TABLETING →
DIRECT COMPRESSION →
ANHYDROUS LACTOSE

Technical brochure
DuraLac® H

MEGGLE
EXCIPIENTS & TECHNOLOGY

MEGGLE's anhydrous lactose grade for direct compression: DuraLac® H

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 compactible 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

DuraLac® H is produced by roller-drying a lactose solution at high temperature to form anhydrous beta-lactose and alpha-lactose crystals at levels approximating 80 % and 20 %, respectively. During anhydrous lactose crystallization, no water is incorporated in the crystal lattice [4]. Subsequent to roller-drying, anhydrous lactose is milled and sieved to the desired particle size distribution, optimizing powder flow and compactibility. DuraLac® H complies with the monograph „Lactose, anhydrous" (Ph. Eur., USP-NF and JP). Because DuraLac® H deforms by brittle fracture during compaction, it is well suited for directly compressed and dry granulated formulations (roller compaction, slugging).

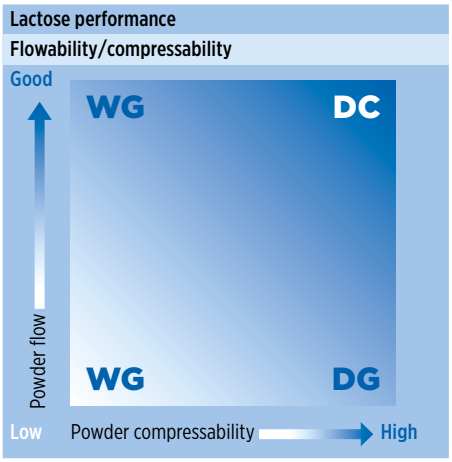


Figure 1: *Powder blend compressability and flowability requirements for various tableting technologies (DC is direct compression, WG is wet granulation, DG is dry granulation) [3].*

Regulatory & quality information

DuraLac® H is MEGGLE's trade name for anhydrous lactose and complies with the current harmonized USP-NF, Ph. Eur., and JP monographs. Specifications and regulatory documents can be downloaded from www.meggle-pharma.com.

MEGGLE's new state-of-the-art, pharma-dedicated production facility in Le Sueur, Minnesota complies with 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 manufacturer and supplier since 2014.

The US site in Le Sueur produces milled alpha-lactose monohydrate and anhydrous lactose to equivalent quality standards and provides the same documentation as the Wasserburg facility. 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.

international excipients certification

Application

DuraLac® H was developed especially for direct compression processes. The following chart provides recommended areas of applications.

- Low to medium dose DC formulations
- Dry granulation (Roller compaction, slugging)
- Capsule filling and sachets

BENEFITS

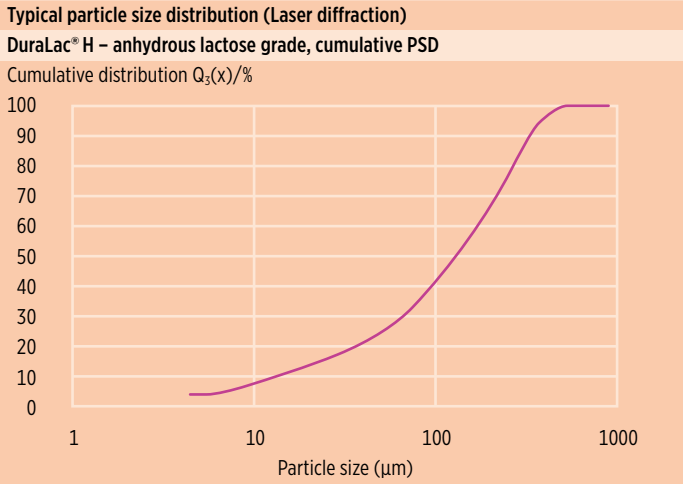
DuraLac® H

- Excellent compactibility
- Good flowability
- Relatively low hygroscopicity (water sorption above 70 % relative humidity)
- High storage stability
- Excipient of choice for formulations requiring low water content

Particle size distribution (PSD)

Figure 2 shows typical laser diffraction particle size distribution data for MEGGLE's anhydrous lactose grade, DuraLac® H.

