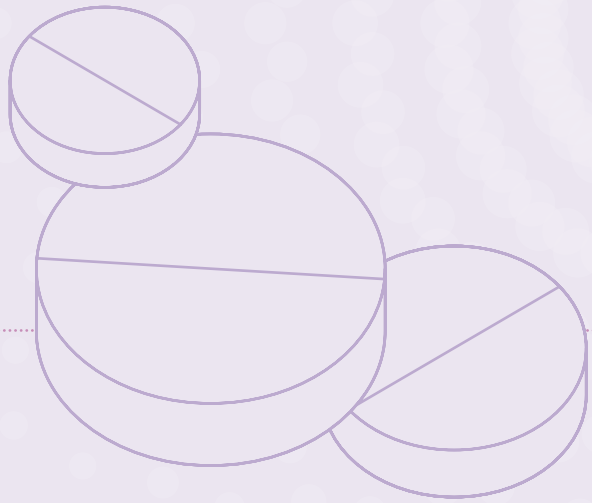
ROQUETTE
Offering the best of nature™

TABLET FORMULATION MADE SIMPLE

Your guide to direct compression without compromise

Selecting the right excipient is key to the success of your direct compression formulation. Read on to discover why PEARLITOL® SD is the first-choice excipient for compression without compromise, and how it can help you **unlock advanced tablet dosage forms in the pharmaceutical space**.



Excipients: key ingredients in your formulation

Direct compression is the most effective and least complex way to produce tablets because it involves minimal process steps. Because of this, it is fast becoming one of the **most common and economical methods of tablet manufacturing** throughout the pharmaceutical industry.

Key attributes of an optimal tablet formulation

- Compresses and compacts
- Good flowability
- Consistent tablet weight
- Content uniformity
- Maintains stability over time
- Dilution potential

The result: A safe and effective tablet with no friability, sufficient hardness and the same disintegration and dissolution time. The chosen excipient should aim to deliver these properties.

Despite its clear advantages, direct compression has its challenges.

The physical properties of the starting materials present in the formulation must be controlled more precisely compared to other tableting methods.

This is because the process and the final drug product are directly impacted by the properties of the raw material (since the raw materials are not altered by granulation steps used in other standard processes). This includes the direct compression excipient used – also called a filler-binder – which can strongly determine the processability of the formulation and overall characteristics of the finished tablet, including flowability of the component powders, hardness, disintegration and dissolution.

The use of poorly controlled or inadequately specified raw materials may lead to several challenges in direct compression, such as poor flowability, inconsistent tablet weight, unsatisfactory tablet strength, lack of content uniformity or segregation and dissolution failure. As such, the key to successful direct compression is critical selection of the excipient and making sure it brings enhanced performance, quality and consistency to the formulation.

> The key to successful direct compression is an excipient that brings **enhanced performance**, **quality** and **consistency**.

Top considerations for direct compression success

There are several technical factors to consider when choosing an excipient for direct compression, including particle size and shape, density, moisture content and composition. That is because these features can affect flowability and compactability of the powder mix, which ultimately drive the tableting process.

Processibility

The powder mix must be homogenous and uniform in weight from batch to batch.

This is to ensure safe and consistent dosing of the active ingredient, i.e. the same API concentration in every tablet.

If segregation of the different components occurs, the distribution of the tablet ingredients is no longer homogenous, and batch-to-batch consistency of the manufactured tablet cannot be guaranteed.

The main risk factor for segregation is wide particle size distribution. Obtaining optimal concentrations of excipients at the correct particle size is therefore key to ensuring uniform mixing and flow of the powder blend.

