

## Dry granulation and its application in dietary supplements manufacturing

### Introduction

A dietary supplement was defined by United States Congress in the Dietary Supplement Health and Education Act (DSHEA), which became law in 1994.

A dietary supplement is a product that is intended to:

- Supplement the diet that bears or contains one or more dietary ingredients (including vitamins, minerals, herbs or other botanicals, amino acids and other substances) or their constituents;
- To be taken by mouth as a pill, capsule, tablet, liquid or suspension;
- Is labeled on the front panel as being a dietary supplement.

The dietary supplement label contains information about the product, like its intended use, direction for use, safety information, and, in addition, it fully, clearly and accurately discloses each ingredient contained in the supplement. Therefore, it should be of importance for consumers to judge the quality of the dietary supplement but based on the label it is difficult to determine the performance, benefits and features like containing the proper amount of ingredients in such a way that their absorption and corresponding efficacy are guaranteed. The grade of quality depends on the production process, which involves the quality control of the manufacturer, the suppliers and other involved parties.

The U.S. Food and Drug Administration (FDA) enforced and issued Good Manufacturing Practices (GMPs) for dietary supplements in 2007. Consequently, the dietary supplement industry released guidance on January 17<sup>th</sup>, 2013, for companies to support the compliance with current Good Manufacturing Practices (cGMPs). By this implementation, manufacturers are now expected to guarantee the identity, purity, strength, and composition of their dietary supplements. For example, the GMPs aim to prevent the inclusion of improper ingredients, the incorrectness of the labeled amount of ingredients, as well as the possibility of (cross-) contamination.

Quality tests of dietary supplements by e.g. Consumer Labs in accordance with the US Pharmacopeia (USP) test methods have alarmed the industry and consumers due to products in form of tablets failing for one or more of the following reasons:

- Much higher/lower levels of nutrients than claimed on the label because of excessive overdose/underdose or inhomogeneity
- Contamination with heavy metals
- Insufficient disintegration rates which resulted in a reduced chance of absorption
- Lower levels of nutrients than claimed on the label because of insufficient shelf life or being destroyed during the manufacturing process e.g. due to too high drying temperatures, too large humidity levels and/or over-compaction

Insufficient disintegration of tablets is often linked to inferior formulations and quality control issues during the manufacture of the tablets (e.g. using too much compaction pressure), including the process steps prior to tableting, e.g. blending and/or granulating.

## Dry granulation of dietary supplements formulations

When it comes to the use of dry granulation with roller compactors as a manufacturing step within the production process of solid dosage forms, it is quite important to use equipment which allows the user to not only control the parameters for granulation, like e.g. granule size or particle size distribution (PSD). The manufacturer must be able to establish in-process specifications for any point, step, or stage in the master manufacturing record where control is necessary to ensure that specifications for identity, purity, strength and composition of the dietary supplement are met, as required by the FDA under Code of Federal Regulations Title 21 Part 111 (CFR 21 Part 111), which describes the cGMP in manufacturing, packaging, labeling, or holding operations for dietary supplements.

In addition, besides having the knowledge and expertise about dry granulation technology it is important for the manufacturer to perform the production processes with equipment which is so precise, especially in the lower press force area, that a perfect density in combination with weight uniformity and optimal flowability of the granules is guaranteed, being a prerequisite for tablets with the desired hardness, disintegration and dissolution rates.

One of the most challenging formulations in form of granules and tablets are heat and humidity sensitive formulations like multivitamins and effervescent mixtures with a high payload of bioactive ingredients. The key to successful processing of these high demanding preparations is a "Quality by Design" (QbD) capable roller compactor which can handle a large range of powder bulk densities, whilst controlling and ensuring an utmost gentle feeding and processing of the powder, thus avoiding an unacceptable increase in temperature above the critical value of some formulation components, which in turn avoids the degradation of the corresponding (active) ingredients.

Gerteis® roller compactors are designed to maintain a maximum measure of process stability and reproducibility throughout its full range of roll pressure by using a small number of process relevant control parameters. All control functions are calibrated, like a patented linear force control system, for achieving and ensuring a long term stable and repeatable process. Gerteis® offers a fully computerized, sensor controlled unit with solid design and state-of-the-art solutions in order to attain the best granulating results, with stable and measurable processing sequences, and with complete validation and replication in compliance with CFR 21 Part 11 as well as fulfilling all requirements for the best execution of Part 111.

With a Gerteis® roller compactor the product process parameters are established very efficiently at lab scale during product development and can be applied to large production machines without any further experiments enabling large scale production more or less the following day, empowering and offering a huge saving in time and costs, whilst eliminating scale up risks more or less completely.

Gerteis® dry granulation offers roller compactors with technology by design, but has been developed significantly further over recent years.

Some of the key advantages of Gerteis are:

- Superior feeding system, allowing you to process the widest range of powder formulations under minimum stress with virtually no increase in temperature (2 - 4°C typically).

- Advanced size reduction system, being an utmost gentle, effective and reproducible method for breaking/milling flakes, thus allowing you to achieve optimal and consistent particle size distribution continuously, making recycling superfluously.
- Compaction unit with a precise control and measurement of roll force in combination with a sophisticated easy to operate gap control feature, both being a prerequisite for always achieving, the same quality within a batch and from batch-to-batch.
- Advanced roller design ensuring negligible process run up and run down, without a need for fines recirculation.
- Special closed loop control of compaction and the feed system to give consistent controllable product density and as add-on, a PAT density tool is available.
- Predictive processing software for rapid processing results.

GERTEIS MASCHINEN + PROZESSENGINEERING AG OFFERS THE PERFECT ROLLER COMPACTOR TECHNOLOGY PLATFORM FOR SUCCESSFUL PROCESSING OF DIETARY SUPPLEMENT FORMULATIONS!

The company was established in 1986 and is headquartered in Jona, Switzerland, ever since. GERTEIS specializes in design, development and production of premium roller compactors for the pharmaceutical, chemical and food industry.

With its innovative technological capabilities for design, development, manufacturing and process optimization, GERTEIS guarantees the optimal solution for your dry granulation needs.

Quality by Design (QbD) 'designed in', Gerteis® dry granulation technology could be the key to your future solid dosage success.

#### OUR BRANDS



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