Figure 3a and 3b depict specified PSD by air-jet sieving and Ro-Tap®. These paramters are also part of the in-process control (IPC).



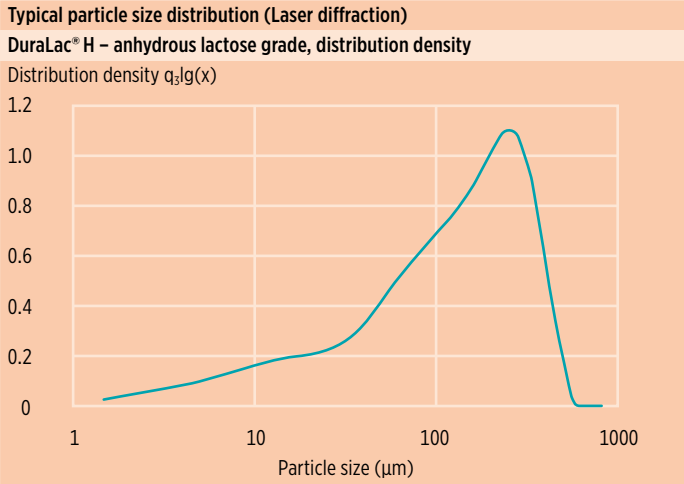


Figure 2: *Typical cumulative PSD and distribution density of DuraLac® H analyzed by Sympatec®/Helos & Rodos.*

Sieve data – anhydrous lactose		
	Lactose type	DuraLac® H
		specified/typical
Particle size distribution	< 45 µm	**NMT 20 %**/16 %
Method: Air-jet sieving	< 150 µm	**40–65 %**/54 %
	< 250 µm	**NLT 80 %**/83 %

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

Sieve data – anhydrous lactose		
	Lactose type	DuraLac® H
		specified/typical
Particle size distribution	< 75 µm	**20–35 %**/23 %
Method: Ro-Tap®	> 75 µm	**6–20 %**/14 %
	< 106 µm	**10–25 %**/15 %
	< 150 µm	**7–15 %**/11 %
	< 180 µm	**15–30 %**/20 %
	< 250 µm	**10–20 %**/17 %

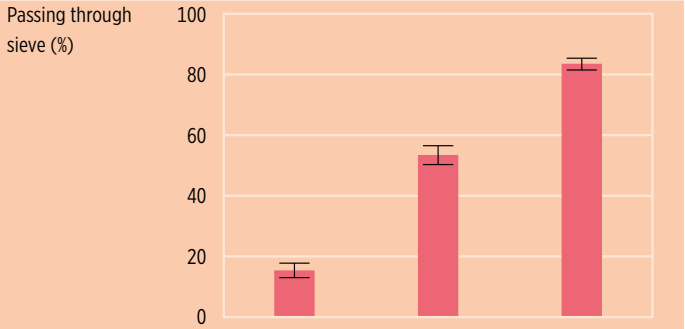
Figure 3b: *Specified PSDs for DuraLac® H by Ro-Tap® in bold letters. Typical values obtained from a permanent in-process control are shown for orientation.*

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)**.

Batch-to-batch consistency – particle size distribution – anhydrous lactose

DuraLac® H



Particle size (µm)	< 45	< 150	< 250
Specified	NMT 20 %	40 – 65 %	NLT 80 %
Mean IPC value (%)	15.5	54.0	83.4
SD (%)	2.5	3.2	1.9

Figure 4: *DuraLac® H provides a very consistent particle size distribution (by air-jet sieving), illustrated by low batch-to-batch variability. Data obtained from a permanent in-process control (IPC) of subsequent batches over 12 months.*

Isotherms

While pure, crystalline alpha-lactose monohydrate demonstrates equivalent equilibrium moisture content during absorption and desorption, anhydrous lactose demonstrates hysteresis, having different equilibrium moisture content upon absorption and desorption. The hysteresis is caused by the conversion of lactose from the anhydrous to hydrated form. Therefore, significant changes in relative humidity during storage should be avoided. DuraLac® H is protected from uncontrolled water uptake, by its aluminum packaging. Therefore, MEGGLE can assure at least 36 months of stability throughout storage (unopened package provided).

