Chemical Engineering Science 188 (2018) 221–237

Contents lists available at ScienceDirect

Chemical Engineering Science

journal homepage: www.elsevier.com/locate/ces

A high-dimensional, stochastic model for twin-screw granulation – Part 1: Model description

Andrew D. McGuire [a], Sebastian Mosbach [a], Kok Foong Lee [a], Gavin Reynolds [b], Markus Kraft [a,c,*]

[a] Department of Chemical Engineering and Biotechnology, University of Cambridge, Philippa Fawcett Dr., Cambridge CB3 0AS, United Kingdom
[b] Pharmaceutical Technology & Development, AstraZeneca, Charter Way, Macclesfield SK10 2NA, United Kingdom
[c] School of Chemical and Biomedical Engineering, Nanyang Technological University, 62 Nanyang Drive, Singapore 637459, Singapore

HIGHLIGHTS

- A novel, four-dimensional population balance model for twin-screw granulation is presented.
- Particle compositions are resolved along the screw barrel.
- The model's performance is assessed at different liquid-solid feed ratios using experimental data.
- We observe qualitative agreement with experimental trends.
- The model framework can be readily extended to higher dimensions.

ARTICLE INFO

Article history:
Received 19 October 2017
Received in revised form 27 April 2018
Accepted 29 April 2018
Available online 18 June 2018

Keywords:
Granulation
Twin-screw
Stochastic
Population balance model

ABSTRACT

In this work we present a novel four-dimensional, stochastic population balance model for twin-screw granulation. The model uses a compartmental framework to reflect changes in mechanistic rates between different screw element geometries. This allows us to capture the evolution of the material along the barrel length. The predictive power of the model is assessed across a range of liquid-solid feed ratios through comparison with experimental particle size distributions. The model results show a qualitative agreement with experimental trends and a number of areas for model improvement are discussed. A sensitivity analysis is carried out to assess the effect of key operating variables and model parameters on the simulated product particle size distribution. The stochastic treatment of the model allows the particle description to be readily extended to track more complex particle properties and their transformations.

1. Introduction

Granulation (also known as agglomeration, pelletisation or balling) is a common method of particle manufacture. The formation of granules is a key process in the food industry, in formation of tablets within the pharmaceutical industry and in the production of fertilisers (Iveson et al., 2001). The granular product will have an optimum size (typically a distribution), porosity, solubility, mechanical strength, shape and flow-ability amongst other properties dictated by the specific application. Granules have several advantages over a simple mixture of the raw ingredients such as better flow-ability; better transport properties (such as limited separation of components and reduced risk of powder explosions); dissolution behaviour and controlled release of Active Pharmaceutical Ingredients (API) (Braumann and Kraft, 2010; Tu et al., 2013).

Twin-screw granulation (TSG) is a relatively new method of continuous granule production and is currently subject to a high degree of research as a viable alternative to batch granulation. TSG consists of a barrel with two co-rotating screws into which raw excipient/API are fed in conjunction with a liquid binder as illustrated in Fig. 1. In these systems, the screws and barrel wall impart a shear force on the material, forming granules which are then conveyed along the barrel towards the outlet, undergoing a number of transformations such as growth/attrition along the way, depending on the processing conditions.

TSG systems have shown many advantages over traditional batch production methods such as the ability to: produce flowable granules with high API content (Shah, 2005); reduce plant foot print (Cartwright et al., 2013); minimise the use of API/excipient during formulation development and ease the scale-up from development to full production (Vercruysse et al., 2015).

* Corresponding author at: Department of Chemical Engineering and Biotechnology, University of Cambridge, Philippa Fawcett Dr., Cambridge CB3 0AS, United Kingdom.
E-mail address: mk306@cam.ac.uk (M. Kraft).

