STARLAC

TABLETING →
DIRECT COMPRESSION →
CO-PROCESSED LACTOSE

Technical brochure
StarLac®

MEGGLE

MEGGLE's co-processed lactose grades for direct compression: StarLac®

General information

Direct compression (DC) tablet manufacture is a popular choice because it provides the least complex, most cost effective process to produce tablets compared to other tablet manufacturing approaches. Manufacturers can blend APIs with excipients and compress, making dosage forms simple to produce [1, 2].

DC technology and the use of modern tableting equipment require that excipients and APIs form a compactable mixture with excellent flowability and low particle segregation tendency [3].

In the pharmaceutical industry, lactose is one of the most commonly used excipients; however, like many other excipients, lactose may not be suitable for direct compression without modification due to insufficient powder flow or/and compaction properties **(figure 1)**.

Product description

Alpha-lactose monohydrate and maize starch (corn starch) are functional excipients used in oral solid dosage forms. Both are naturally derived and well established in the pharmaceutical industry. Lactose is frequently used as a diluent or direct compression binder. Starch can be used as a binder for wet or dry applications, disintegrant, and diluent. In an effort to establish synergistic functional performance, such as enhanced compactibility and faster tablet disintegration, lactose and starch were co-spray-dried to form a monoparticulate system. StarLac® comprises 85 % alpha-lactose monohydrate and 15 % native maize starch. StarLac® provides compaction and lubricant insensitivity characteristics desired for direct compression, and the hydration properties desired for rapid API release. Additionally, StarLac®'s flowability is superior compared to a physical blend of the individual components in equivalent ratio.

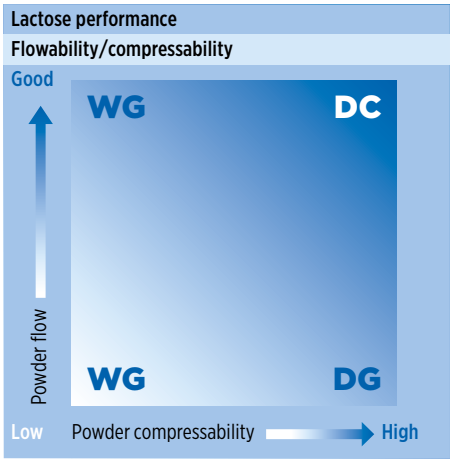


Figure 1: *Powder blend compressability and flowability requirements for various tableting technologies (DC is direct compression, WG is wet granulation, DG is dry granulation) [3].*

Regulatory & quality information

The raw materials used to produce StarLac®, alpha-lactose monohydrate and maize starch, comply with Ph. Eur., USP-NF, and JP monograph requirements. Since no chemical modifications occur during co-processing, individual chemical identities are maintained. Therefore, StarLac® can be considered as a physical blend of alpha-lactose monohydrate and native maize starch [4].

A StarLac® drug master file (DMF) is available during FDA (Food and Drug Administration) drug product submission review and approval. The native maize starch used during StarLac® manufacture is GMO-free (genetically modified organism) and gluten-free. Specifications and regulatory documents can be downloaded from www.meggle-pharma.com.

Our pharma-dedicated production facility in Wasserburg, Germany is certified according to DIN ISO 9001:2015 and has implemented GMP according to the Joint IPEC-PQG (Good Manufacturing Practices Guide for Pharmaceutical Excipients) and USP-NF General Chapter <1078> GOOD MANUFACTURING PRACTICES FOR BULK PHARMACEUTICAL EXCIPIENTS. MEGGLE has been an EXCiPACT™-certified excipient manufacture and supplier since 2014.

The Wasserburg facility demonstrates MEGGLE's complete lactose production capability range, including sieving, milling, agglomeration, spray-drying, and co-processing. Additionally MEGGLE is a member of IPEC (International Pharmaceutical Excipients Council).

