

The unique position of DFE Pharma Lactose



MCC

Starch

Lactose

Inhalation

Superdisintegrants

The pursuit of excipient excellence

We are DFE Pharma



We are the global leader in excipient solutions. We develop, produce and market excipients for oral solid dose and dry powder inhalation formulations. Our customers are pharmaceutical companies, operating globally, regionally and locally.

The pursuit of excipient excellence

Excipient excellence is a pursuit that will never be fully achieved. What is excellent today will be outdated tomorrow. That's why to us the pursuit of excipient excellence is a way of life. A source of inspiration. Excipient excellence is what guides us on our way to developing and producing the best possible excipient solutions for our customers. Today, tomorrow, always.

• **Leading in expertise**

We are here to help you create pharmaceutical products that set the new standard.

• **Leading in supply**

We are here to ensure you can always produce your products. No matter what happens.

• **Leading in time to market**

We are here to help you grow by minimising the time to market.

We invite you to join us in our pursuit of excipient excellence.

Pursuit 'the act of striving towards an ideal with strong determination.'

Lactose

Your Lactose by DFE Pharma

Our lactose has been used as an excipient for more than a century. Because of its versatility, it is the backbone of many successful formulations. We can supply it to you from multiple production sites around the globe. In any quantity, and always with the same consistent high quality. That's why we are the global market leader: a truly unique position.

We have been producing pharmaceutical lactose for over 100 years. As we control the complete supply chain – from meadow to final delivery – we can guarantee that our products are of exceptionally high quality. Our dedicated production sites in Europe and New Zealand enable us to ensure continuity of supply, even during extreme market situations.

DFE Pharma assures you a continuous supply of the best lactose excipients and associated services available. In order to meet your current and future expectations we continuously invest in improving our quality standards and production technologies. Our staff specialises in providing extensive technical support and developing innovative solutions to meet your specific challenges.

DFE Pharma supplies more than 30 pharmaceutical lactose grades off the shelf from multiple production sites. In addition, we develop customised products to meet your specific requirements. To simplify the selection of your lactose grade, we have created three product ranges:

> KEY RANGE

A selection of highly consistent lactose products suitable for most of your Oral Solid Dose Form (OSDF) applications. These grades are part of a formulator's first choice during the start of a new OSDF project. This range includes milled, sieved and direct compression products (spray-dried, granulated and anhydrous lactose grades).

>> SPECIALTY RANGE

A unique, broad range of milled and sieved lactose products with specific particle size distributions, accompanied by direct compression lactose products that provide unique functional properties helping you in your application.

>>> CUSTOMISED RANGE

A fully customised lactose product to meet your specific needs mutually developed in the shortest possible time.

Applications & product groups

Pharmaceutical lactose is used in a wide variety of Oral Solid Dosage Forms such as tablets, capsules, sachets, pellets and others, as well as in applications such as dry powder inhalers. The type of pharmaceutical product, and the associated process used to make that product, mainly determines the selection of the appropriate type of lactose. Within the DFE Pharma key- and specialty range you will find a lactose excipient for your application.

Pharmaceutical lactose is made by crystallisation and drying, followed by secondary processing to create the variety of products available. A brief description of the different types of pharmaceutical lactose is found below.

To assist you in finding the best type of lactose for your application we can also offer you the product finder at www.dfepharma.com/productfinder. To find out more about the chemistry and functionality of lactose please visit the knowledge base on our website.

Sieved lactose

Pharmaceutical α -lactose monohydrate is sieved to produce relatively narrow size distributions. The products flow well and are therefore typically used in applications such as sachet filling, capsule formulations and direct compression where good flow is of key importance. In direct compression, sieved lactose is used to improve the flow of the formulation mix in conjunction with direct compression lactose to impart good compaction properties. DFE Pharma offers sieved lactose under the product names Lactochem[®] and Pharmatose[®].