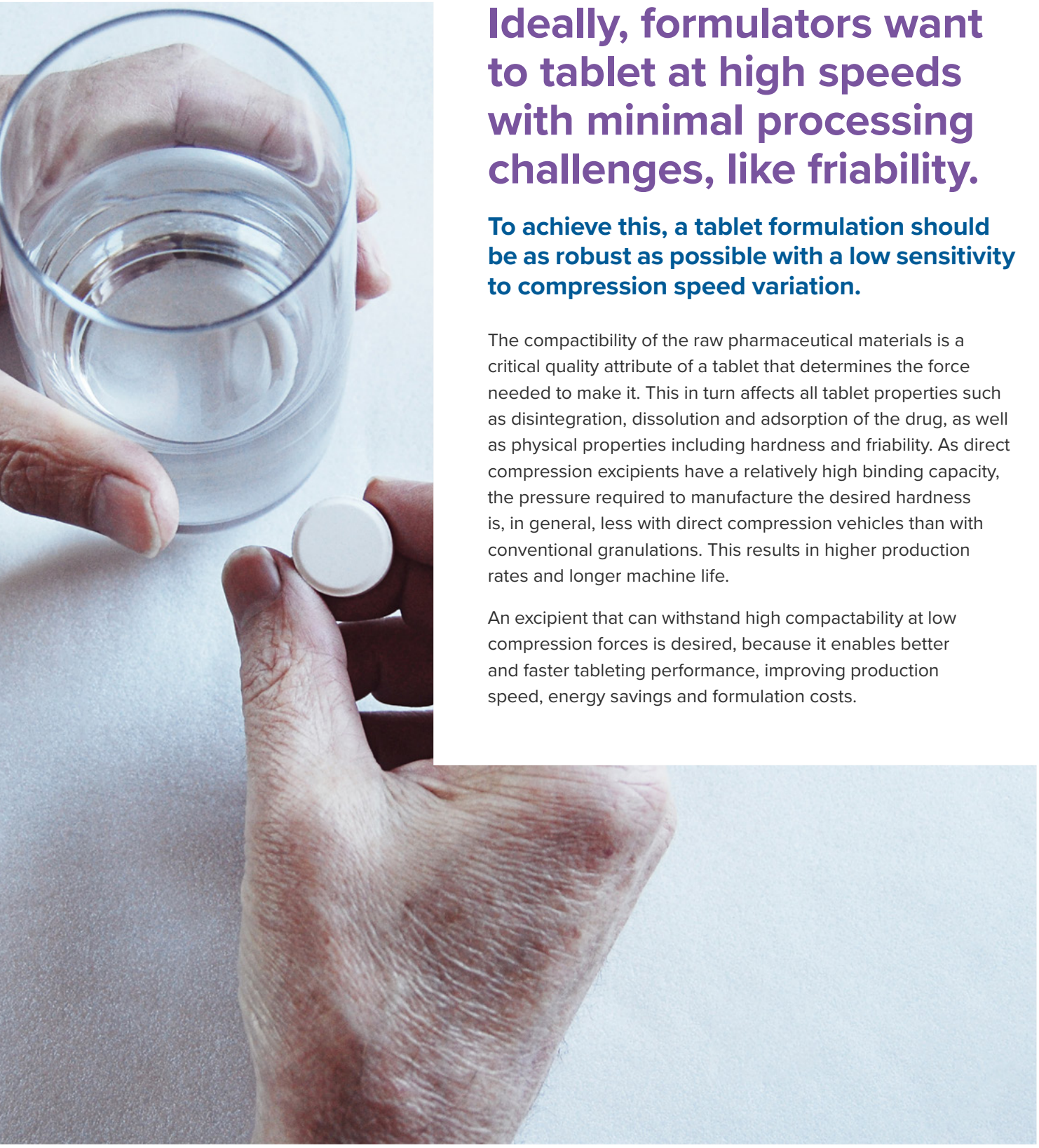
To overcome this, it is important for an excipient to have narrow particle size distribution and controlled particle size. The API particle size must also closely match the excipient's particle size for a homogenous powder blend.

There is also a need for adequate flowability of the tablet mass during direct compression since the powders flowability characteristics impact the overall tablet process. Flowability is determined by numerous factors, such as the shape, size and surface properties of powder particles, their mutual interactions, and environmental conditions, such as humidity.

Low flowability of the powder may cause technological problems; the most serious being uneven filling of the tablet press, substantial differences in the mass and inadequate tablet hardness.

> An excipient with **good flow properties** is **essential**.

Tableting properties



Ideally, formulators want to tablet at high speeds with minimal processing challenges, like friability.

To achieve this, a tablet formulation should be as robust as possible with a low sensitivity to compression speed variation.