MEGGLE invests considerably in the sustainability of raw material sourcing, production standards, and efficiency. We are actively engaged in environmental protection. In order to guarantee the quality of our products, our commitment and adherence to established pharmaceutical standards remains is our highest priority.

Application

StarLac® has been specifically designed for direct compression and may be used in other formulation development approaches as well. In comparison to a physical blend of the individual components, StarLac® provides superior flow, improved compactibilty, decreased lubricant sensitivity, and hardness-independent tablet disintegration. As StarLac® possesses brittle and plastic deformation characteristics, it also can be used in dry granulation formulations.

- Direct compression
- ODT formulations
- Dry granulation (Roller compaction, slugging)

BENEFITS

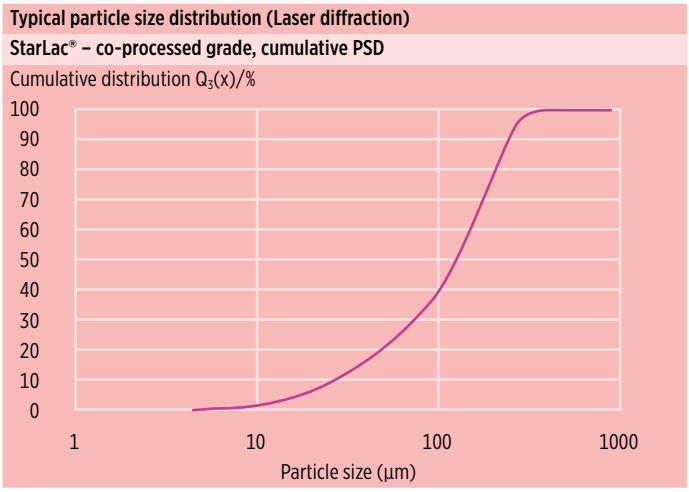
StarLac®

- Excellent compactibility
- Excellent flowability
- Rapid, hardness-independent tablet disintegration
- Compaction and hydration properties do not dendent on hydrophobic lubricant type or level

Particle size distribution (PSD)

Figure 2 shows typical laser diffraction particle size distribution data for StarLac®. StarLac® possesses a narrow PSD that supports homogenous powder blend preparation, essential for achieving good tablet quality.

Figure 3 depicts the specified PSD range and typical average values by air-jet sieving. These parameters are constantly monitored through in-process control (IPC) testing and are part of the StarLac® particle size distribution specification.



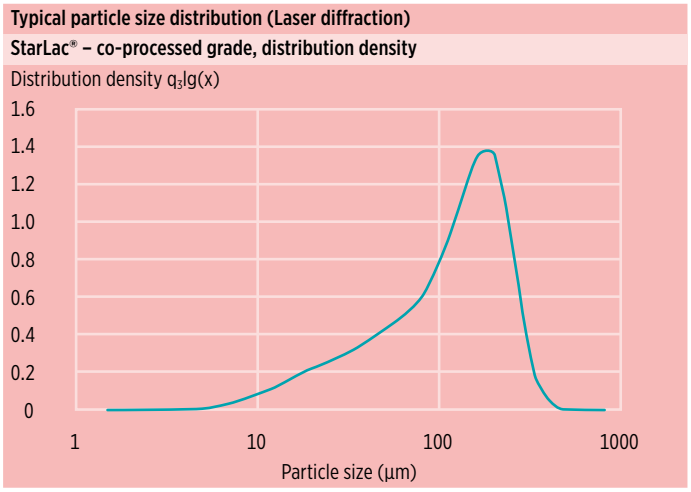


Figure 2: *Typical cumulative PSD and distribution density of MEGGLE's StarLac®. Analyzed by Sympatec®/Helos & Rodos particle size analyzer.*

Sieve data – co-processed lactose		
	Lactose type	**StarLac®**
		specified/typical
Particle size distribution	< 32 µm	**NMT 15 %**/ 6 %
Method: Air-jet sieving	< 160 µm	**35–65 %**/49 %
	< 250 µm	**NLT 80 %**/90 %
	< 315 µm	/99 %

