

Table of Contents

Abstract.....	i
Keywords	vi
Declaration of Academic Integrity	vii
Certificate from Supervisor	viii
Certificate of the External Examiner and ODEC	ix
Acknowledgments	x
Table of Contents	xii
List of Tables	xvii
List of Figures.....	xx
List of Schemes.....	xxix
Abbreviations and Symbols	xxxi

Chapter 1

1.1 Introduction	1
1.1.1 Intermolecular Interactions	2
1.1.2 Supramolecular Synthons and Graph Set Notation	3
1.2 Organic Solid Forms	4
1.2.1 Cocystals/Salts	5
1.2.2 Salt-Cocrystal Continuum	8
1.2.3 Hydrates and Solvates.....	10
1.2.4 Coamorphous Solids.....	11
1.2.5 Eutectics and Solid Solutions	11
1.2.6 Polymorphism and Stoichiometric Cocrystals.....	12
1.3 Preparation of Multicomponent Crystalline Phase	14
1.3.1 Solid-state grinding.....	14
1.3.2 Solvent-mediated grinding.....	14
1.4 Characterization	15
1.5 Physicochemical Properties	16
1.5.1 Dissolution Rate and Solubility	16
1.5.2 Membrane Permeability.....	19
1.5.3 Bioavailability.....	21
1.5.4 Stability.....	23
1.5.5 Mechanical Properties	26
1.6 Marketed Pharmaceutical Cocrystals and Salts	28

1.7	Summary	28
1.8	References	29

Chapter 2

2.1	Abstract	43
2.2	Introduction	43
2.3	Results and Discussion.....	45
2.3.1	Synthesis of Molecular Salt and Isolation of Polymorphs.....	45
2.3.2	Characterization of Product Phases	46
2.3.3	Phase Stability.....	53
2.3.4	Solubility Measurement	54
2.3.5	Synthon Energy Calculation	55
2.3.6	Membrane Permeation Behaviour	56
2.4	Summary	57
2.5	Experimental Section	58
2.5.1	Materials	58
2.5.2	Synthesis of Dimorphic Molecular Salt Hydrates	58
2.5.3	Vibrational Spectroscopy (FT-IR)	58
2.5.4	Differential Scanning Calorimetry (DSC)	58
2.5.5	Thermogravimetric Analysis (TGA).....	59
2.5.6	Powder X-ray Diffraction (PXRD).....	59
2.5.7	Single Crystal X-ray Diffraction (Single crystal X-RD)	59
2.5.8	Hirshfeld Surface Analysis and Energy Frameworks	59
2.5.9	DFT Calculation.....	59
2.5.10	Cambridge Structural Database (CSD).....	60
2.5.11	Solubility Measurements	60
2.5.12	Membrane Permeability	60
2.6	References	60

Chapter 3

3.1	Abstract	65
3.2	Introduction	65
3.3	Results and Discussion.....	67
3.3.1	Synthesis of Molecular Salts.....	67
3.3.2	Characterization of Product Phases	68
3.3.3	Hydrogen Bond Synthon and CSD Survey.....	77
3.3.4	Phase Stability Study	78

3.3.5	Solubility Measurement.....	80
3.3.6	Membrane Permeation Behaviour	83
3.3.7	Hirshfeld Surface Analysis	86
3.4	Summary	87
3.5	Experimental Section.....	87
3.5.1	Materials	87
3.5.2	Synthesis of Molecular Salt Hydrates.....	88
3.5.3	Vibrational Spectroscopy (FT-IR).....	88
3.5.4	Differential Scanning Calorimetry (DSC)	88
3.5.5	Thermogravimetric Analysis (TGA)	89
3.5.6	Powder X-ray Diffraction (PXRD).....	89
3.5.7	Single Crystal X-ray Diffraction (Single Crystal X-RD)	89
3.5.8	Cambridge Structural Database (CSD).....	89
3.5.9	DFT Calculation	89
3.5.10	Hirshfeld Surface Analysis	90
3.5.11	Phase Stability	90
3.5.12	Solubility Study	90
3.5.13	Permeability Study.....	90
3.6	References	91

Chapter 4

4.1	Abstract	95
4.2	Introduction.....	95
4.3	Results and Discussion.....	97
4.3.1	Synthesis of Molecular Salts	97
4.3.2	Characterization of Product Phases	98
4.3.3	Stability Study	109
4.3.4	Solubility determination in various pH media.....	111
4.3.5	Membrane Permeation Behaviour	113
4.3.6	Hirshfeld Surface Analysis	116
4.4	Summary	117
4.5	Experimental Section	117
4.5.1	Materials	117
4.5.2	Synthesis of Molecular Salts	117
4.5.3	Vibrational Spectroscopy.....	118
4.5.4	Thermal Analysis.....	118

4.5.5	Powder X-ray Diffraction	118
4.5.6	Single Crystal X-ray Diffraction.....	119
4.5.7	Cambridge Structural Database (CSD).....	119
4.5.8	DFT Calculation.....	119
4.5.9	Hirshfeld Surface Analysis	119
4.5.10	Phase Stability Study	119
4.5.11	Solubility Study	119
4.5.12	Membrane Permeability Study	120
4.6	References	120

Chapter 5

5.1	Abstract	124
5.2	Introduction	124
5.3	Results and Discussion.....	126
5.3.1	Synthesis of Molecular Salts.....	126
5.3.2	Characterization of product phases	127
5.3.3	Phase Stability Study	135
5.3.4	Solubility determination in various pH media	136
5.3.5	Membrane Permeation Behaviour	138
5.4	Summary	141
5.5	Experimental Section	141
5.5.1	Materials	141
5.5.2	Synthesis of Molecular Salts.....	141
5.5.3	Vibrational Spectroscopy.....	142
5.5.4	Differential Scanning Calorimetry (DSC)	142
5.5.5	Thermogravimetric Analysis (TGA).....	142
5.5.6	Powder X-ray Diffraction (PXRD)	143
5.5.7	Single Crystal X-ray Diffraction (Single Crystal X-RD)	143
5.5.8	Hirshfeld Surface Analysis	143
5.5.9	Solubility Measurements	143
5.5.10	Membrane Permeability Study	144
5.6	References	144

Chapter 6

6.1	Abstract	149
6.2	Introduction	149
6.3	Results and Discussion.....	151

6.3.1	Synthesis of Molecular Salts	151
6.3.2	Characterization of Product Phases	151
6.3.3	Conformational variation of drug	158
6.3.4	Solubility Measurement.....	159
6.3.5	Membrane Permeability Behaviour.....	161
6.3.6	Hirshfeld Surface Analysis	163
6.4	Summary	164
6.5	Experimental Section	165
6.5.1	Materials	165
6.5.2	Synthesis of Molecular Salts	165
6.5.3	Vibrational Spectroscopy.....	165
6.5.4	Differential Scanning Calorimetry (DSC)	166
6.5.5	Thermogravimetric Analysis (TGA)	166
6.5.6	Powder X-ray Diffraction (PXRD).....	166
6.5.7	Single Crystal X-ray Diffraction (Single Crystal X-RD)	166
6.5.8	Hirshfeld Surface Analysis	166
6.5.9	DFT Calculation	166
6.5.10	Cambridge Structural Database (CSD).....	167
6.5.11	Solubility Measurements	167
6.5.12	Membrane Permeability.....	167
6.6	References	167
Chapter 7		
	References	175
Appendix	A