The compactibility of the raw pharmaceutical materials is a critical quality attribute of a tablet that determines the force needed to make it. This in turn affects all tablet properties such as disintegration, dissolution and adsorption of the drug, as well as physical properties including hardness and friability. As direct compression excipients have a relatively high binding capacity, the pressure required to manufacture the desired hardness is, in general, less with direct compression vehicles than with conventional granulations. This results in higher production rates and longer machine life.

An excipient that can withstand high compactability at low compression forces is desired, because it enables better and faster tableting performance, improving production speed, energy savings and formulation costs.

Stability

With direct compression, tablet manufacture can be carried out without the involvement of moisture and heat. Hence, product stability is almost always ensured.

However, moisture sensitive APIs remain challenging in direct compression formulations and can experience shorter shelf life.

An excipient can contribute to the tablet's stability. Here, it is important to consider the physical, mechanical and chemical properties of the excipient as these factors can impact various formulation parameters related to the stability of the API, like disintegration, dissolution and shelf life of the final product.

A non-hygroscopic excipient, for example, prevents the tablet from absorbing moisture (by creating a moisture barrier), protecting the active ingredient. This is especially beneficial for APIs that are moisture sensitive.

Once the right excipient has been determined for the formulation, it must also demonstrate no physical or chemical instabilities. An excipient that exhibits quality control and consistency in performance is essential for ensuring a robust and stable formulation.

> "A non-hygroscopic excipient positively influences the stability of a tablet because it does not absorb moisture from the environment."

Rapid disintegration and dissolution

Fast tablet disintegration in the body is critical for ensuring that the active ingredient is released quickly to treat the patient.

The disintegration and dissolution profile of the tablet must also remain the same from batch to batch to ensure each tablet elicits the same effect.

Disintegration and dissolution of the dosage form, and the active ingredient, is greatly influenced by the excipient choice.

An excipient that is fast dissolving in water and compatible with all tablet shapes helps to support drug release in the body. Generally, accelerated dissolution is observed for tablets based on spray-dried materials compared to those containing a granulated direct compression excipient.

> “**Disintegration** and **dissolution** is greatly influenced by the excipient choice.”

A direct compression excipient should possess the following:

Technical properties

- Compressible and free-flowing
- Compactable
- High density
- Water-soluble
- High dilution potential
- Non-hygroscopic
- Chemically inert

Nutritional characteristics

- Sweetness
- Cooling effect
- Non-cariogenic
- Good gastrointestinal tolerance

Unlock your next formulation with mannitol

Direct compressional mannitol is a superior excipient with distinct advantages, such as excellent compatibility, compactability and higher intrinsic dissolution rate compared to other binder-fillers. It is also considered compatible with almost all drugs, is an inert substance, demonstrates high stability properties and produces a semi-sweet, smooth, cool taste (aligned with patient compliance).

Interestingly, mannitol is also the only excipient offering two opposite properties:

- In aqueous solution: high solubility, up to 18 g/100 mL at 20°C
- In powder form: very low hygroscopicity, does not adsorb water at 20°C up to 96% relative humidity.

This means it allows fast disintegration, even in the hardest tablets and offers moisture control for moisture-sensitive actives.

To date, numerous commercial grades of mannitol have been produced by different manufacturers to deal with the various demands related to tablet manufacturing. Spray-dried mannitol powders, in particular, have been used successfully for a long time.

> “Mannitol can help you **simplify the production of your tablets** via direct compression, **without compromising performance**.”

