solids development

Filling the gap between powder and technology

DRY GRANULATION
SUMMARY

ROLLER COMPACTOR

SOLIDS DEVELOPMENT CONSULT – YOUR TRUSTED PARTNER FOR EFFICIENT FORMULATION AND PROCESS DEVELOPMENT

www.solids-development.com

About Us

Solids Development is your specialist for efficient formulation and process development of solid dosage forms. As experts and problem solvers for your challenges in the development and production of tablets and granules, we offer comprehensive services - from formulation work, through scale-up, to solving production problems.
Below you will find a summary of our LinkedIn posts on the topic of Dry Granulation.

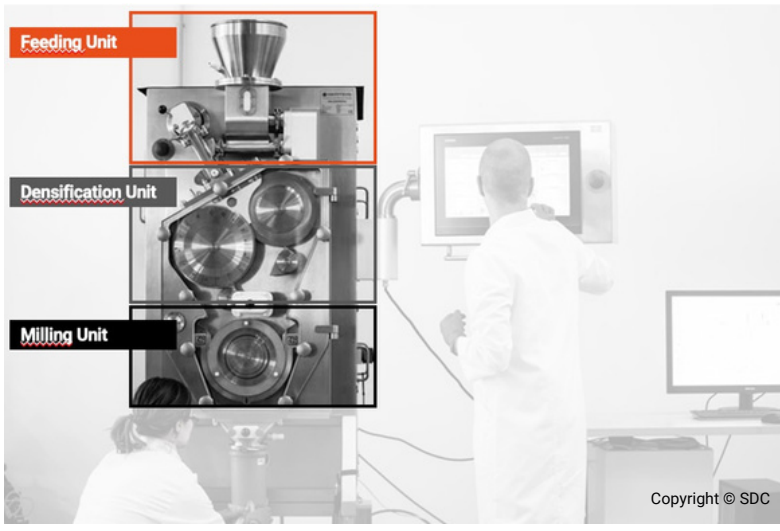
Roller Compactor - Summary of important aspects

The Necessity of Granulation for Quality Assurance in Tabletting

Tablet manufacturing is a highly precise process where granulation plays a central role in ensuring quality and efficacy. This step is crucial for improving flowability, ensuring dose uniformity, increasing tablet strength, and enhancing the dissolution rate. Particularly when processing micronized active pharmaceutical ingredients (APIs) or poorly flowing formulations, granulation is indispensable. It helps to overcome challenges in the homogeneity of the mixture and ensures that the tablets meet required criteria such as hardness, dissolution rate, consistent weight, and dose uniformity.

Introduction to Dry Granulation – Functional Units of Roller Compactors

Dry granulation, also known as roller compaction, is a method where powder is densified between two rollers without adding any liquid. This process is particularly beneficial when the addition of liquid is undesirable, or the materials are heat sensitive. Roller compactors consist of three main components: the feeding unit, the densification unit, and the milling unit. Each unit plays a specific role in the process and contributes to the efficiency and quality of granulation.