Figure 3: *Specified PSDs for StarLac® by air-jet sieving in bold letters. Typical values obtained from a permanent in-process control are shown for information.*

Batch-to-batch consistency

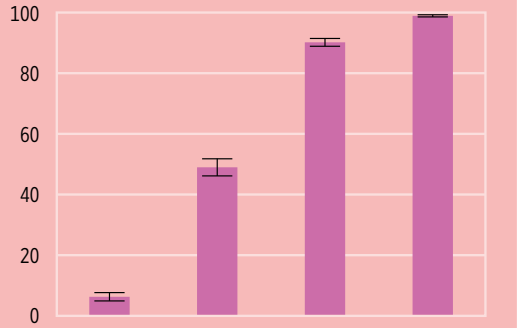
Batch-to-batch consistency for all lactose products can be attributed to MEGGLE's long history and experience in lactose manufacture, and broad technical expertise. Constant in-process and final product testing ensures consistency and quality **(figure 4)**.

Isotherms

StarLac® exhibits moderate moisture uptake under high relative humidity conditions due to the starch influence on the observed equilibrium moisture content **(figure 5)**.

Batch-to-batch consistency – particle size distribution – co-processed lactose

StarLac®



Particle size (µm)	< 32	< 160	< 250	< 315
Specified	NMT 15 %	35 – 65 %	NLT 80 %	
Mean IPC value (%)	6.1	48.9	90.3	99.0
SD (%)	1.4	2.8	1.3	0.5

Figure 4: *StarLac®'s consitent particle size distribution (by air-jet sieve analysis) illustrated by low batch-to-batch variability. Data obtained from a permanent in-process control (IPC) of subsequent batches over 12 months.*

Sorption isotherm (Dynamic vapor sorption at 20 °C)

StarLac®

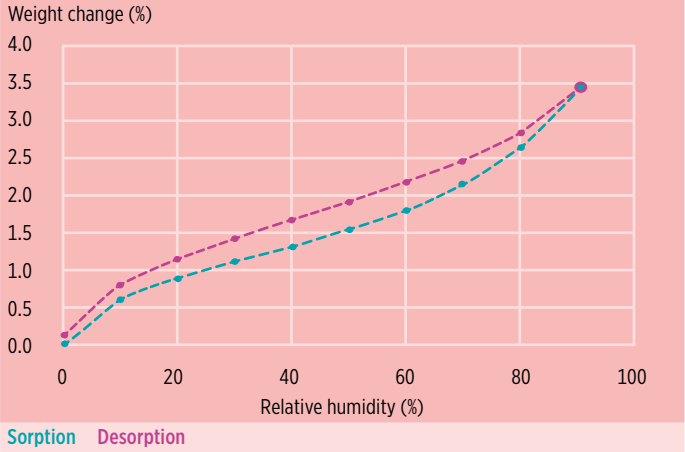


Figure 5: *Sorption-desorption isotherm (20 °C) of StarLac®, SPSx-1µ moisture sorption test system.*

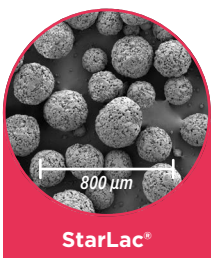


Figure 6: *SEM image of MEGGLE's StarLac® by ZEISS Ultra 55 FESEM (U = 5 kV; Au/Pd sputtered).*

Scanning electron micrograph (SEM)

StarLac® is nearly spherical in shape due to the co-spray-drying manufacturing process. StarLac®'s overall morphology reduces blend segregation and improves finished dosage form content uniformity **(figure 6)**.