Introducing

PEARLITOL® SD

A mannitol you can rely on every time

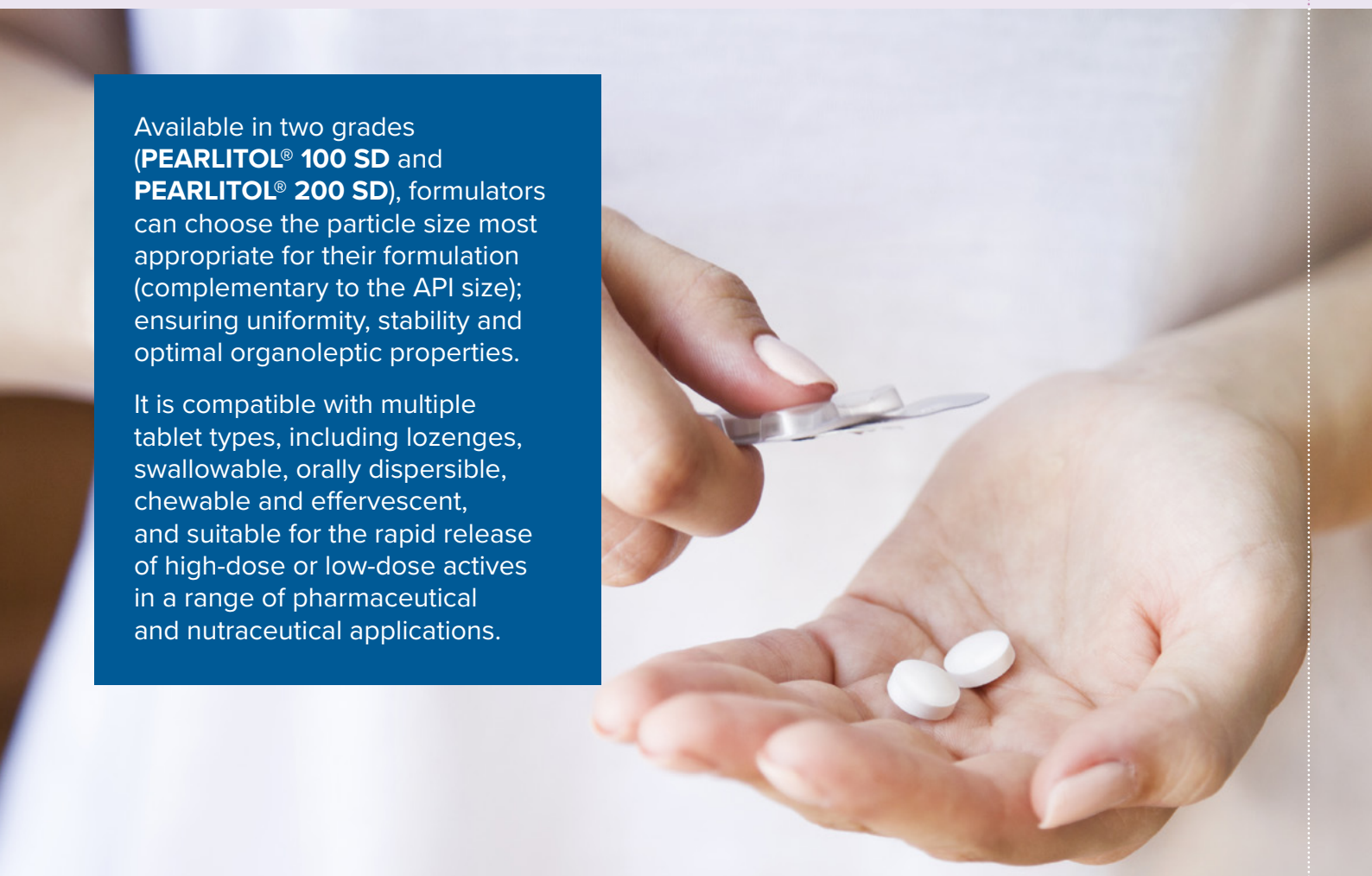
PEARLITOL® SD is an easy-to-use, spray-dried mannitol with superior, consistent performance. Designed for direct compression, it offers all of the benefits of mannitol, and more.

The excipient's **outstanding functional properties** enable compression of the most challenging and unstable formulations **without compromising** tablet quality.

This allows the creation of robust, high-quality tablets without the need for additives. PEARLITOL® SD also operates on a much wider range of compression forces allowing formulators to adjust manufacturing parameters to compensate formulation performance fluctuation.

Available in two grades (**PEARLITOL® 100 SD** and **PEARLITOL® 200 SD**), formulators can choose the particle size most appropriate for their formulation (complementary to the API size); ensuring uniformity, stability and optimal organoleptic properties.

