammatory markers.....	78
4.5	Consequences on inflammatory markers.....	79
4.6	Effect on liver biochemical parameters.....	80
4.7	PCR confirmation of standard bacterial strains.....	81
4.8	Effect on gut dominant microbial phyla.....	82
4.9	Effect on gut dominant microbial genera.....	85
4.10	Effect on microbial metabolites.....	87
4.11	Effect on bile salt hydrolase (BSH) producing bacteria.....	88
4.12	Effect on adipose tissue histopathology.....	89
4.13	Effect on toll like receptors (TLRs) expression.....	89
4.14	Effect on NOD like Receptors (NLRs) expression.....	91
4.15	Effect on inflammatory gene expression.....	92
4.16	Effect on SCFA receptor and insulinotropic modulation.....	94
	Discussion.....	95-106
<hr/>		
	Objective 2.....	107-126
<hr/>		

4.17	Fourier-transform infrared spectroscopy (FT-IR).....	107
4.18	Formulation and optimization of the cefdinir microspheres.....	109
4.19	<i>In Vitro</i> drug release analysis from enteric coated cefdinir microspheres.....	110
4.20	Drug release kinetic analysis.....	112
4.21	Optimization of the enteric coated linezolid microspheres.....	113
4.22	<i>In Vitro</i> Drug release analysis from enteric coated linezolid microspheres.....	115
4.23	Release kinetic analysis for linezolid microspheres.....	116
4.24	Scanning electron microscopy (SEM) of formulated microspheres.....	117
4.25	<i>In Vitro</i> antimicrobial study of microspheres.....	118
4.26	<i>Ex-vivo</i> antimicrobial study of microspheres.....	119
	Discussion.....	121-126
Objective 3.....		127-155
4.27	Effect on oral glucose tolerance test (OGTT) assay.....	127
4.28	Effect on physiological and blood biochemical parameters.....	129
4.29	Effect on inflammatory and liver biochemical parameters.....	130
4.30	Effect on gut dominant bacterial phyla.....	131
4.31	Effect on gut dominant bacterial genera.....	134
4.32	Effect on short chain fatty acids (SCFAs).....	136
4.33	Effect on toll like receptors (TLRs) expression.....	137
4.34	Effect on NOD like receptors (NLRs) expression.....	139
4.35	Effect on inflammatory genes expression.....	140
4.36	Effect on GPCR and insulinotropic modulation.....	142
4.37	Effect on adipokines expression.....	143
4.38	Effect on peroxisome proliferator-activated receptors (PPARs).....	144
	Discussion.....	146-155
5.	Summary and Conclusions.....	157-163
6.	References.....	165-196
7.	List of Publications.....	197-200