

Unit Operation Literature Review Outline

Tablet Formation & Encapsulation

Nathan LeRoy | 10/3/2018

Abstract:

Oral dosage forms are the most popular dosage form due to their ease of use, consistency, and lack of required professional experience. Lately, pro-biotics have seen a rise in popularity for their digestive health benefits. A pro-biotic in an oral dosage form makes the bio-acquisition of the API easily available to everyone. Two of the most popular dosage forms are compressed tablets and gelatin capsules. This review will go through the unit process of created both, and the associated pros and cons of each. Both have fundamental process parameters that affect performance and allow predictability of outcomes. However, at the end of the day, a gelatin capsule is the most desirable form due to the lack of shear which may be seen in tablet compression, and due to the lack of a need for excipients.

Themes:

1. Methods and Factors of Tablet Formation

a. Overview of tablet presses, factors determining performance, and scaling:

i. **The effect of processing parameters on pharmaceutical tablet properties**

By: [Sinka, IC](#) (Sinka, I. C.)^[1]; [Motazedian, F](#) (Motazedian, F.)^[1]; [Cocks, ACF](#) (Cocks, A. C. F.)^[2]; [Pitt, KG](#) (Pitt, K. G.)^[3]

The preferred drug delivery system today is represented by tablets, which are manufactured using high speed rotary presses where the powder material is compressed in a die between rigid punches. Compression represents one of the most important unit operations because the shape, strength and other important properties of the tablets are determined at this time. These properties are dictated not only by the characteristics of the powder constituents (which are determined by the properties of the constituents, mixing and granulation), but also by the selection of process parameters imposed by production machinery. This paper focuses on the die fill and the compaction parameters.

ii. **Understanding effects of process parameters and forced feeding on die filling**

By: Goh, HP (Goh, Hui Ping)[1] ; Heng, PWS (Heng, Paul Wan Sia)[1] ; Liew, CV (Liew, Celine Valeria)[1]

Abstract:

Die filling is a critical step during pharmaceutical tablet production and is still not well understood due to the rather complex interplay between particle attributes, die orifice diameter and fill energetics. While shoe-die filling models have been used to simulate die filling conditions, they typically lack the sophistication of the actual production-scale, feeder-based die filling conditions. The relationship between tableting process parameters and filling into die orifices of different diameters by powders of different flowabilities requires critical examination and

understanding. In this study, a special die filling contraption was designed and custom-made to simulate the effects of gravity, suction and feeder paddle assistance as present in modern rotary tablet presses. Die fill performance was studied using powders with different flow properties. Suction impact was greatest on die fill, in particular, for small orifice diameters and less permeable powders. Effect of paddle velocity on die fill was greater for compressible powders and larger orifice diameters. In comparison to suction and paddle velocity, forced feeding did not significantly affect die fill performance. Relationship between process parameters and die fill performance was found to be highly dependent on the material and orifice diameter.

b. Particle Size Distribution and Modeling/Predicting Granulation Processes:

i. **Model development and prediction of particle size distribution, density and friability of a comilling operation in a continuous pharmaceutical manufacturing process**

By: [Metta, N](#) (Metta, Nirupaplava)^[1]; [Verstraeten, M](#) (Verstraeten, Maxim)^[2]; [Ghijs, M](#) (Ghijs, Michael)^[2,3]; [Kumar, A](#) (Kumar, Ashish)^[4]; [Schafer, E](#) (Schafer, Elisabeth)^[4]; [Singh, R](#) (Singh, Ravendra)^[1]; [De Beer, T](#) (De Beer, Thomas)^[2]; [Nopens, I](#) (Nopens, Ingmar)^[3]; [Cappuyns, P](#) (Cappuyns, Philippe)^[4]; [Van Assche, I](#) (Van Assche, Ivo)^[4] [...More](#)

Abstract:

The comilling process plays an important role in solid oral dosage manufacturing. In this process, the granulated products are comminuted to the required size distribution through collisions created from a rotating impeller. In addition to predicting particle size distribution, there is a need to predict other critical quality attributes (CQAs) such as bulk density and tapped density, as these impact tablet compaction behavior. A comprehensive modeling approach to predict the CQAs is needed to aid continuous process modeling in order to simulate interaction with the tablet press operation. In the current work, a full factorial experiment design is implemented to understand the influence of granule strength, impeller speed and residual moisture content on the CQAs. A population balance modeling approach is applied to predict milled particle size distribution and a partial least squares modeling approach is used to predict bulk and tapped density of the milled granule product. Good agreement between predicted and experimental CQAs is achieved. An R-2 value of 0.9787 and 0.7633 is obtained when fitting the mean particle diameters of the milled product and the time required to mill the granulated material respectively.

2. Methods and Factors of Capsule Filling

a. Fundamentals of Capsule Filling

i. **Pharmaceutical Production, an Engineering Guide. IChemE. pp. 126–129**

Bill Bennett; Graham Cole, (2003)

The encapsulation process is an alternative to tablet compression, which also masks unpleasant-tasting actives. It can also have advantages where compression could result in a compacted tablet with unacceptably long or short dispersion time in the upper alimentary system. As with

tablets, the gelatin barrier can be further coated with 'enteric' materials which ensure dissolution or dispersion only in that part of the system where optimum effect is produced.

3. Final Formulations, Filling, and Packaging

a. Fundamentals and Key aspects

i. **Final formulation, filling and packing pilot plants**

Bill Bennett; Graham Cole, (2003)

The equipment used in this type of pilot plant is a smaller version of the production scale equipment. Facilities are usually built to cope only with certain types of products. For example, a facility to manufacture tablets is likely to be able to cope with a large variety of different products because the processes involved in making tablets are similar even if the active ingredient is completely different. However, this facility would be completely different to one making inhalation products even if the tablet and the inhalation product contained the same active ingredient.

Conclusion:

Oral dosage forms provide everyone with an easy and readily available opportunity to take the active ingredients they need to improve their health. A gelatin capsule is the ideal form for a probiotic due to its lack of excipients, its resistance to relative humidity changes, and its ability to gently store and dispense the API.