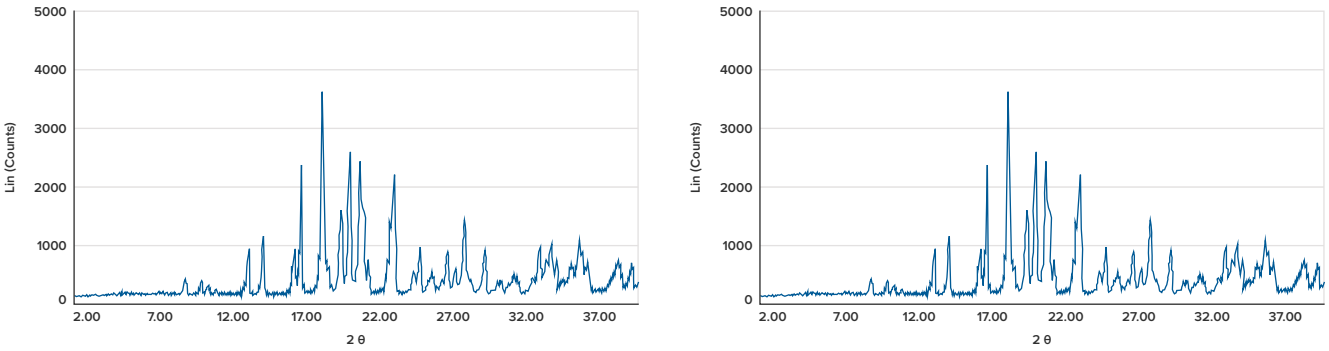
It is compatible with multiple tablet types, including lozenges, swallowable, orally dispersible, chewable and effervescent, and suitable for the rapid release of high-dose or low-dose actives in a range of pharmaceutical and nutraceutical applications.



The PEARLITOL® SD difference

Consistent quality

PEARLITOL® SD is remarkably stable by nature, ensuring stability whatever the formulation or manufacturing process. It promises tablet robustness and quality – with no evolution of the formulation – even at high temperatures.

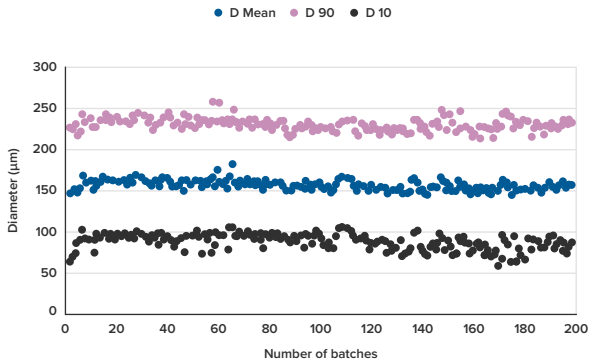


X-Ray diffraction of PEARLITOL® 200SD before and after heating 8 hours at 140°C.
PEARLITOL® SD is made of a high purity, stable polymorph that ensures no evolution of the formulation.

Superior, reliable functionality

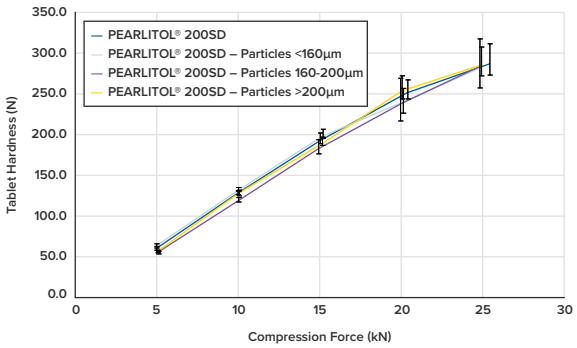
PEARLITOL® SD offers exceptional compactability and hardness. Its compactability has been optimized via spray drying to control particle size – ensuring a reproducible product and high-performance batch after batch.

This boosts productivity, guaranteeing reliable dosing and performance of each and every tablet. In addition, the tableting properties do not change after long-term storage, i.e. no evolution of compactability is observed.



Spray drying ensures control of the particle size for a consistent, high-performance product.

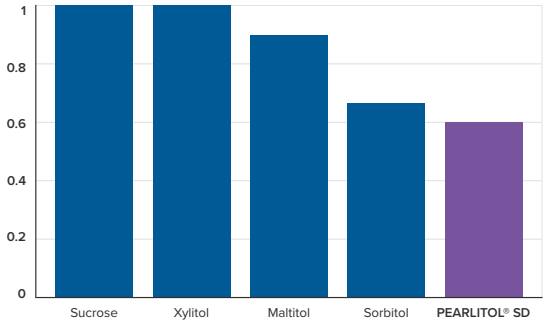
KORSCH XP1, 10 mm diameter flat tablet, 420 mg tablet weight, 1.2 % magnesium stearate



Comparison of the tabletability of PEARLITOL® 200SD to particle size cuts. Minor variations in PEARLITOL® SD's particle size has no impact on compression behavior, therefore delivering adequate formulation robustness and tablet hardness.