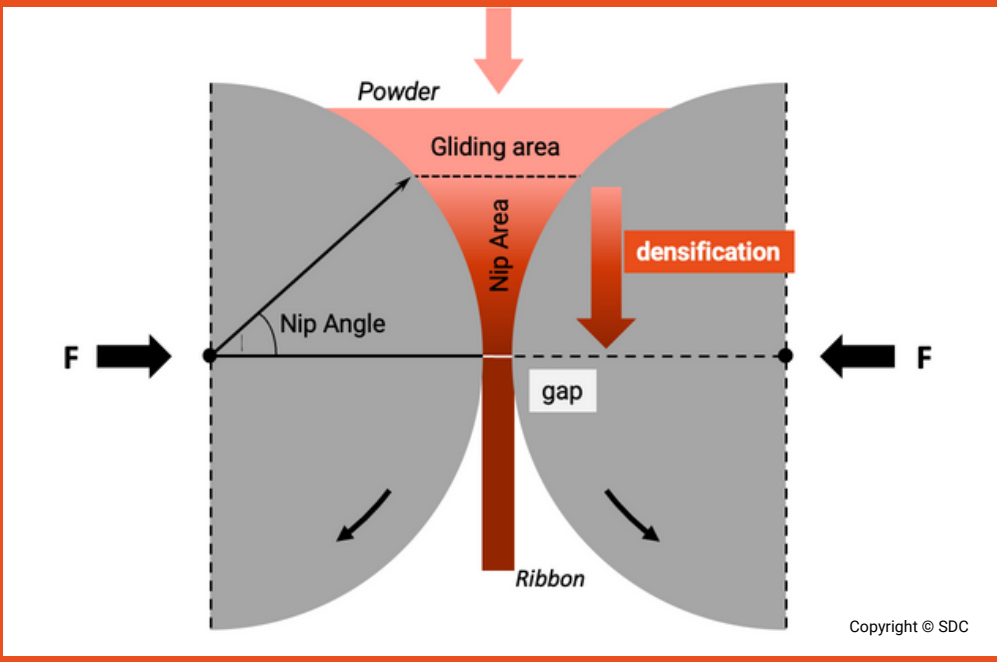


The Feeding Unit

The feeding unit, consisting of a hopper and one or two augers, is crucial for the delivery of powder to the densification unit. A constant feed is essential to ensure consistent quality of the granules. Different manufacturers implement various designs to achieve a uniform feed regardless of bulk density and flowability. The construction and design of the feeding unit are therefore pivotal for the success of the entire granulation process.

The Densification Unit

The densification unit, where the powder is densified between two counter-rotating rollers into a ribbon, is central to the quality of the granules. The specific roll force, roll gap, and roll speed are the main parameters that determine the properties of the ribbon and thus of the granules. Different machine builders arrange the rollers horizontally, vertically, or inclined, and the diameter and width of the rollers vary. Choosing the right configuration and settings is crucial for achieving the desired granulate quality.

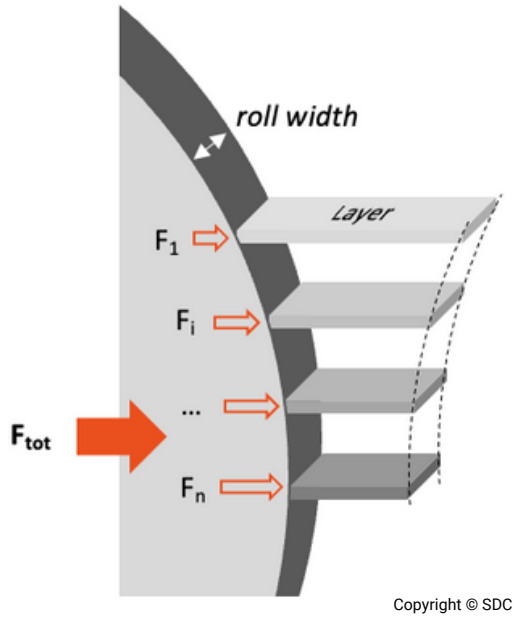


Understanding Nip Angles in Powder Compaction

The nip angle is determined by the roll force and roll gap. A deeper understanding of this angle is essential for optimizing the compaction process. Barbara Fretter and Michael Schupp have provided valuable insights into this in their article in Scientist Live on December 11, 2023. They explain how lower bulk densities require larger nip angles and affect compaction efficiency.
We are happy to share the link to the article in Scientist Live.

The Specific Roll Force

The specific roll force, expressed in kN/cm, is a critical parameter in roller compaction as it directly influences the density of the ribbon and thus the quality of the granules. The force is proportional to the roll width, and the use of the unit kN/cm allows for the transfer of force parameters to rollers of different widths. The specific roll force influences compaction efficiency and the properties of the resulting granulate.