MEGGLE's anhydrous lactose grade, DuraLac® H, contains no water of crystallization. In addition, as illustrated in **figure 5** by a sorption isotherm (dynamic vapor sorption), anhydrous lactose is not hygroscopic and does not absorb water significantly even when relative humidity is increased to 70 % and above. This makes DuraLac® H the excipient of choice for low moisture formulation applications, especially when moisture-sensitve APIs need to be protected.

Sorption isotherm (Dynamic vapor sorption at 20 °C)

DuraLac® H

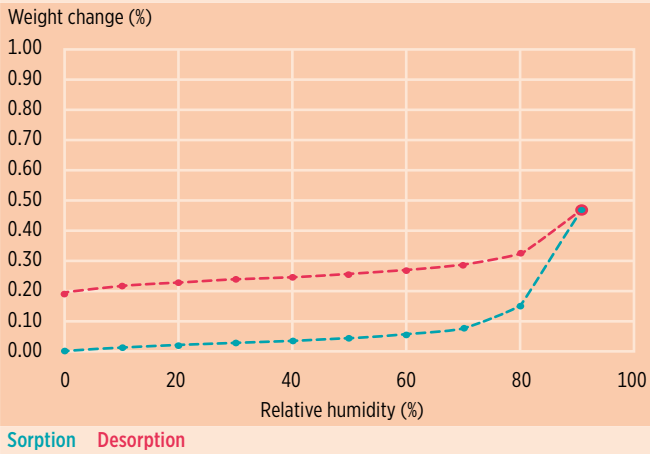


Figure 5: *Sorption-desorption isotherms (20 °C) of DuraLac® H. Analysis performed by SPSx-1µ moisture sorption test system.*

Scanning electron micrograph (SEM)

Lactose monohydrate and anhydrous lactose exhibit different morphology. Where lactose monohydrate products are defined typically by monoclinic spheroidal, "tomahawk-shaped" monocrystals, anhydrous lactose consists of micro-crystal clusters of beta- and alpha-lactose, both in the anhydrous form **(figure 6)**. This characteristic shape results from the roller-drying and milling processes.

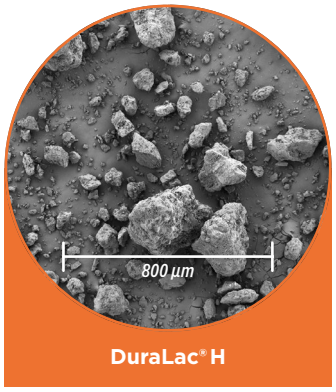


Figure 6: *SEM image of MEGGLE's DuraLac® H by ZEISS Ultra 55 FESEM (U = 5 kV; Au/Pd sputtered).*

Functional related characteristics

Powder flow

It is well-known that particle size and shape influence powder flowability. Particles smaller than 100 µm tend to be more cohesive and less freely flowing, whereas larger, denser particles tend to be more freely flowing. Particle morphology also significantly affects powder flow characteristics. Regarding flowability, **figure 7** demonstrates that particle shape and structure are more important than the particle size distribution. Due to its shape, the anhydrous lactose flowability is moderate, but improves significantly with lubricant and/or glidant addition.

Flowability can be described for example by the material's 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 values of 31–35° indicate "good flowability", and in general, worsens with steeper angles. **Figure 8** shows typical flowability indices for DuraLac® H, indicating its moderate flowability.