Patient-friendly formulation

With excellent non-cariogenic and sugar-free attributes, PEARLITOL® SD improves the organoleptic properties of tablets by bringing taste masking, natural sweetness and a cooling effect to formulations. This makes it suitable for pharmaceuticals addressing all types of patient populations, including pediatric patients, and also means it helps to optimize drug compliance.

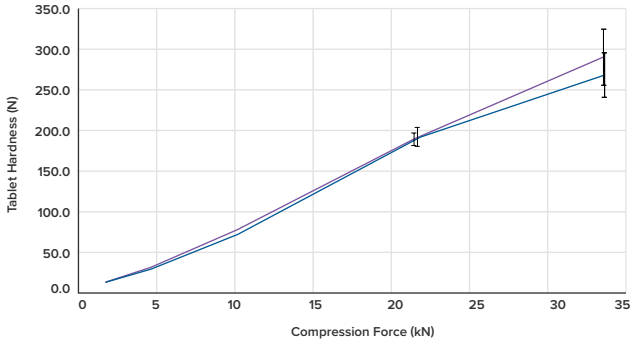


Sweetness index of PEARLITOL® SD compared to other polyols.

Cost savings

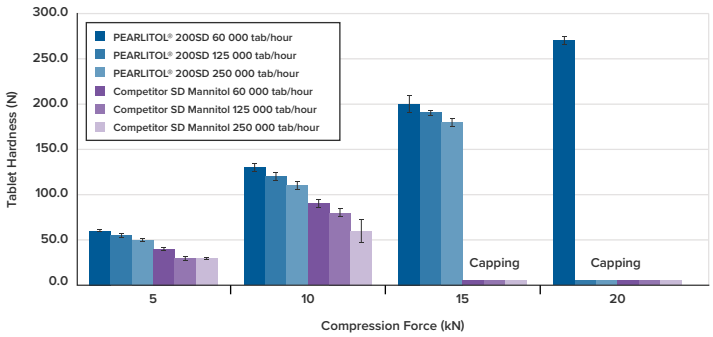
The excipient's broad-spectrum compatibility with tablet shape and processes enables faster formulation development. Low speed sensitivity and improved compressibility maximizes productivity, thus lowering maintenance costs and saving energy. As such, manufacturers are able to achieve the same tablet hardness with 30% less energy consumption when compared to competitor mannitol products.

STYLCAM compression simulator, 0.6% magnesium stearate, D 11.28 flat punch, 400 mg tablet weight



Compression was tested on equipment simulating a high-speed rotary press. Comparison of the tabletability of PEARLITOL® 200SD at 100,000 tablets/hour (green curve) and 200,000 tablets/hour (grey curve). Low speed sensitivity with PEARLITOL® maximizes productivity and results in cost savings.