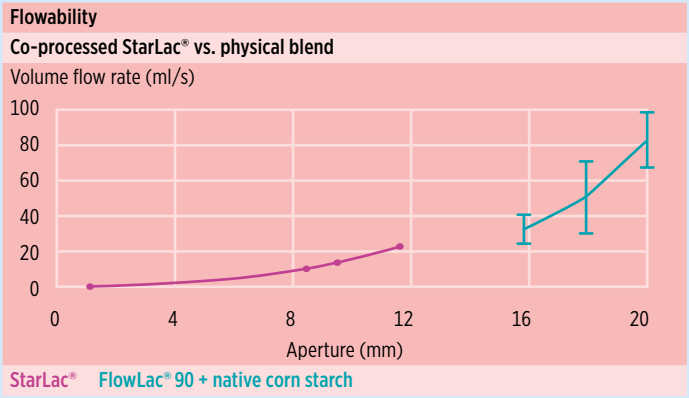


Figure 7: *Volume flow rate (ml/s) as a function of aperture size (mm diameter) for StarLac® and a comparable physical blend analyzed by a FlowRatex®.*

Functional related characteristics

Powder flow

In assessing powder flow using a FlowRatex® apparatus, StarLac® exhibited superior flowability compared to a physical blend made up of spray-dried lactose and maize starch. The simple blend of individual ingredients showed greater flow variation compared to StarLac® **(figure 7)**. StarLac® also possessed lower flowability index (StarLac® = 2 mm, physical blend = 16 mm), indicating superior flowability **(figure 8)**.

Flowability can also be described by the Hausner ratio, Carr's index, or angle of repose. A Hausner ratio below 1.25 or Carr's index below 20 indicates that powders are freely flowing. Angle of repose describes "good flowability" between 31–35°, and in general, worsens with steeper angles. **Figure 9** shows typical flowability indices for StarLac®, indicating excellent flowability.

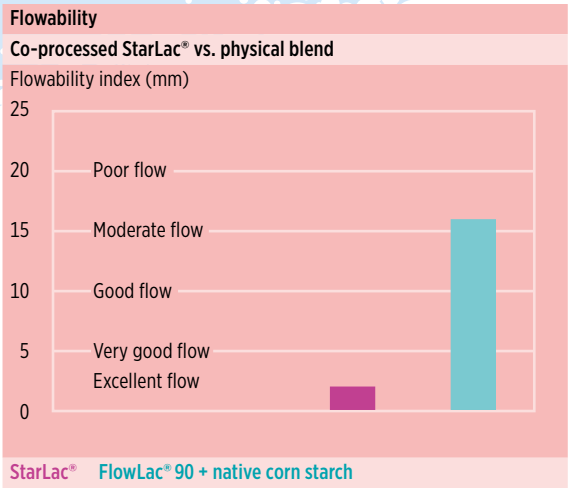


Figure 8: *Flowability index of StarLac® and its corresponding physical blend. Smaller values indicate better flowability.*

Flowability

StarLac® – co-processed lactose

	Angle of repose (°)	Density bulk (g/l)	Density tapped (g/l)	Hausner ratio	Carr's index (%)
StarLac®	29	540	670	1.24	19.40

Figure 9: *Flowability/processability related parameters of StarLac®. Pharmacopoeial methods (Ph. Eur.) were used.*

Compactibility and friability

StarLac® shows excellent compactability even at low to moderate compaction pressure **(figure 10)**. Low friability (< 1 %) is given **(figure 11)**, eliminating the need for a protective coating.

