TABLE OF CONTENTS

S. No.	Description	Page Number
	Declaration	I
	Abstract	II-III
	Acknowledgement	IV-V
	Table of Contents	VI-XIII
	List of Figures	XIV-XX
	List of Tables	XXI-XXII
	List of Abbreviations	XXIII-XIV
Chapter 1	Introduction	1-42
1.1	Biological functions of vitamin D	1
1.2	Recommended dietary intake of vitamin D	2
1.3	Risk factors	4
1.4	Population under risk factor	4
1.5	Vitamin D Compounds	5
1.5.1	Vitamin D2 (Ergocalciferol)	6
1.5.2	Vitamin D ₃ (Cholecalciferol)	7
1.5.3	Vitamin D analogues	9
1.6	Formulation Approaches	11
1.6.1	Solid Dispersion	13
1.6.1.1	Advantages of solid dispersion	15
1.6.1.1.1	Particle size reduction:	15
1.6.1.1.2	Enhanced wettability	16
1.6.1.1.3	Higher porosity of particles	16
1.6.1.1.4	Drug in amorphous state:	17
1.6.1.2	Classifications of solid dispersion	17

1.6.1.2.1	First generation of solid dispersion	17
1.6.1.2.2	Second generation of solid dispersion	18
1.6.1.2.3	Third generation solid dispersions	19
1.6.1.2.4	Fourth generation of solid dispersion	20
1.6.1.3	Selection of suitable carriers for solid dispersion	21
1.6.1.4	Mechanism of drug release from solid dispersion	21
1.6.1.4.1	Drug diffusion	22
1.6.1.4.2	Carrier controlled release	22
1.6.1.5.	Recrystallization inhibitors as excipients in solid dispersion	23
1.6.1.6	Methods for the preparation of solid dispersion	24
1.6.1.6.1	Kneading technique	25
1.6.1.6.2	Melting technique	25
1.6.1.6.3	Co-precipitation technique	26
1.6.1.6.4	Co-grinding strategy	26
1.6.1.6.5	Solvent evaporation technique	26
1.6.1.6.6	Electrostatic spinning technique	27
1.6.1.6.7	Melt extrusion strategy	27
1.6.1.7	Characterization of solid dispersion	27
1.6.1.7.1	Thermal analysis techniques	27
1.6.1.7.2	X-ray crystallography	28
1.6.1.7.3	Spectroscopy	29
1.6.1.7.4	Dissolution studies	29
1.6.1.7.5	Scanning electron microscopy	30
1.6.1.8	Solid dispersion of vitamin D	30
1.6.2	Solid lipid nanoparticles (SLNs)	32
•	•	

1.6.3	Nano-emulsion	33
1.6.4	Self-emulsifying drug delivery system (SEDDS)	37
1.6.5	Nanoparticles	38
1.7	Future perspective on vitamin D formulations	40
Chapter 2	Literature Review	43-51
Chapter 3	Research Envisaged and Plan of Work	52-55
3.1	Research envisaged	52
3.2	Objectives	53
3.3	Plan of work	53
Chapter 4	Bioactive and Excipients Profile	56-63
4.1	Bioactive (Cholecalciferol) Profile	56
4.2	Excipient Profile	57
4.2.1	Hydroxypropylmethylcellulose Acetate Succinate (HPMC-AS)	57
4.2.2	Polyvinylpyrrolidone (PVP)	58
4.2.2.1	Significance of chain length of polyvinylpyrrolidone	59
4.2.2.2	Ratio of bioactive molecule to polyvinylpyrrolidone	59
4.2.2.3	Safety profile of polyvinylpyrrolidone	59
4.2.3	Poloxamer	60
4.2.4	Cremophor	61
4.2.5	Oleic acid	62
4.2.6	Polyethylene glycol (PEG)	63
Chapter 5	Experimental Details (Materials and Methods)	64-86
5.1	Materials	64
5.2	Equipments	65
5.3	Preformulation studies of Bioactive (cholecalciferol)	66

5.3.1	Determination of solubility	66
5.3.2	Determination of partition co-efficient	66
5.3.3.	Evaluation of melting point	67
5.4	Methods for the Determination of Cholecalciferol	67
5.4.1	Preparation of standard curve of cholecalciferol in PBS	67
5.4.2.	Preparation of standard curve of cholecalciferol in ethanol	67
5.4.3.	HPLC method for determination of cholecalciferol	68
5.5	Strategy I: Development and characterization of enteric polymer-based solid dispersion for cholecalciferol delivery	68
5.5.1	Preparation of HPMCAS based solid dispersion	68
5.5.2	Production of physical mixture	69
5.5.3	Determination of practical yield	69
5.5.4	Determination of cholecalciferol concentration in solid dispersion	69
5.5.5	Fourier transform–infra red spectroscopy (FT-IR)	70
5.5.6	Scanning electron microscopy (SEM)	70
5.5.7	Differential scanning calorimetry analysis	70
5.5.8	Characterization of solid dispersion using X-ray diffraction analysis	71
5.5.9	Effect of formulation on viability of mimics of intestinal cells (caco-2 cells)	71
5.5.10	Dissolution study	72
5.5.11	Determination of relative bioavailability of cholecalciferol	73
5.5.12	Stability study	73
5.5.13	Statistical analysis	73