https://doi.org/10.1016/j.ces.2018.04.076
0009-2509/

Nomenclature

Roman symbols

B	breakage fragment distribution [–]
d	particle diameter [m]
d_{max}	maximum primary particle diameter [m]
d_{min}	minimum primary particle diameter [m]
F	breakage kernel [s^{-1}]
g_{break}	breakage frequency [s^{-1}]
h_{l}	thickness of external binder layer [m]
h_{a}	height of surface asperities [m]
I_{drop}	droplet inception rate [$s^{-1}\,m^{-3}$]
I_{solid}	solid inception rate [$s^{-1}\,m^{-3}$]
k_{att}	breakage rate constant [$s\,m^{-3}$]
k_{col}	collision rate constant [m^3]
k_{comp}	compaction rate constant [–]
k_{nuc}	nucleation rate constant [s^{-1}]
k_{pen}	penetration rate constant [$kg^{1/2}\,m^{-7/2}\,s^{-3/2}$]
k_{reac}	number of compartments [–]
K_{coag}	coagulation kernel [$m^3\,s^{-1}$]
K_{col}	size independent collision kernel [$m^3\,s^{-1}$]
K_{nuc}	nucleation kernel [$m^3\,s^{-1}$]
l_{e}	external liquid volume [m^3]
l_{i}	internal liquid volume [m^3]
$l_{\text{i}\rightarrow\text{e}}$	volume of liquid transferred to exterior during compaction [m^3]
LSR	operating liquid solid mass flowrate ratio [–]
$\tilde{m}$	harmonic mean particle mass [kg]
$\bar{m}_{\text{feed}}$	number average feed particle mass [kg]
$\dot{M}_{\text{feed}}$	solid mass flowrate [$kg\,s^{-1}$]
n_{screw}	screw speed [$rev\,s^{-1}$]
N	number of particles [–]
N_{exp}	number of experimental conditions [–]
N_{response}	number of simulation/experimental responses [–]
OF	fitting objective function [–]
p	pore volume [m^3]
Δp_{comp}	compaction pore reduction [m^3]
q_0	primary particle number distribution [m^{-1}]
$q_{0,\mathbb{X}_{\text{incept}}}$	primary particle number distribution on $\mathbb{X}_{\text{incept}}$ [–]
q_3	primary particle volume distribution [m^{-1}]
r_{pen}	particle penetration rate [$m^3\,s^{-1}$]
$\tilde{R}$	harmonic mean particle radius [m]
R_{incept}	primary particle inception rate [s^{-1}]
R_{droplet}	droplet inception rate [s^{-1}]
R_{inflow}	particle inflow rate [s^{-1}]
R_{outflow}	particle outflow rate [s^{-1}]
s_{o}	original solid volume [m^3]
s^*	pore saturation limit [–]
t	time [s]
T_{break}	breakage operator [–]
T_{coag}	coagulation transform [–]
T_{comp}	compaction transform [–]
T_{nuc}	nucleation growth transform [–]
U_{col}	particle collision velocity [$m\,s^{-1}$]
v	particle volume [m^3]
$v_{\text{nuc}}^{\text{max}}$	maximum particle volume permitted to join nucleus [m^3]
$v_{\text{parent}}^{\text{min}}$	minimum volume for breakage [m^3]
v_{drop}	droplet volume [m^3]
V_{real}	compartment volume [m^3]
$V_{\text{real,T}}$	total volume of all compartments [m^3]
$\dot{V}_l$	binder flowrate [$m^3\,s^{-1}$]
x	particle vector [m^3]
x_{drop}	droplet particle vector [m^3]
x_{nuc}	nuclei particle vector [m^3]
y_{exp}	experimental fitting response [m]
y_{sim}	simulation fitting response [m]
z	compartment index [–]

Greek symbols

α	effective droplet diameter parameter [–]
α_{daughter}	breakage distribution parameter [–]
β_{daughter}	breakage distribution parameter [–]
ε	particle porosity [–]
ε_{bed}	particle bed packing fraction [–]
$\varepsilon_{\text{granule}}$	Hagrasy agglomerate porosity definition [–]
ε_{min}	minimum particle porosity [–]
μ_{binder}	binder viscosity [Pa s]
λ	concentration measure [m^{-3}]
ν	breakage product parameter [–]
ρ_{env}	envelope density [$kg\,m^{-3}$]
ρ_{l}	binder density [$kg\,m^{-3}$]
ρ_{s}	solid density [$kg\,m^{-3}$]
ρ_{true}	true density [$kg\,m^{-3}$]
ϕ	liquid saturation [–]
ϕ_{max}	maximum liquid saturation [–]
σ	fitting response scaling factor [m]
τ	compartment residence time [s]
ϕ	test function [–]
χ_{frag}	breakage parameter [–]

Another advantage of TSG equipment is the variable configuration of the device available to the operator during formulation development. Each screw in the TSG system is composed of numerous screw *elements* which may be of varying geometry. Different types of element act differently on the particle mass passing through them and thus the screw element configuration may be altered to produce a granular product with different physical properties. The screw speed, liquid feed rate and powder feed formulation may also be varied in this way, resulting in a system with an exceptionally large operating space. The complexity and variability of the TSG system therefore requires a deep understanding of the underlying process in order to predict, and more importantly,

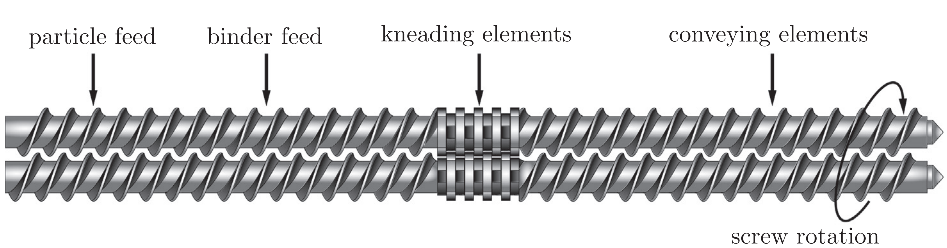

Fig. 1. Twin-screw granulator.