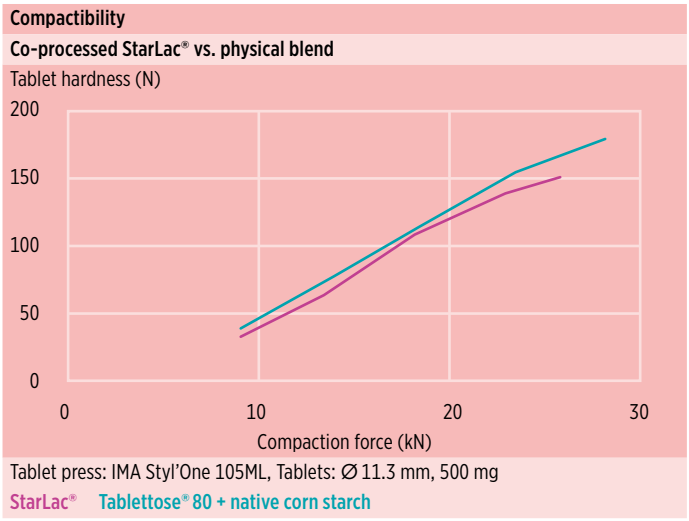


Figure 10: *Tablet hardness profile for StarLac® compared to a physical blend of the individual components. Tablets were produced using a tablet press: IMA Styl'One fittet with 11.3 mm punches. Average tablet weight was targeted at 500 mg.*

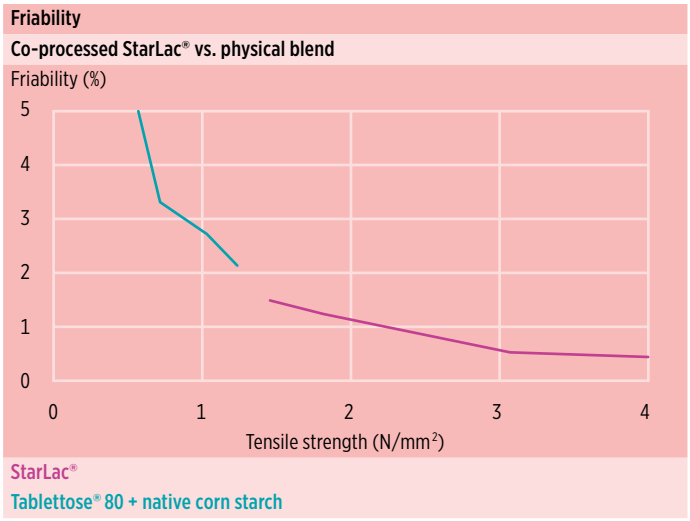


Figure 11: *Friability of tablets produced either with StarLac® or its corresponding physical blend.*

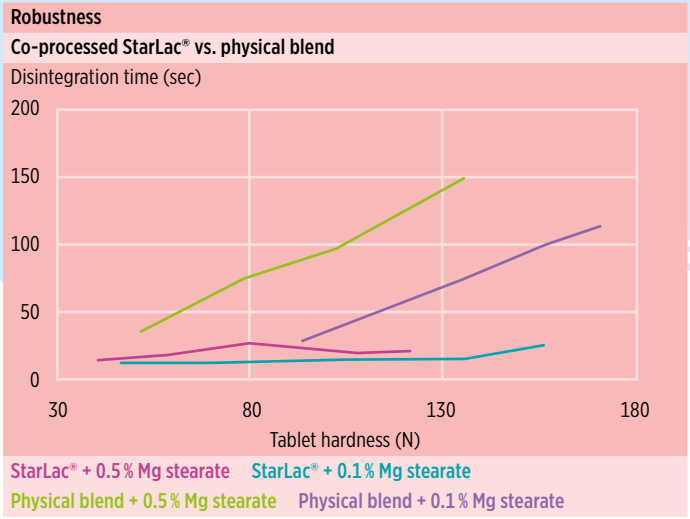


Figure 12: *Tablet disintegration profile showing StarLac® and its corresponding physical ad-mixture. Tablet hardness and lubricant level hardly impact disintegration time.*

Disintegration and Dissolution

Superior hydration characteristics make StarLac® ideal where rapid tablet disintegration is desired. In addition, StarLac® tablet disintegration is independent of lubricant level and tablet hardness. A physical blend comprising lactose and starch demonstrated significant lubricant sensitivity and tablet hardness dependency, by comparison **(figures 12 and 13)**. As a result of tablet disintegration data, follow-up studies revealed accelerated API dissolution when using StarLac® **(figure 14)**. The hardness independent and lubricant insensitivity exhibited by StarLac® also make it a candidate for orally disintegrating/dispersible tablet (ODT) applications.

