



Contents

List of Symbols	VII
1 Introduction and state of the art	1
1.1 Aim and structure of this work	2
1.2 Granulation and its applications	3
1.3 Dry granulation	3
1.3.1 Physics in dry granulation	4
1.3.1.1 Heckel model	6
1.3.1.2 Kawakita model	7
1.3.1.3 Cooper & Eaton model	8
1.3.1.4 Model comparison	8
1.3.1.5 Attraction mechanisms of particles	10
1.3.2 Roller compaction	12
1.3.2.1 Setup of roller compactors	12
1.3.2.2 Gap control	16
1.3.2.3 Deaeration	16
1.3.2.4 Ribbon split	18
1.3.2.5 Comminution in screen mill	18
1.3.2.6 Similarities between roller compaction and high-pressure roller mills	19
1.3.3 Tableting	20
1.3.4 Other dry granulation processes	21
1.4 Wet granulation	22
1.4.1 Fluidized bed	22
1.4.2 High shear mixer	24
1.4.3 Twin screw granulation	25
2 Powder properties	27
2.1 Stress transmission in powder	27
2.2 Flowability	27
2.3 Tableting specific properties	28
3 Modeling approaches for roller compaction	31
3.1 Johanson model	31
3.1.1 Johanson's compressibility factor K	33



3.1.2	Johanson model analysis	34
3.1.3	Extended Johanson models	35
3.2	Finite element method	36
3.3	Discrete element method assisted models	37
4	Fundamentals of discrete element method	39
4.1	Contact models in discrete element method	42
4.1.1	Hertz-Mindlin contact model	43
4.1.2	Walton & Braun contact model	45
4.1.3	Luding contact model	46
4.1.4	Thakur et al. contact model	47
4.1.5	JKR contact model	48
4.2	Non-spherical particles	49
4.2.1	Bonded-particle model	49
4.2.2	Multi-sphere particles	52
4.2.3	Superquadrics	53
4.2.4	Polyhedral particles	53
4.3	Time discretization in discrete element method	53
5	Discrete element method adjustment and calibration	55
5.1	Roller compaction contact model	55
5.1.1	Thakur et al. damping adjustment	55
5.1.2	Calibration of the roller compaction	56
5.1.2.1	Assumptions	58
5.1.2.2	Compaction	59
5.1.2.3	Shear cell	60
5.2	Ribbon breakage simulation	61
5.2.1	Hertz-Mindlin contact model for connected particles	63
5.2.2	Bonded-particle model	63
5.2.3	Calibration of breakage	65
5.3	Software tools	68
5.3.1	MUSEN	70
5.3.2	GPU cluster	70
5.3.3	General calibration of discrete element method parameters	71
6	Methods in post-processing and experiments	73
6.1	Analysis in discrete element method	73
6.1.1	Stress on walls	73
6.1.2	Internal stress	74
6.1.3	Porosity analysis	74
6.1.4	Particle velocity	75
6.2	Computed tomography	76
6.2.1	Physics in computed tomography	76
6.2.2	Cone beam micro computed tomography	77
6.2.3	Errors in computed tomography	78



6.2.4	Gray values and porosity determination using computer tomography images	79
6.3	Particle tracing	80
7	Results	85
7.1	Roller compaction	85
7.1.1	Pseudo-2D simulation	85
7.1.1.1	Setup description	86
7.1.1.2	Roller stress	88
7.1.1.3	Velocity analysis	90
7.1.1.4	Porosity	93
7.1.1.5	Discussion of pseudo-2D simulations	94
7.1.2	Roller compaction simulation	95
7.1.3	Net stresses	98
7.1.4	Summary	102
7.2	Comminution	103
7.2.1	Discrete element method simulation setups	105
7.2.2	Analysis of particle size distribution	105
7.2.3	Post processing concept	107
7.2.4	Validation	110
7.2.5	Porosity-size distribution	112
7.3	Combined reduced-order framework of roller compaction and tableting	114
7.3.1	Porosity model	114
7.3.2	Tensile strength model	115
7.3.3	Parameterization and application of the combined model . . .	117
7.3.4	Sensitivity analysis	119
7.3.5	Response-surface maps	120
7.3.5.1	Porosity	120
7.3.5.2	Tensile strength	120
7.3.6	Limitations	121
7.3.7	Summary	122
8	Conclusion	125
A	Kawakita-plot	129
B	Comminution model: post processing interim results	131
C	Roller compaction simulation additions	133
D	Sensitivity of combined reduced-order model	135
E	Deaeration in roller compaction process	137