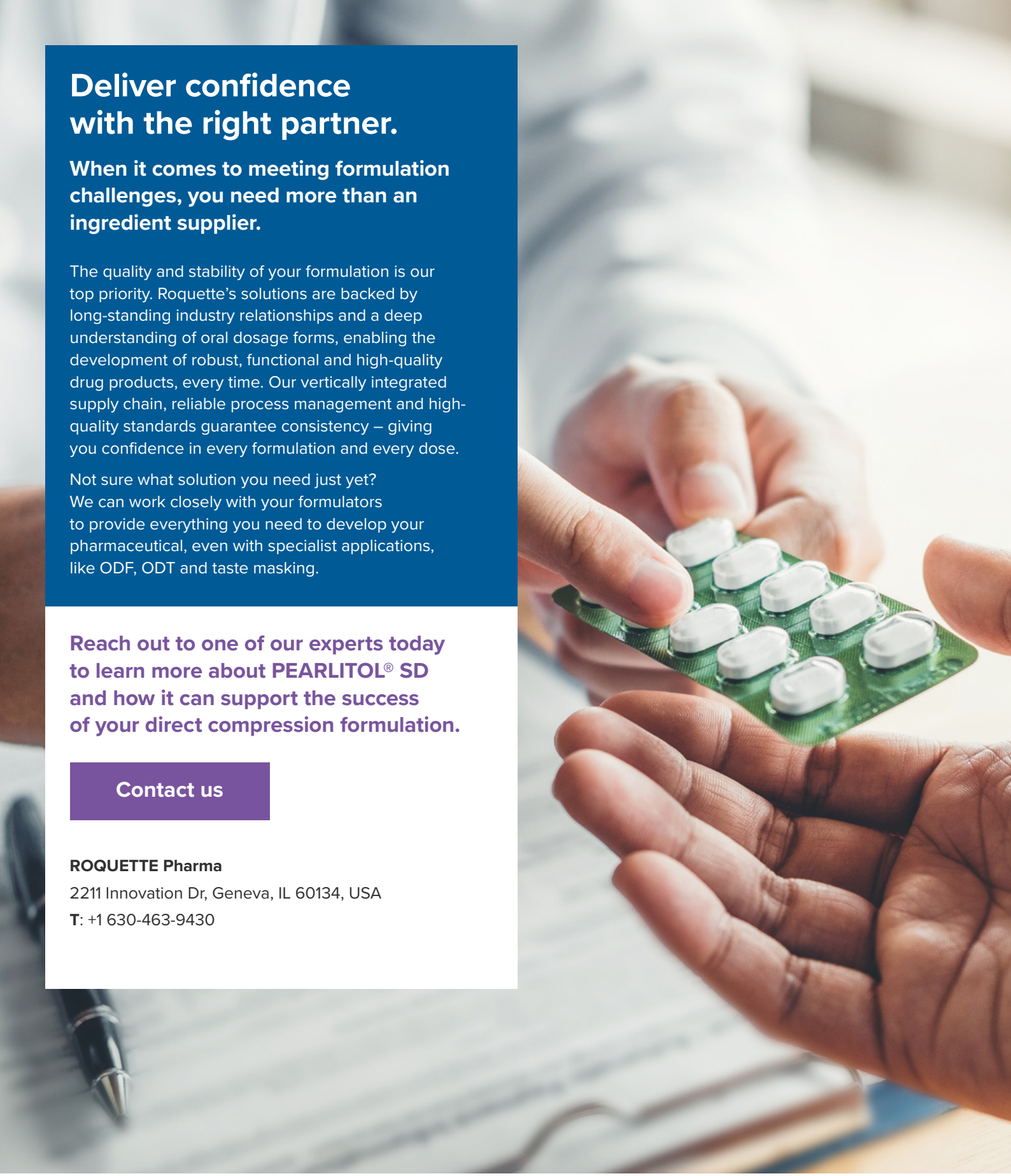
PEARLITOL® 200SD and competitor mannitol with 1.2% of MgSt - D10R9 concave punch



Tabletability of PEARLITOL® 200SD versus competitor spray-dried mannitol. PEARLITOL® SD is superior to competitor mannitol – enabling greater tablet hardness, even at increased speeds.

Technical and formulation support

PEARLITOL® SD is underpinned by Roquette's extensive expertise and technical know-how in solid oral dosage formulations, and 40 years' experience supplying industry-leading, plant-based excipients and raw materials that can be tailored to your pharmaceutical. Plus, PEARLITOL® SD is QbD-backed, with usage-specific documentation to support qualification and registration processes.



Deliver confidence with the right partner.

When it comes to meeting formulation challenges, you need more than an ingredient supplier.

The quality and stability of your formulation is our top priority. Roquette's solutions are backed by long-standing industry relationships and a deep understanding of oral dosage forms, enabling the development of robust, functional and high-quality drug products, every time. Our vertically integrated supply chain, reliable process management and high-quality standards guarantee consistency – giving you confidence in every formulation and every dose.

Not sure what solution you need just yet? We can work closely with your formulators to provide everything you need to develop your pharmaceutical, even with specialist applications, like ODF, ODT and taste masking.

Reach out to one of our experts today to learn more about PEARLITOL® SD and how it can support the success of your direct compression formulation.

Contact us

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