TABLE OF CONTENTS

S. NO.	Title	PAGE NO.
	Declaration	ii
	Abstract	iii-vii
	Acknowledgement	viii-ix
	Table of contents	X-XV
	List of figures	xvi-xvii
	List of tables	xviii-xix
	List of publications	XX
	List of abbreviations	xxi-xxii
CHAPTER 1	INTRODUCTION	1-36
1.1	Inflammatory bowel diseases	1
1.2	Epidemiology	5
1.3	Etiology	5
1.4	Factors responsible for ulcerative colitis	7
1.5	Pathogenesis of ulcerative colitis	9
1.6	Signs and symptoms of ulcerative colitis	12
1.7	Currently used drugs therapy in the management of ulcerative colitis	16
1.8	Mesalamine as a potent antioxidant and anti- inflammatory drug	16
1.9	Probiotics role in ulcerative colitis.	18
1.10	Challenges in the treatment of ulcerative colitis	20
1.11	Strategies for the management of ulcerative colitis	21
1.11.1	Microparticles as carrier	21
1.11.2	Pellets as carrier	24
1.12	Polymer selection	24
1.12.1	Profile of cellulose acetate phthalate	24
1.12.2	Enzyme based polymer	25
1.13	Excipients profile	26
1.13.1	Span 80	26

1.13.2	Isooctane	27
1.13.3	Light liquid paraffin	28
1.13.4	Microcrystalline cellulose	28
1.14	Need for colon-specific drug delivery system	29
1.14.1	pH-dependent system	30
1.14.2	Microflora-activated systems	32
1.15	Research envisaged	33
1.16	Research aim and objectives	33
1.17	Plan of work	34
CHAPTER 2	LITERATURE REVIEW	37-46
CHAPTER 3	EXPERIMENTAL (MATERIALS AND	47-80
	METHODS)	
3.1	Materials and equipment	47
3.1.1	Chemicals and excipients	47
3.1.2	Equipment used	48
3.2	Preformulation studies of Mesalamine	50
3.3	Organoleptic properties	51
3.4	Development of the analytical methods	53
3.4.1	UV- visible spectroscopy studies	53
3.4.1.1	Preparation of standard curve of drug in PBS 7.4	53
3.4.1.2	Preparation of standard curve of drug in 0.1N HCl	53
3.5	HPLC method for Mesalamine determination	54
3.6	Screening of probiotic strain based on the antioxidant and inflammatory property	55
3.7	Formulation development	56
3.7.1	Preparation and optimization of pectin	56
	microparticles	
3.7.1.1	Coating of pectin microparticles	57
3.7.2	Characterization of prepared microparticles	57
3.7.2.1	Drug loading and entrapment efficiency	57
3.7.2.2	Particle morphology	58
3.7.2.3	Particle size analysis, polydispersity index and	58

	Zeta potential analysis	
3.7.2.4	FTIR Spectroscopy	58
3.7.2.5	X-ray diffraction (XRD) determination	58
3.7.2.6	Differential Scanning Calorimetry	59
3.7.2.7	In vitro drug release	59
3.7.2.8	Release and viability count of <i>S. boulardii</i> from the coated microparticles during dissolution	59
3.8	<i>In vivo</i> efficacy studies using TNBS-induced colitis model in Wistar rat	60
3.8.1	In vivo studies	60
3.8.2	Induction of colitis by TNBS	61
3.8.3	Morphological studies	62
3.8.4	Biochemical studies	64
3.8.5	Measurement of serum markers	66
3.9	Histopathology study	66
3.10	Stability study	66
3.11	Pharmacokinetic studies for microparticles formulation	67
3.12	Statistical evaluation	68
3.13	Preparation and optimization of pellets formulation	68
3.13.1	Preparation of uncoated pellets	68
3.13.2	Coated pellets preparation	70
3.14	<i>In vitro</i> characterization of drug-probiotic-loaded pellets	71
3.14.1	Drug loading and entrapment efficiency	71
3.14.2	Pellets morphology	71
3.14.3	Sphericity studies	71
3.14.4	Micrometric properties	72
3.14.5	Determination of moisture content	74
3.14.6	Mucoadhesive test	75
3.14.7	FTIR Spectroscopy	75
3.14.8	X-ray diffraction (XRD) determination	75