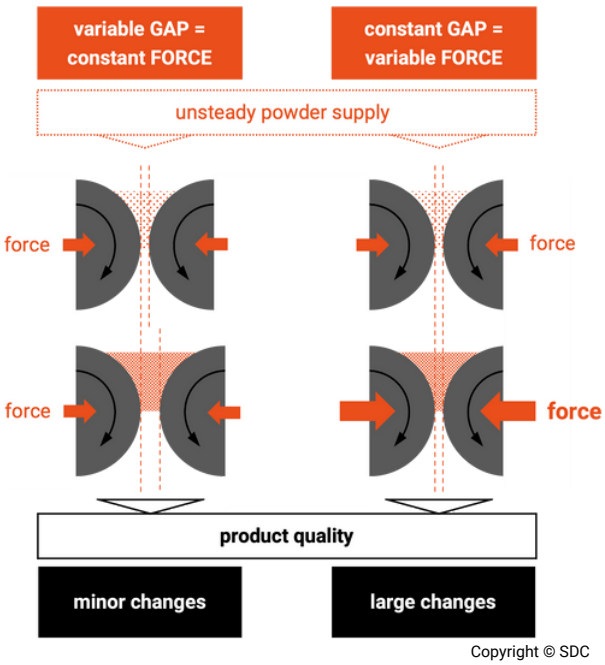
IDraw-in Problems and Solutions

Draw-in problems, often caused by insufficient frictional forces, can be addressed by adjusting the roll surface or minimizing powder lubrication. The use of rolls with indentations can improve frictional forces by changing the friction from powder-metal to powder-powder. These adjustments enhance the process's efficiency and securing the quality of the granules.

We are happy to share the link to the article in Scientist Live.

Fixed vs. Variable GapRoller Compactors

The choice between roller compactors with fixed or variable roll gaps has significant impact on the quality of the granules. The fixed gap compactors have a constant gap during the process. When it comes to fluctuation in the powder supply, this results in changing specific roll forces, the main driver for the quality of granules. Roller compactors with variable gaps can handle fluctuations in the powder supply. One roll is movebale and so the gap varies, but the force stays constant, leading to more consistent product quality.



Influence of Force and Gap on Granulate Quality

As already mentioned, the specific roll force and roll gap are the main drivers for the ribbon density and thus for the quality of the granules. Careful tuning of these parameters is essential for optimizing the granulation process. Hartmut vom Bey and Barbara Fretter provide a comprehensive overview of the effects of force and gap in their article. They emphasize that a higher specific roll force leads to denser ribbons, while a larger gap reduces compaction and thus ribbon density.

We are happy to share the link to the article in Scientist Live.

At-Gap Density as an Alternative to Ribbon Density

The densification unit, where the powder is densified between two counter-rotating rollers into a ribbon, is the central unit in roller compaction. The specific roll force, roll gap, and roll speed are the main parameters that determine the properties of the ribbon and thus of the granules. Different machine builders arrange the rollers horizontally, vertically, or inclined, and the diameter and width of the rollers vary. Choosing the right configuration and settings is crucial for achieving the desired quality.

$$densiy = \frac{mass\ [g]}{volume\ [cm^3]}$$

Collected granules (e.g. for 2 min)

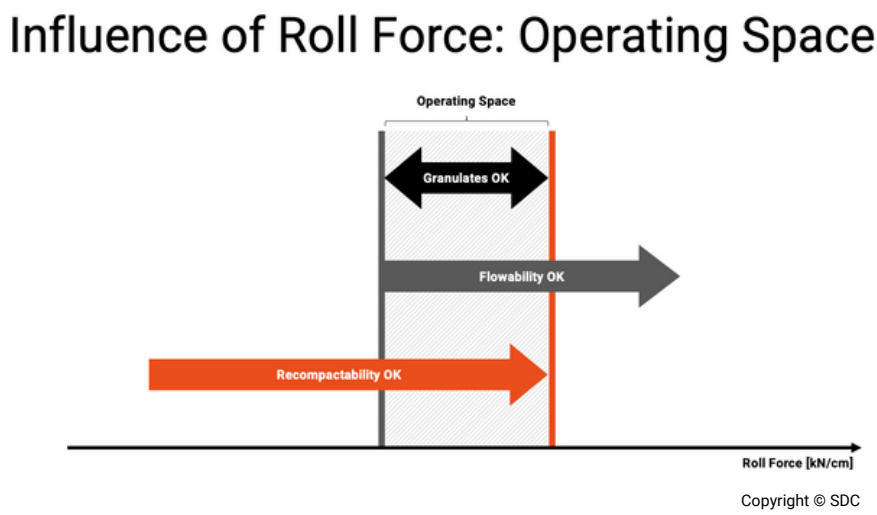
$$\frac{volume}{min} = gap * roll\ width * roll\ circumference * rpm$$