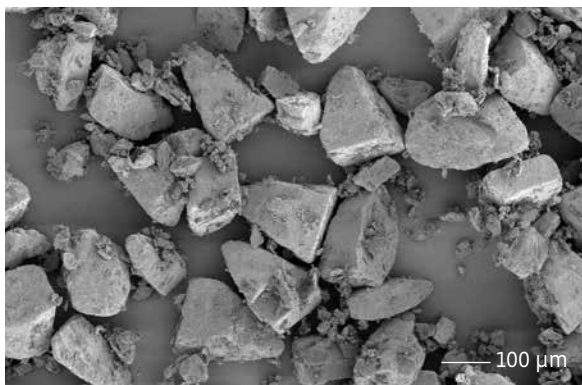


Figure 1: Sieved lactose.

Milled lactose

Pharmaceutical α -lactose monohydrate is mechanically milled to varying degrees of fineness. The available grades differ in their particle size distributions. Due to its fine nature, milled lactose tends to flow less well, but its relatively high surface area means that it is highly compactable. Milled lactose is therefore used primarily in wet granulation applications for tablets and capsules and for spheres made by extrusion-spheronisation. DFE Pharma offers milled lactose under the product names Lactochem[®] and Pharmatose[®].

Spray-dried lactose

Finely milled lactose monohydrate is suspended in water and spray-dried to give spherical agglomerates of crystalline lactose monohydrate in a matrix of amorphous lactose. The result is a product that both flows and compresses well. Spray-dried lactose is therefore very well suited to direct compression applications. DFE Pharma offers spray-dried lactose under the brand names Lactopress[®] Spray Dried and SuperTab[®] SD. Specialty range products offer improved functionality compared to the key range products.

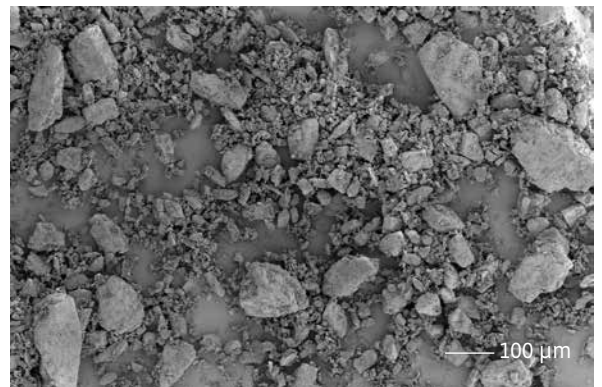


Figure 2: Milled lactose.

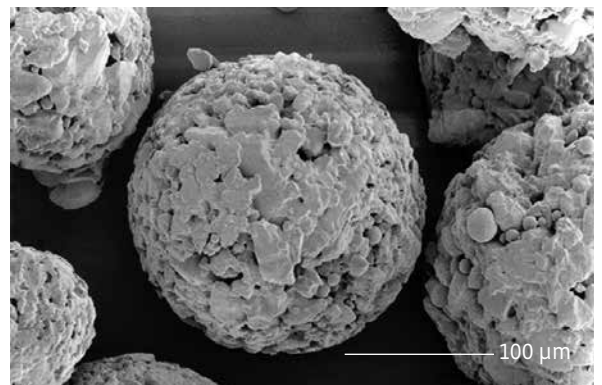


Figure 3: Spray-dried lactose.

Granulated Lactose

Milled lactose monohydrate is fluid bed processed to give agglomerates of lactose monohydrate. These agglomerates exhibit good flow and compaction properties and are therefore suitable in direct compression applications. In capsule formulations agglomerated lactose monohydrate forms strong plugs under the application of light compaction forces. In combination with its excellent flowability it is therefore the lactose monohydrate of choice for hard capsule formulations. DFE Pharma offers granulated lactose under the brand names Lactopress® Granulated and SuperTab® GR.

Anhydrous lactose

A solution of lactose is rapidly dried at high temperature to form anhydrous lactose which is then milled and sieved to the required particle size distribution. Anhydrous lactose offers the best compactability of all grades of lactose, and it is well suited to direct compression applications. Due to the absence of crystal water anhydrous lactose is also suitable in formulations containing moisture sensitive drugs. It is the recommended form of lactose for dry granulation because its brittle nature allows re-compaction without loss of tabletability. DFE Pharma offers anhydrous lactose under the brand names Lactopress® Anhydrous and SuperTab® AN. The specialty range products offer a selection of particle size distributions for improved flow or low dusting.