5.6	Strategy II: Development and Characterization of Delayed Release HPMC Capsules (DRHCap) for Efficient Delivery of Cholecalciferol Solid Dispersion	74
5.6.1	Preparation of DRHCap-SD of cholecalciferol	74
5.6.2	Physical mixture preparation	75
5.6.3	Percentage practical yield of SD-PVP	75
5.6.4	Determination of cholecalciferol content in SD-PVP	75
5.6.5	Solubility determination of cholecalciferol in SD-PVP	75
5.6.6	FT-IR spectroscopy of cholecalciferol, SD-PVP and excipients	76
5.6.7	Morphological examination using scanning electron microscopy	76
5.6.8	Differential scanning calorimetry analysis	76
5.6.9	X-ray diffraction analysis	76
5.6.10	Effect of formulation of viability of Caco-2 cells	77
5.6.11	Dissolution study	78
5.6.12	Flow properties	78
5.6.13	Stability study	79
5.6.14	Statistical analysis	79
5.7	Strategy III: Development and Characterization of Self-emulsifying Drug Delivery Systems (SEDDS) for Cholecalciferol	79
5.7.1	Selection of oil, surfactant and co-surfactant	79
5.7.2	Preparation of pseudo-ternary phase diagram	80
5.7.3	Development of self-emulsifying drug delivery system (SEDDS)	80
5.7.4	Characterization of self-emulsifying drug delivery system	81
5.7.4.1	Evaluation of self-emulsification	81

5.7.4.2	Morphological examination by transmission electron microscopy	82
5.7.4.3	Determination of average particle diameter and zeta potential of SEDDS	82
5.7.4.4	Drug content	82
5.7.5	In-vitro stability assessment in SGF and SIF	82
5.7.6	In vitro dissolution study	83
5.7.7	In-vitro bio-accessibility	83
5.7.8	Evaluation of compatibility of the formulation with the caco-2 cells	85
5.7.9	Stability study	86
5.7.10	Statistical analysis	86
Chapter 6	Results and Discussion	87-133
6.1	Preformulation Studies of Cholecalciferol	87
6.1.1	Determination of solubility	87
6.1.2	Determination of partition co-efficient	87
6.1.3	Determination of melting point	87
6.2	Methods for Determination of Cholecalciferol	87
6.2.1	Standard curve of cholecalciferol in PBS	87
6.2.2	Standard curve of cholecalciferol in ethanol	88
6.2.3	HPLC method for determination of cholecalciferol	89
6.3	Strategy I: Development and Characterization of Enteric Polymer-based Solid Dispersion for Cholecalciferol Delivery	89
6.3.1	Preparation of HPMCAS-based solid dispersion	89
6.3.2	Fourier transform – Infra red (FT-IR) spectroscopy	91
6.3.3	Scanning electron microscopy (SEM)	96
6.3.4	Thermal analysis	99

6.3.5	X-ray diffraction analysis	100
6.3.6	Effect of formulation on viability of mimics of intestinal cells (caco-2 cells)	101
6.3.7	Dissolution study	102
6.3.8	Relative bioavailability of cholecalciferol	105
6.3.8	Stability study	106
6.4	Strategy II: Development and Characterization of Delayed Release HPMC capsules for Efficient Delivery of Cholecalciferol Solid Dispersion	108
6.4.1	Preparation of DRHCap-SD of cholecalciferol	108
6.4.2	FT-IR spectroscopy	109
6.4.3	Scanning electron microscopy	110
6.4.4	Differential scanning calorimetry (DSC) analysis	113
6.4.5	X-ray diffraction analysis	115
6.4.6	Effect of formulation on viability of Caco-2 cells	116
6.4.7	In vitro dissolution	117
6.4.8	Flow properties	118
6.4.9	Stability study	119
6.5	Strategy III: Development and Characterization of Self-emulsifying Drug Delivery Systems for Cholecalciferol	122
6.5.1	Solubility in various excipients	122
6.5.2	Preparation of pseudo-ternary phase diagram	122
6.5.3	Characterization of self-emulsifying drug delivery system	124
6.5.3.1	Assessment of self-emulsification	125
6.5.3.2	Morphological examination by transmission electron microscopy	125
6.5.3.3	Determination of emulsion particle size and zeta potential	126

7.2	Conclusion References	144 146-177
7.1	Summary	134
Chapter 7	Summary and Conclusion	134-145
6.5.8	Stability study	132
6.5.7	Effect of formulation on viability of Caco-2 cells	131
6.5.6	In-vitro bio-accessibility of cholecalciferol	130
6.5.5	In vitro dissolution study	129
6.5.4	In-vitro stability assessment in SGF and SIF	128
6.5.3.4	Cholecalciferol content in the SEDDS formulation	127