

The chemistry and physics behind compression process in the pharmaceutical industry

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Renan Marcel Bonilha Dezena,¹ Paulo César Pires Rosa²

¹Preformulation Specialist Consultant, Brazil

²Faculty of Pharmaceutical Sciences, University of Campinas (UNICAMP), Brazil

Correspondence: Renan Marcel Bonilha Dezena, Preformulation Specialist Consultant, Campinas, São Paulo, Brazil, Tel 5519991361228, Email rena_marcel@hotmail.com

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Background

Since the beginning, the use of oral solids in therapy has always predominated due to the ease of administration, decreased perception of unpleasant flavors and odors, thus enabling greater adherence to treatment, in addition to greater stability when compared to other pharmaceutical forms.¹⁻³ Inventor William Brockedon patented the first compressor in 1843 for compressing potassium and calcium oxide. Subsequently, through the growing interest regarding the compression of graphite powder, the feasibility of applying the technology for the production of medicines was observed.¹⁻³

The main steps for manufacturing oral solids are direct compression, dry granulation and wet granulation. The direct compression process provides greater productivity, however, due to limitations inherent to the formulation, it is necessary to use dry or wet granulation (Figure 1).¹⁻³

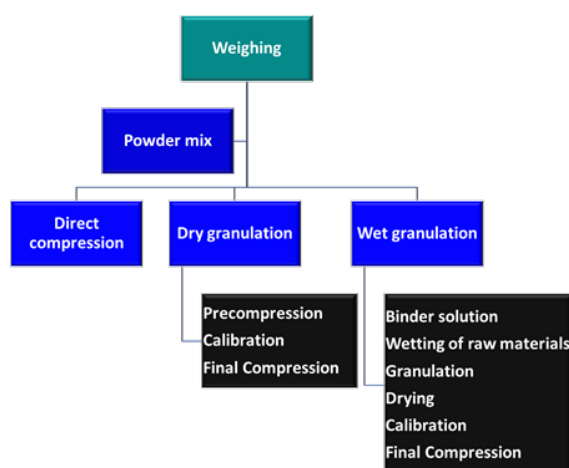


Figure 1 Main steps for manufacturing oral solids.

Example of limitations inherent to the formulation:

- Uniformity, density, fluidity, porosity and compressibility.¹⁻³

The advantage of dry granulation is related to situations in which the drug is sensitive to heating from a drying unit operation step during the wet granulation process and also susceptible to the formation of pseudopolymorphs (hydrates or solvates) when in contact with the granulating solution or even chemical hydrolysis reactions.¹⁻³ Potential manufacturing deviations related to granulation are slow disintegration, changes in dissolution profile, adhesion in both punch and press die.¹⁻³

An eccentric compressor briefly presents the following stages, as shown in figure 2.

The application of a compressive force on the particles of a given formulation will cause a deformation in the material. This phenomenon, which is associated with the intensity/duration of the

compression force and the physicochemical characteristics of the formulation, can present itself as elastic, plastic and destructive.^{4,5}

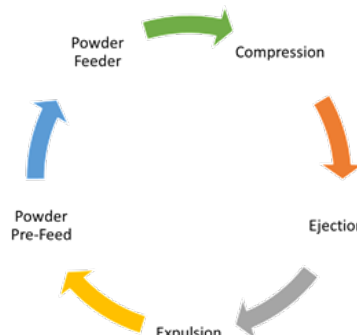


Figure 2 Eccentric compressor stages.

In elastic deformation, the particles of the formulation return to their original volume after the compression force is removed. In plastic deformation, the particles of the formulation do not return to their original volume after the compression force is removed, remaining compacted. Finally, in destructive deformation, fragmentation and compaction occur (Figure 3).^{4,5}

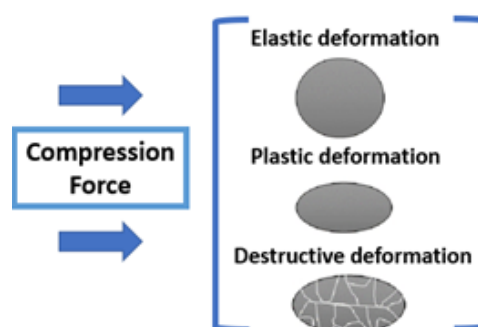


Figure 3 Different types of particle deformation under compression force.

Scientific studies have shown that crystallinity is an extremely important physical property, and, in this way, it would be possible to predict the behavior and type of deformation. There is a tendency that crystalline compounds undergo elastic or destructive deformation (brittle fragmentation) whereas semi-crystalline and amorphous compounds undergo plastic deformation.^{6,7}

As an example, we can highlight alpha-lactose monohydrate as a fragile material and microcrystalline cellulose as a plastic material when subjected to the direct compression process.^{6,7} In the compression process, regarding the compressibility of the powders, as essential as the physical mechanisms involved (elastic and/or plastic deformations and fragile fragmentation), we can highlight the mechanism of interparticle bonding and the area where these bonds are active.¹⁻⁷

According to the literature, there are five main types of interactions between characterized particles:

- a. Partial merger.¹
- b. Crystallization.¹
- c. Binders.¹
- d. Capillarity and surface tension.¹
- e. Attraction between solid particles (molecular and electrostatic forces).¹

Summary

Therefore, it is essential to have in-depth knowledge of the physical and chemical properties of excipients and drugs through pre-formulation studies for the design of quality pharmaceutical products that are viable in terms of the production process.

Acknowledgments

None.

Conflicts of interest

Authors declare that there is no conflict of interest.

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