

Accepted Manuscript

Computational approaches to predict the effect of shear during processing of lubricated pharmaceutical blends

William R. Ketterhagen, Matthew P. Mullarney, John Kresevic, Daniel Blackwood



PII: S0032-5910(18)30393-0
DOI: doi:[10.1016/j.powtec.2018.05.023](https://doi.org/10.1016/j.powtec.2018.05.023)
Reference: PTEC 13396
To appear in: *Powder Technology*
Received date: 24 January 2018
Revised date: 27 April 2018
Accepted date: 11 May 2018

Please cite this article as: William R. Ketterhagen, Matthew P. Mullarney, John Kresevic, Daniel Blackwood , Computational approaches to predict the effect of shear during processing of lubricated pharmaceutical blends. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Ptec(2017), doi:[10.1016/j.powtec.2018.05.023](https://doi.org/10.1016/j.powtec.2018.05.023)

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Computational approaches to predict the effect of shear during processing of lubricated pharmaceutical blends

William R. Ketterhagen*, Matthew P. Mullarney, John Kresevic, and Daniel Blackwood

Worldwide Research & Development, Pfizer Inc., Groton, CT 06340

Keywords: lubrication, tensile strength, powder feeding, encapsulation, discrete element method, compartment model

* Corresponding Author.

Current address: Drug Product Development, Research and Development, AbbVie Inc., North Chicago, Illinois 60064

E-mail address: bill.ketterhagen@abbvie.com (W.R. Ketterhagen)

Abstract

In the production of pharmaceutical tablets and capsules, a lubricant such as magnesium stearate is often added to the powder blend or granulation in order to reduce friction and, in some cases, minimize sticking to the manufacturing equipment surfaces. If the lubricated blend is exposed to excessive shear during the processing steps prior to tableting or encapsulation, adverse effects on quality attributes of the final dosage form may be observed. These could include an increase in wetting contact angle, a slowdown in disintegration and/or dissolution, and a reduction in the tensile strength of compacts. In this work, two different computational modeling approaches are proposed to predict the effect of shear during the processing of lubricated pharmaceutical blends on drug product quality attributes. In this case study, an agitated powder feed system is examined, but the approach could be readily extended to other powder processing operations. First, a framework for the prediction of lubrication-based tensile strength reduction using the discrete element method (DEM) is proposed. This approach utilizes a companion study in a lab-scale, high-shear mixer to map the DEM predictions of extent of shear to an experimentally relevant tensile strength prediction. Second, a compartment model (CM) approach is proposed to model the powder flow and lubrication in the feed system. The tensile strength predictions from these two different approaches both compare favorably to experimental measurements of tensile strength.

Download English Version:

<https://daneshyari.com/en/article/6674563>

Download Persian Version:

<https://daneshyari.com/article/6674563>

[Daneshyari.com](https://daneshyari.com)