Micronised lactose

DFE Pharma is the only lactose supplier in the world that produces micronised lactose. Micronised lactose has extremely small particles (90% is less than 10 micron). The product is used to create a pre-blend with the API to prevent segregation.

What should I use?

Different formulations have different characteristics therefore there is not a single answer to this question.

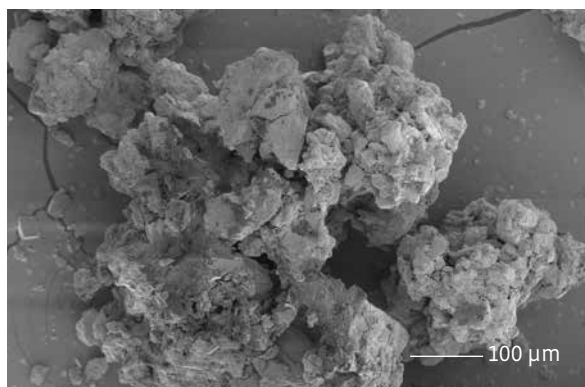


Figure 4: Granulated lactose.

However based on experience the following guideline can be used as a starting point:

	Tablets			Other solid dosage forms		
	Wet Granulation	Dry Granulation	Direct Compression	Capsules	Sachets	Spheres
Sieved lactose	o	o	+	+++	+++	o
Milled lactose	+++	+	o	+	o	+++
Spray-dried lactose	+	o	+++	++	+++	+
Granulated lactose	+	o	+++	+++	+++	+
Anhydrous lactose	+	+++	+++	+++	+	+

Dry granulation in this overview includes roller compaction and slugging. Spheres in this overview are made by extrusion spheronisation.

- +++ Highly recommended
- ++ Recommended
- + Possible but not recommended
- o Not advised

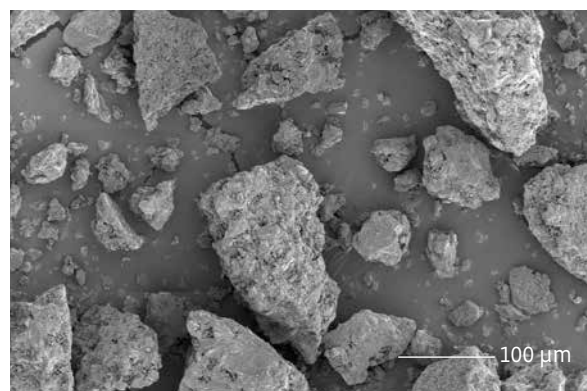


Figure 5: Anhydrous lactose.

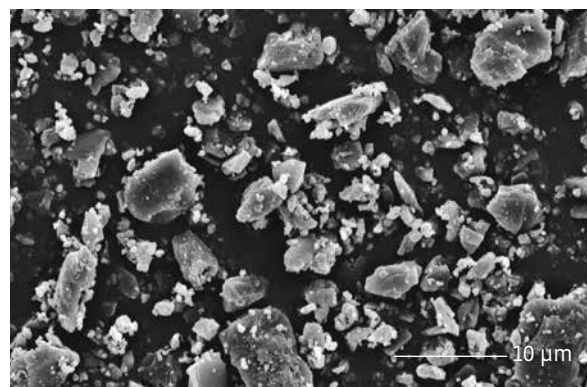


Figure 6: Micronised lactose.



DFE Pharma Key range

Our key range products are high quality lactose excipients for all common OSDF applications such as tablets, sachets and capsules. The key range includes milled, sieved and direct compression products. When starting a new OSDF project these lactose products are part of a formulator's first choice. Products with comparable specifications can usually be sourced from multiple DFE Pharma production locations.

Pharmacopoeia

All key range products comply with the latest editions of the USP-NF, Ph.Eur. and JP.

Packaging

DFE Pharma key range products are available in the standard size packaging as described in the table below. Other packaging options may be available upon request. Please contact us for options.