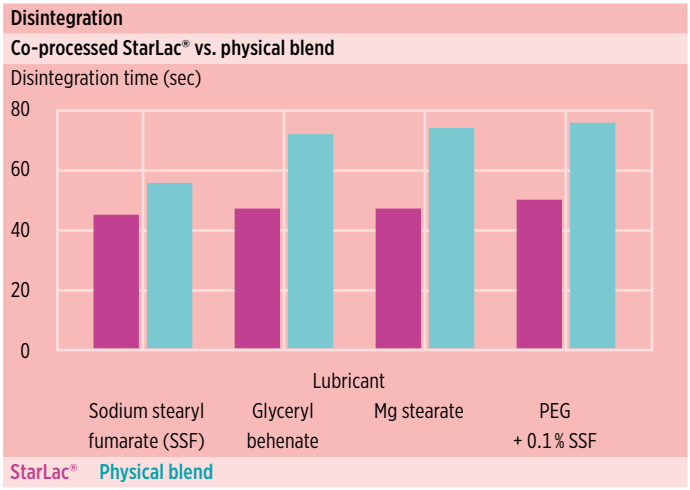


Figure 13: *Tablet disintegration time for tablets produced with StarLac® compared to a physical blend of the individual ingredients. Powders were lubricated to 0.5 % as shown.*

Packaging and shelf life

Packaging material complies with Regulation (EC) No.1935/2004 and 21 CFR 174, 175, 176, 177 and 178. Stability tests have been performed according to ICH guidelines and an ongoing stability program is implemented. **Figure 15** provides an overview about packaging size and material, and product shelf life.

Packaging and shelf life			
StarLac®			
	Size	**Material**	**Shelf life**
StarLac®	25 kg	Paper bag with PE-EVOH-PE inliner	36 Months

Figure 15: *Packaging and shelf life of MEGGLE's StarLac®.*

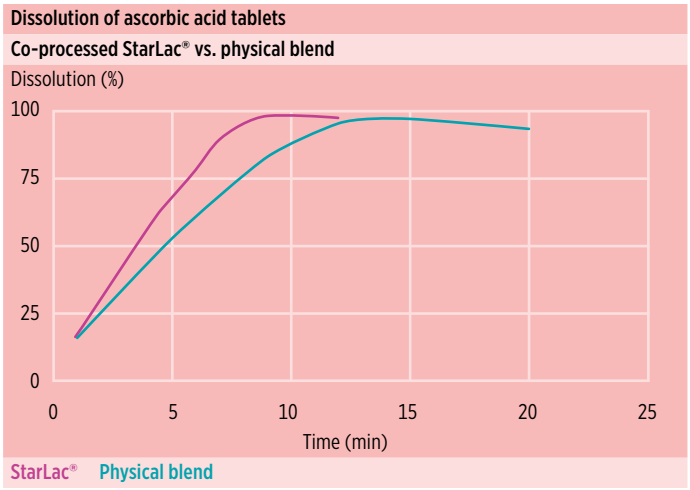


Figure 14: *Dissolution profiles for ascorbic acid formulations (30 % loading) produced with StarLac® compared to a physical blend.*

Literature

[1] Meeus, L. (2011). Direct Compression versus Granulation. Pharmaceutical Technology, 23(3).

[2] Kristensen, H. G., Schaefer, T. (1987). Granulation: A Review on Pharmaceutical Wet-Granulation. Drug Development and Industrial Pharmacy, 13(4–5), 803–872.

[3] Mîinea, L. A., Mehta, R., Kallam, M., Farina, J. A., Deorkar, N. (2011). Evaluation and Characteristics of a New Direct Compression Performance Excipient, 35(3).

[4] Guideline on Excipients in the Dossier for Application for Marketing Authorization of a Medicinal Product. EMEA/CHMP/QWP/396951/2006.

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