The Operating Space in Roller Compaction

The operating space is the area in which the granules can be produced with sufficient flowability and still result in strong tablets . By applying force to a powder, a part of the bonding sites between the particles is used to form the ribbon. These bonding sites are lost for making tablets. The higher the force, the lower the recompactability of the powder. This is why the operating space is an important aspect defining the process and its boundaries. Apply as much force as needed, but as less as possible!

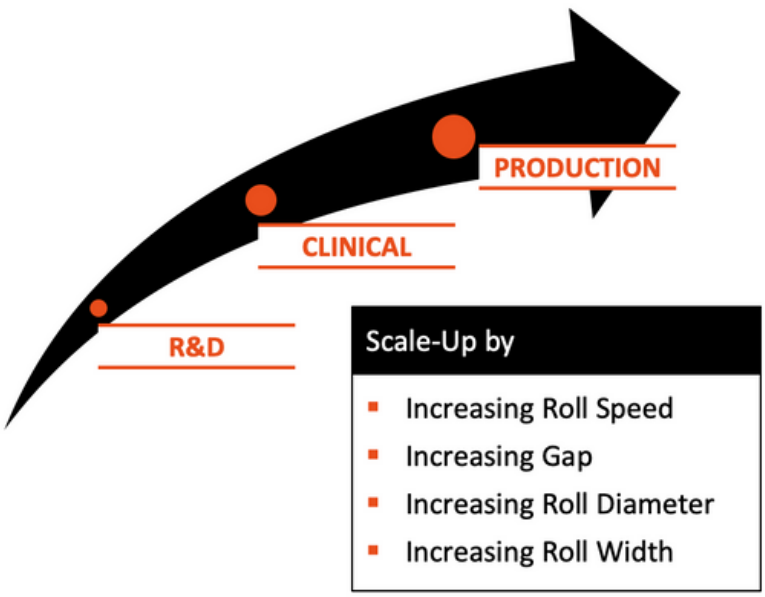
The Milling Unit

The milling unit determines the particle size distribution of the granules. Depending on the grinding properties of the material, the granulator type and settings as well as the sieve type and size needs to be set. The milling systems must mill the ribbons/flakes as gently as possible to achieve a good-flowing granulate. Additionally, it is important that the milling unit delivers a reproducible particle size distribution independent from adapting the throughput.



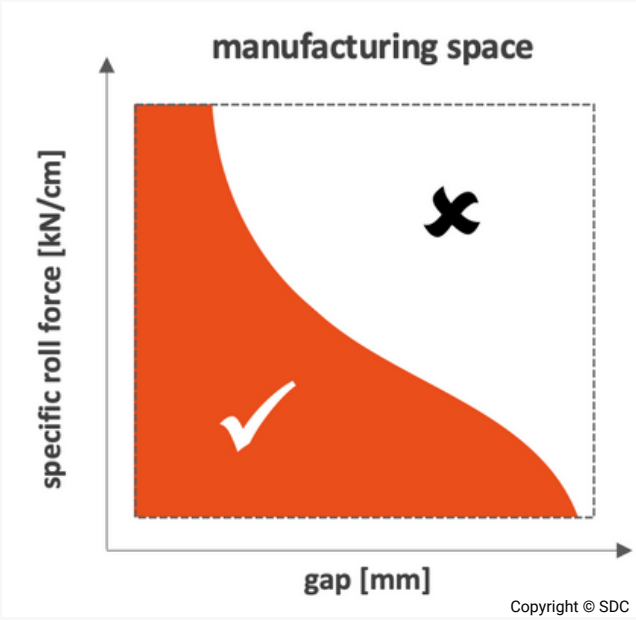
Scale-Up in Roller Compaction

In roller compaction the scale-up from lab scale to production scale is straight forward and can be performed with only few experiments. The influencencing factors are well known. Often, they can be predicted or at least easily corrected for. Hartmut vom Bey and Barbara Fretter discuss the details in scaling up in dry granulation on Scientist Live.