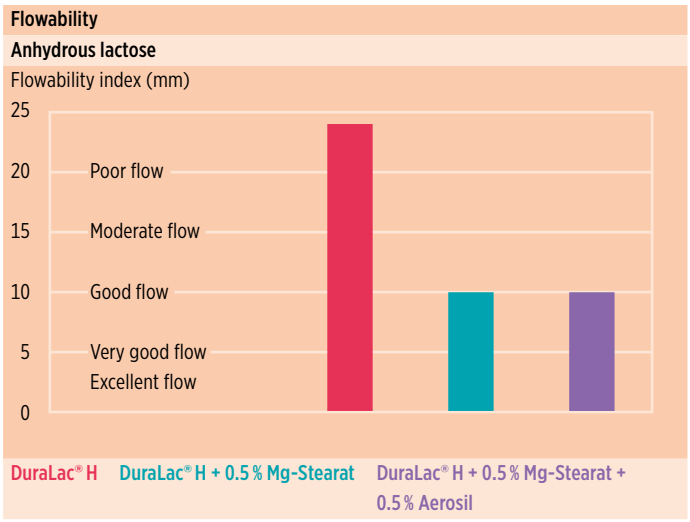


Figure 7: *Flowability index of DuraLac® H, and its mixture with Magnesium stearate or additionally Aerosil.*

Flowability

DuraLac® H – anhydrous lactose

	Angle of repose (°)	Density bulk (g/l)	Density tapped (g/l)	Hausner ratio	Carr's index (%)
DuraLac® H	42	670	880	1.31	23.86

Figure 8: *DuraLac®'s typical powder technological parameters, in order to characterize its flowability. Pharmacopoeial methods were used.*

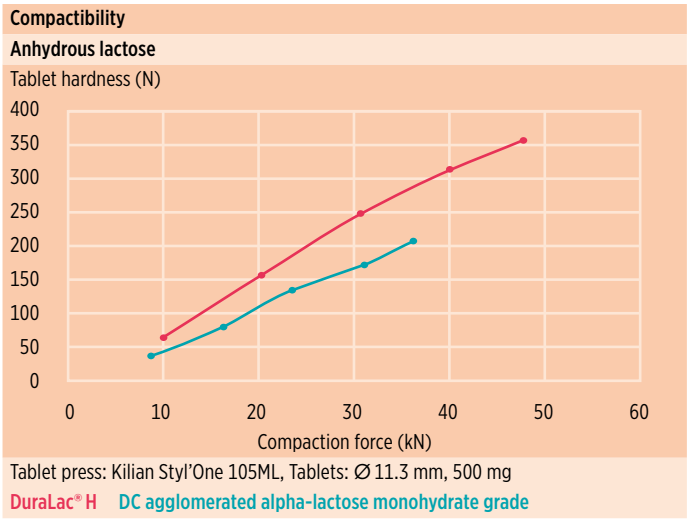


Figure 9: *Force-hardness profile of DuraLac® H compared to DC agglomerated alpha-lactose monohydrate.*

Powder compressability

During compaction, DuraLac® H fragments, exposing clean surfaces having numerous binding sites. This provides the functional performance needed to produce robust tablets in direct compression and granules having desired characteristics for high-speed tableting and capsule filling processes. **Figure 9** shows that tablets made with DuraLac® H achieve higher tablet hardness yield than comapcts produced from agglomerated alpha-lactose monohydrate (DC grade).

Packaging and shelf life

DuraLac® H

	Size	Material	Shelf life
DuraLac® H	25 kg	Carton box with an aluminum laminated inliner	36 Months

Figure 10: *Packaging and shelf life of MEGGLE's DuraLac® H.*

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 10** provides an overview about packaging size and material, and product shelf life.

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] Lerk, C. F. (1993). Consolidation and Compaction of Lactose. Drug Development and Industrial Pharmacy, 19(17–18), 2359–2398.

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