3.14.9	Differential Scanning Calorimetry	75
3.14.10	In vitro drug release	76
3.14.11	Release and viability count of S. boulardii from	76
	the coated microparticles during dissolution	
3.15	In vivo studies	77
3.15.1	Induction of colitis and drug administration in	77
	Wistar rats	
3.15.2	Macroscopic characters assessment	77
3.16	Determination of MPO, LPO and GSH	78
3.17	Measurement of serum markers	78
3.18	Histopathological assessment	79
3.19	Stability study	79
3.20	Pharmacokinetic studies of prepared pellets	79
	formulation	
3.21	Statistical analysis	80
CHAPTER 4	RESULTS AND DISCUSSION	81-130
4.1	Preformulation parameters	81
4.1.1	Physical state	81
4.1.2	Melting point	81
4.1.3	Partition coefficient	81
4.1.4	Solubility profile of Mesalamine	82
4.1.5	FTIR spectroscopy	83
4.2	Analytical method development	83
4.2.1	Standard curve of Mesalamine in PBS 7.4	84
4.2.2	Standard curve of Mesalamine in 0.1 N HCL	84
4.3		
	Determination of antioxidant activity by using	85
4.2.1	nitric oxide assay	
4.3.1	nitric oxide assay Anti-inflammatory effect evaluation of	85 87
4.3.1	nitric oxide assay Anti-inflammatory effect evaluation of probiotics (<i>S. boulardii</i> and <i>L.acidophilus</i>) Preparation optimization and characterization of	
	nitric oxide assay Anti-inflammatory effect evaluation of probiotics (<i>S. boulardii</i> and <i>L.acidophilus</i>) Preparation optimization and characterization of Mesalamine loaded probiotic based	87
4.4	nitric oxide assay Anti-inflammatory effect evaluation of probiotics (<i>S. boulardii</i> and <i>L .acidophilus</i>) Preparation optimization and characterization of Mesalamine loaded probiotic based microparticles	87 87
	nitric oxide assay Anti-inflammatory effect evaluation of probiotics (<i>S. boulardii</i> and <i>L.acidophilus</i>) Preparation optimization and characterization of Mesalamine loaded probiotic based	87

	based microparticles	
4.4.3	Drug loading and entrapment efficiency	88
4.4.4	Particle morphology	89
4.4.5	Determination of particle size, PDI and Zeta potential analysis	90
4.4.6	Compatibility study through FTIR spectroscopy	90
4.4.7	X-ray diffraction (XRD) analysis	91
4.4.8	DSC analysis	92
4.4.9	In vitro drug release	94
4.4.10	In vitro probiotic release and viability count	95
4.5	Stability study	96
4.6	In vivo studies	97
4.6.1	Assessment of bodyweight	97
4.6.2	Macroscopic activity score	98
4.6.3	Diarrhoea assessment during the treatment period	99
4.6.4	Effect of microparticles formulation on MPO in TNBS induced colitis in rats	99
4.6.5	Effect of microparticles formulation on LPO in TNBS induced colitis in rats	100
4.6.6	Effect of microparticles formulation on GSH in TNBS induced colitis in rats	101
4.6.7	Determination of C-reactive protein	102
4.6.8	Determination of ESR	102
4.6.9	Determination of WBC	103
4.7	Pharmacokinetics estimation	103
4.8	Histopathology examination	105
4.9	Pellets formulation results	107
4.9.1	Preparation and optimization of uncoated drug and probiotic-loaded pellets	107
4.10	<i>In vitro</i> characterization of drug probiotic-loaded pellets	110
4.10.1	Drug loading and entrapment efficiency	110
4.10.2	Pellets morphology	110
4.11	Sphericity studies	111
4.12	Micrometric and other properties	112

	APPENDIX	
	REFERENCES	141-158
5.2	Conclusion	140
5.1	Summary	131-140
CHAPTER 5	SUMMARY AND CONCLUSION	131-140
4.25	Histopathological analysis	129
4.24.1	Pharmacokinetics estimation	127
4.24	In vivo studies	127
4.23	Determination of WBC	127
4.22	Determination of ESR	126
4.21	Determination of C-reactive protein	126
4.20.4	Effect of formulation on GSH in TNBS induced colitis in rats	125
4.20.3	Effect of formulation on LPO in TNBS induced colitis in Wistar rats	124
4.20.2	Effect of formulation on MPO in TNBS Induced colitis in Wistar rats	123
	period	
4.20.1.3	Diarrhoea assessment during the treatment	122
4.20.1.2	Macroscopic activity score	121
4.20.1.1	Assessment of body weight	121
4.20.1	Morphological studies	121
4.20	In vivo results	121
4.19	Stability study	110
4.18	<i>In vitro</i> probiotic release and viability count	117
4.10	In vitro drug release	110
4.15	XRD assessment DSC analysis	115 116
4.14	Compatibility study through IR spectroscopy	114
4.13	Mucoadhesive evaluation	112