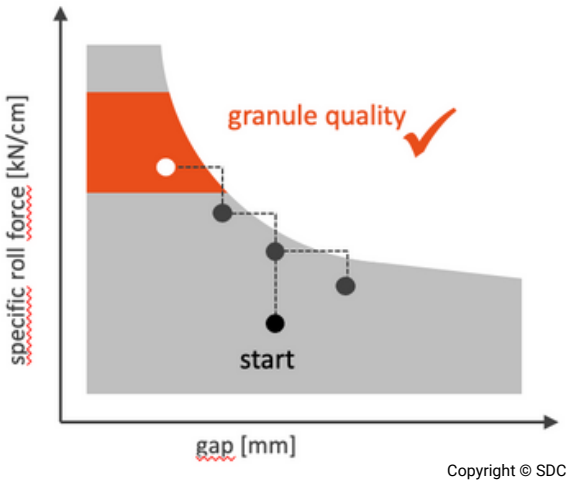
The Manufacturing Space

The manufacturing space maps the physical boundaries of specific roll forces and gaps in which a product can be produced with a given configuration of the roller compactor. The representation of specific roll force against the gap shows the combinations of force and gap that can be processed. Larger gaps often carry the risk of draw-in problems. The same risk appears with too high specific roll forces, which also might densify the material too much and then lead to an overload of the roll torque. Adjustments in the formulation or settings of the roller compactor, especially the roll types, can expand the manufacturing space. Knowledge of the boundaries of the manufacturing space is crucial for process development, scale-up, planning of trials, and understanding potential manufacturing problems. It is important to note that the manufacturing space provides answers to processability, but not necessarily to the quality of the granules.



First Experiments in Developing a Dry Granulate – Our Approach

In the early phase of developing new drugs, it is often a challenge to gain maximum information with a limited amount of API. When processing a formulation into a dry granulate for the first time, the interactions between the formulation and the roller compactor are mostly unknown. This is especially true for products with a limited manufacturing space and a small operating range where the granulate quality is good. A rigid experimental plan carries the risk of being either uninterpretable or missing the small operating range. Our approach for first experiments in dry granulation avoids this risk. By adhering to the general rule of roller compaction – "realize as little densification as possible but as much as necessary" – the starting point is at a medium gap and a moderate roll force. Higher densification is achieved by increasing the roll force. Once the limit of the manufacturing space is reached, the gap should be reduced, allowing the forces to be increased further resulting in stronger densification, and so on. Using this approach minimizes the first experiments and maximizes the outcome, significantly saving time and material.



Small Scale Development of Dry Granulates

To save material, we use our Small Scale Method, which is especially important when the API is only available in limited quantities or the costs of the API are very high. In this method, we replace the ribbons by tablets. The tablets are made on a compaction simulator or single punch press and then milled to granules using a special handmill. These granules are then analyzed regarding flowability, recompactabilty, PSD etc. As shown in the graph, the recompactability of the granules from tablets are the same as from the foller compactor. The same applies to the PSD, if you use the right handmill. This method can save material by a factor of 20.

Here are the main features of the Small Scale approach summarized:

Resource Conservation and Cost Reduction: By significantly reducing the amount of material needed, the approach minimizes costs and conserves valuable resources, especially for expensive or rare APIs.

Efficient Process Design: Instead of ribbons, tablets are used, which are produced on a compaction simulator or a single punch machine and then milled into granules. This allows for precise control and high quality of the final product.