Product overview

	Form	Shelf life / standard packaging*	Production location
Lactochem® Crystals	Sieved	36 months / 25 kg paper bags	Borculo, the Netherlands
Pharmatose® 100M	Sieved	36 months / 25 kg paper bags	Veghel, the Netherlands
Lactochem® Fine Powder	Milled	36 months / 25 kg paper bags	Borculo, the Netherlands
Pharmatose® 200M	Milled	36 months / 25 kg paper bags	(EU) = Veghel, the Netherlands (NZ) = Kapuni, New Zealand
Lactopress® Spray Dried 250	Spray-dried	18 months / 25 kg carton box	Borculo, the Netherlands
SuperTab® 11SD	Spray-dried	(EU) = 24 months / 40 kg HDPE drum (NZ) = 24 months / 30 kg carton box	(EU) = Nörten-Hardenberg, Germany (NZ) = Kapuni, New Zealand
Lactopress® Granulated	Granulated	36 months / 25 kg paper bag	Nörten-Hardenberg, Germany
SuperTab® 30GR	Granulated	36 months / 40 kg HDPE drum	Nörten-Hardenberg, Germany
Lactopress® Anhydrous	Anhydrous	24 months / 25 kg carton box	Borculo, the Netherlands
SuperTab® 21AN	Anhydrous	24 months / 50 kg HDPE drum	Nörten-Hardenberg, Germany

*All standard packaging include polyethylene inner liners.

KEY RANGE

SPECIALTY RANGE

CUSTOMISED RANGE

DFE Pharma Specialty range

Specialty range products have been produced and supplied by DFE Pharma for many years with an excellent track record in quality and consistency.

Our specialty grades offer extra choices compared to the key range products. The number of milled and sieved lactose products represents the broadest range of particle size distributions available anywhere. You can find your best fitting product using the grade finder tool on our website (www.dfepharma.com/gradefinder). The direct compression products within this range have been developed with different functional properties compared to the key range products. They provide extra functionality to help in your formulation. SuperTab® 22AN, for example, provides additional functionality with superior flowability. Some further examples are detailed below.

A full overview of our specialty range products can be found in the overview table in this brochure. Please also visit our website for more information or contact your sales representative for the selection of the most suitable grade for your application!

Examples

Lactochem® Regular Powder Low Endotoxin

For formulations with defined requirements around endotoxin levels, finding the right lactose can be a challenge. Lactochem® Regular Powder Low Endotoxin will provide you comfort that endotoxin levels are minimised. Special selection and processing has been implemented creating extra controls to achieve the security of low endotoxin levels.

SuperTab® 24AN

We proudly introduce to you our latest specialty grade: SuperTab® 24AN, agglomerated anhydrous lactose. This unique product combines the benefits of granulated and anhydrous lactose resulting in our best directly compressible lactose product made to date. For a full list of functional advantages follow the link to the product website.



SuperTab® 14SD

SuperTab® 14SD combines unique high speed processing capabilities with extra compactability. The high surface area for bonding makes this product the best compactable direct compression lactose grade available.

Pharmacopoeia

All specialty range products comply with the latest editions of the USP-NF, Ph.Eur. and JP.

Packaging

DFE Pharma specialty range products are available in the standard size packaging. Other packaging options may be available upon request. Please contact us for options.

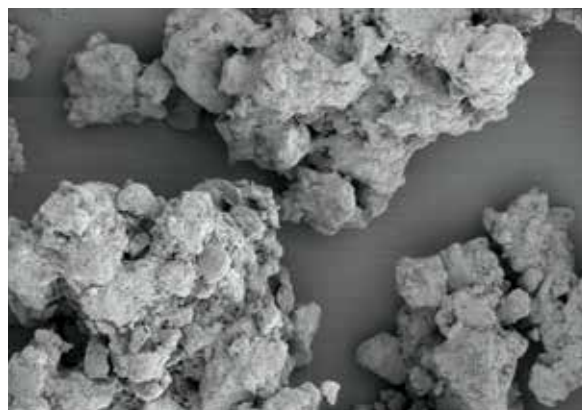


Figure 7: SuperTab® 24AN.

KEY RANGE

SPECIALTY RANGE

>>> CUSTOMISED RANGE

DFE Pharma Customised range

The DFE Pharma customised range is not a real product range, but rather a well defined process. It is our way to develop new lactose products and services specifically for you. This encompasses any of your specifications, demands, production processes or applications that we currently are not able to meet.

