

CONTENTS

Content	Page No.
Abstract	i–iv
Declaration	v
Certificate of the Supervisor	vi
Acknowledgements	vii–ix
Table of Contents	x–xiv
List of Tables	xv
List of Figures	xvi–xviii
Abbreviations	xix–xx
Chapter 1: Introduction	1–67
1.1. Background and Significance	2
1.2. Rationale for Nutraceutical-Based Oral Therapy	3
1.2.1. Therapeutic Potential of Curcumin	4
1.2.2. Therapeutic Potential of Lipoic Acid	5
1.3. Challenges in Oral Delivery of Curcumin and Lipoic Acid	6
1.3.1. Limited Bioavailability and Stability	6
1.3.2. Approaches to Address Bioavailability Challenges	6
1.4. Overview of Biopolymer-Based Systems for Controlled Oral Delivery	7
1.4.1. Criteria for Selecting Biopolymeric Carriers	8
1.4.2. Need for Controlled Drug Release	9
1.4.3. Advantages of oral route of delivery	10
1.4.4. Mechanisms of Controlled Release in the Gastrointestinal (GI) Tract	11
1.5 Recent Advances in Biopolymeric Controlled Release Platforms	12
1.5.1 Polysaccharide-Based Systems	12
1.5.1.1. Alginate	12
1.5.1.2. Carrageenan	14
1.5.1.3. Chitosan	17

CONTENTS

1.5.2 Protein-Based Systems	
1.5.2.1. Gelatin	20
1.5.2.2. Soy flour	23
1.5.3. Enhancing Stability and Performance with Inorganic Materials	25
1.5.3.1. Montmorillonite (MMT): Layered structure and high surface area	25
1.5.3.2. Magnesium Oxide (MgO) Nanoparticles: Matrix reinforcement and putative antidiabetic effects.	26
1.5.3.3. Halloysite Nanotubes (HNTs): Tubular architecture and versatile drug loading	28
1.5.4 Crosslinking Strategies	31
1.5.4.1. Physical (Ionic) Crosslinking	31
1.5.4.2. Chemical Crosslinking	32
1.5.4.3. Optimisation of Crosslinking Parameters	34
1.5.5. Role of Particle Size in Controlled Oral Drug Delivery Systems	35
1.5.6. Surfactants	37
1.6. Fabrication techniques for polymeric controlled release vehicles	39
1.6.1. Ionic Gelation Method	40
1.6.2. Polyelectrolyte Complexation (PEC)	41
1.6.3. Emulsification-Solvent Evaporation Method	43
1.6.4. Spray Drying Method	45
1.6.5. Coacervation Method	47
1.6.6. Nano-precipitation (Solvent Displacement) Method	49
1.6.7. Supercritical Fluid (SCF) Technology	50
1.7. Scope and Objectives	52
1.8. References	54
Chapter 2: Materials and Methods	68-81
2.1. Materials	69
2.2. Methods	70

CONTENTS

2.2.1. Calibration curve of α -Lipoic acid	70
2.2.2. Calibration curve of Curcumin	71
2.2.3. Preparation of Glutaraldehyde crosslinked Lipoic acid loaded ChitosanMMT-Alginate complex	72
2.2.4. Preparation of Glutaraldehyde crosslinked Lipoic acid loaded GelatinHalloysite-Carrageenan complex	72
2.2.5. Preparation of a glutaraldehyde-crosslinked curcumin-loaded MgO-doped chitosan–carrageenan complex	73
2.2.6. Preparation of Glutaraldehyde crosslinked Curcumin loaded MgO doped Soy flour-MMT complex	74
2.2.7. Calculation of process yield	74
2.2.8. Calculation of drug loading and drug encapsulation efficiency	75
2.3 Characterisation	75
2.3.1. Fourier Transform Infrared Spectroscopy (FTIR)	75
2.3.2. X-ray Diffraction (XRD)	76
2.3.3. Scanning Electron Microscopy (SEM)	77
2.3.4. Field Emission Scanning Electron Microscopy (FESEM)	77
2.3.5. Energy Dispersive X-ray (EDX) Spectroscopy	78
2.4 <i>In Vitro</i> Drug Release Studies	78
2.5 Biological Assays	78
2.5.1 2-NBDG Glucose Uptake Assay	78
2.5.2 MTT Cell Viability Assay	79
2.6 Statistical Analysis	79
2.7 References	80
Chapter 3: Results and Discussion	82-140
3.1. Chitosan-Alginate Complex for the Controlled Delivery of α -Lipoic Acid: Modulation by Montmorillonite and Glutaraldehyde	83
3.1.1. Process Yields, Drug Encapsulation Efficiency, and Drug Loading Efficiency	83
3.1.2. <i>In vitro</i> drug release studies	84

CONTENTS

3.1.3. Characterisation	86
3.1.3.1. Fourier transform infrared spectroscopy	86
3.1.3.2. X-ray diffraction study	89
3.1.3.3. Scanning electron microscope (SEM) study	91
3.1.4. Glucose Uptake Assay	92
3.1.5. Cell Viability Assay	94
3.2. Gelatin-Halloysite Nanotube-Carrageenan Polyelectrolyte Complex for pH-Responsive Delivery of Lipoic Acid	96
3.2.1. Process yields, drug encapsulation efficiency, and drug loading efficiency	96
3.2.2. <i>In Vitro</i> Release Studies	98
3.2.3. Characterisation	99
3.2.3.1. Fourier transform infrared spectroscopy	99
3.2.3.2. X-ray diffraction study	102
3.2.3.3. Field-Emission Scanning Electron Microscopy (FESEM) Analysis	103
3.2.4. 2-NBDG uptake assay	104
3.2.5. Cell viability assay	106
3.3. Magnesium Oxide-Doped Chitosan-Carrageenan Complex for Controlled Oral Delivery of Curcumin	108
3.3.1. Process yield, drug loading and drug encapsulation efficiency	108
3.3.2. <i>In Vitro</i> Drug Release Study	109
3.3.3. Characterisation	111
3.3.3.1. Fourier transform infrared spectroscopy	111
3.3.3.2. X-ray diffraction study	113
3.3.3.3. Field emission scanning electron microscopy (FESEM) and energy dispersive X-ray spectroscopy (EDX)	114
3.3.4. 2-NBDG uptake assay	117
3.3.5. Cell viability assay	120

CONTENTS

3.4. Development Of a pH-Responsive Soy Flour– Montmorillonite–Magnesium Oxide Complex for Sustained Release of Curcumin in Antidiabetic Therapy	122
3.4.1. Process Yield, Drug Loading and Drug Encapsulation Efficiency	122
3.4.2. <i>In Vitro</i> Drug Release Study	124
3.4.3. Characterisation	126
3.4.3.1. Fourier transform infrared spectroscopy	126
3.4.3.2. X-ray diffraction study	128
3.4.3.3. Field Emission Scanning Electron Microscopy (FESEM) study	129
3.4.4. 2-NBDG uptake assay	131
3.4.5. Cell viability assay	132
3.5. References	135
Chapter 4: Conclusion and Future Scope	142-149
4.1. Conclusion	143
4.2. Future Scopes	147
Appendix- List of Publications	a