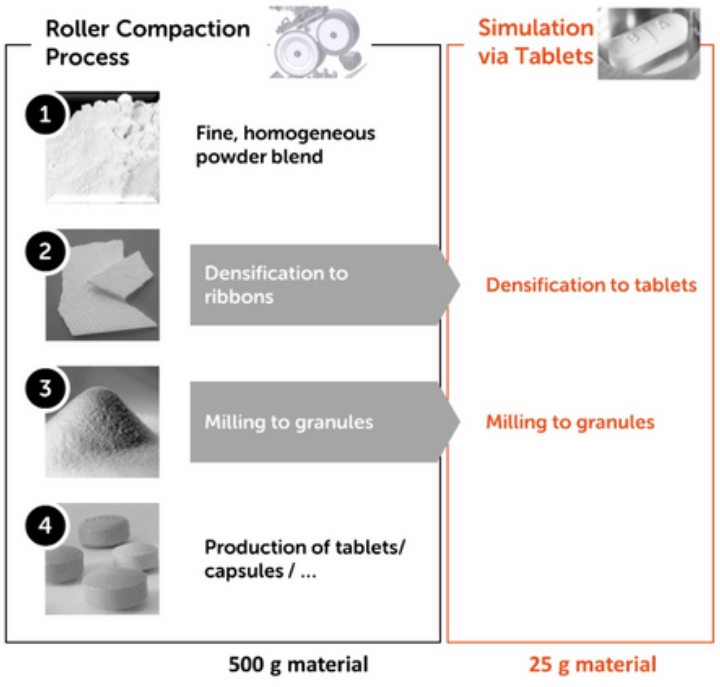
Quality Assurance through Analysis: The granules are analyzed for flowability, recompactability, and particle size distribution (PSD) to ensure the quality and specifications of the product.

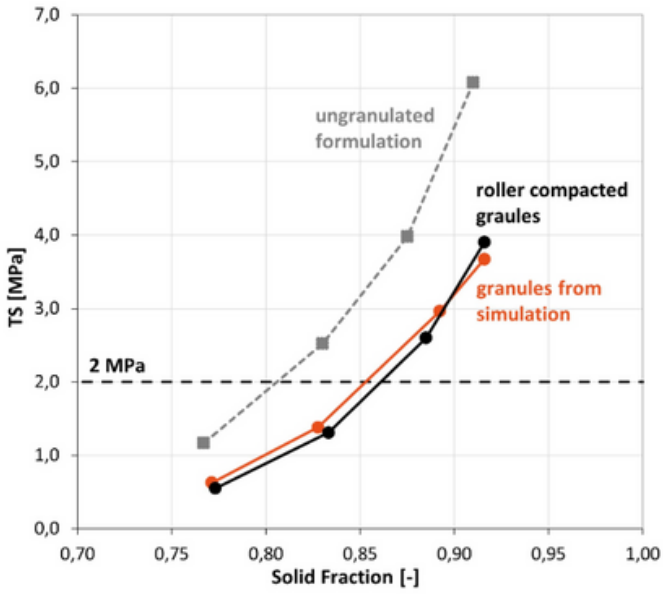
Significant Material Savings: The approach can reduce the material requirement by a factor of 20 or more, which is particularly important for limited availability or valuable APIs.

Strategic Solution for Development Challenges: The Small Scale approach offers a strategic solution to develop efficient and effective products without wasting resources and maximizing the quality and efficacy of the final product.

In summary, the Small Scale approach enables cost-efficient and resource-saving product development by reducing material needs, ensuring quality, and optimizing the development process.

If you want to optimize your product development while saving resources and costs, the Small Scale approach is the solution. Feel free to contact us to learn how we can address your specific challenges and improve your development processes with our proven approach. Let's pave the way together for efficient and successful product development. We look forward to hearing from you! **Contact us!**





That's what Solids Development stands for.

Filling the gaps between powder and technological: Our expertise in the field of granulation and tabletting stands firm.

For more information, please visit our homepage www.solids-development.com.

Our range of services includes Formulation Development, Transfer & Scale-up, Production Optimization, and Measurement & Process Engineering. We are passionate about sharing knowledge and are committed to fostering growth through our comprehensive training programs.

Follow us on our LinkedIn Campany-Page and stay updated with various topics under #DrRob.

We are here to support and accompany you at every step of your manufacturing process.

Every partnership begins with a non-binding conversation, and we are eager to start that dialogue with you. Feel free to contact us and let's unlock the potential of your products together. Your success is our mission. We look forward to you.

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Dr. Barbara Fretter & Maarten Lammens

Do you have challenges for which you need support?

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