The process is designed in such a way that based on mutual agreement and partnership milestones are set and products will become available. When you require a customised grade DFE Pharma will form a dedicated project team. At least your sales representative, the product manager and R&D manager will participate. You can expect exceptionally well trained people with a passion to deliver precisely what is needed to get your product(s) to the market. Our goal is to build a bridge between your application and our capabilities.

The DFE Pharma steps for a successful customisation project are:

Initiation phase

During this phase all your specific needs for this customisation project are described and verified with our capabilities. This will already involve extensive communication between our respective departments. We will move to the next phase when we have a joint fit.

Development phase

A dedicated project team will initiate small scale development to meet your needs. You will receive development product for your internal evaluation. This phase may include multiple steps to achieve the desired result. After your approval we will move to the upscaling phase.

Upscaling phase

The development product is handed over to our Process Development Department for large scale production trials. You will assess if this trial product still meets your requirements. Small adjustments based on your evaluation can still be incorporated in this phase.

Validation phase

In this phase, the manufacturing process is validated according to our internal procedures based on cGMP standards. Upon successful completion of our validation and clearance of this product, you can use it for your commercial production.

Commercial phase

The new lactose product is embedded in our regular organisation and will be supplied according to the agreed conditions.

Customised range process

Initiation phase	Development phase	Upscaling phase	Validation phase	Commercial phase
<ul style="list-style-type: none"> Understanding your requirements Verification of our capabilities Mutual agreement on process 	<ul style="list-style-type: none"> Set up project team Small scale development Your evaluation Feedback loops Approval 	<ul style="list-style-type: none"> Transfer to Process Development Large scale trial Your evaluation Feedback loops Final approval 	<ul style="list-style-type: none"> Validation Clearance Project end 	<ul style="list-style-type: none"> Product is available for your future demands

Overview of all DFE Pharma lactose OSDF grades

Please find below an overview of all DFE pharmaceutical lactose products.

Grade	Key / Special	Sieved	Milled	Spray-dried	Granulated	Anhydrous	Direct compression	Wet granulation	Dry granulation	Capsules	Sachets	Spheres
Lactochem® Crystals	K	x								x	x	
Pharmatose® 100M	K	x								x	x	
Lactochem® Fine Powder	K		x					x				x
Pharmatose® 200M	K		x					x				x
Lactopress® Spray Dried 250	K			x			x			x	x	
SuperTab® 11SD	K			x			x			x	x	
Lactopress® Granulated	K				x		x			x	x	
SuperTab® 30GR	K				x		x			x	x	
SuperTab® 21 AN	K					x	x		x	x		
Lactochem® Coarse Crystals	S	x								x	x	
Lactochem® Fine Crystals	S	x								x	x	
Lactochem® Extra Fine Crystals	S	x								x	x	
Pharmatose® 50M	S	x								x	x	
Pharmatose® 60M	S	x								x	x	
Pharmatose® 70M	S	x								x	x	
Pharmatose® 80M	S	x								x	x	
Pharmatose® 90M	S	x								x	x	
Pharmatose® 110M	S	x								x	x	
Pharmatose® 125M	S	x								x	x	
Lactochem® Coarse Powder	S		x					x				x
Lactochem® Regular Powder	S		x					x				x
Lactochem® Powder	S		x					x				x
Lactochem® Extra Fine Powder	S		x					x				x
Lactochem® Super Fine Powder	S		x					x				x
Pharmatose® 130M	S		x					x				x
Pharmatose® 150M	S		x					x				x
Pharmatose® 350M	S		x					x				x
Pharmatose® 450M	S		x					x				x
Lactopress® Spray Dried	S			x			x			x	x	
SuperTab® 14SD	S			x			x			x	x	
Lactopress® Anhydrous	S					x	x		x	x		
Lactopress® Anhydrous Powder	S					x	x		x			
Lactopress® Anhydrous Fine Powder	S					x	x		x			
SuperTab® 22 AN	S					x	x		x	x		
SuperTab® 24 AN	S					x	x		x	x		
Lactochem® Regular Powder Low Endotoxin	S						x	x				



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DMV-Fonterra Excipients GmbH & Co. KG - Warranty

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