DURALAC

TABLETING →
DIRECT COMPRESSION →
ANHYDROUS LACTOSE

Technical brochure
DuraLac® H

MEGGLE
EXCIPIENTS & TECHNOLOGY

MEGGLE 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)**.

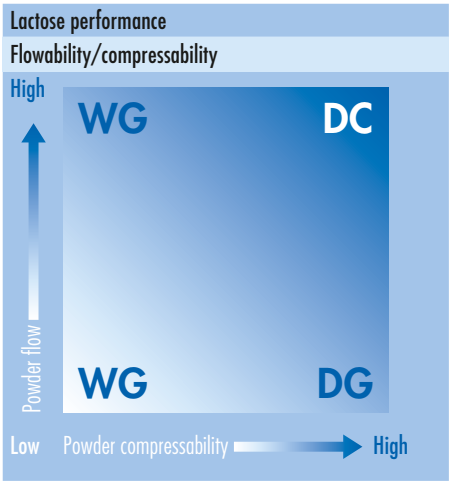


Figure 1: Powder blend compressability and flowability requirements for various tableting technologies (DC is direct compression, WG is wet granulation, DG is dry granulation) [3].

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 resulting only in the non-hygroscopic anhydrous form [4]. Subsequent to roller-drying, anhydrous lactose is milled and sieved to the desired particle size distribution, optimizing powder flow and compactability. Because DuraLac®H deforms by brittle fracture during compaction, it is well suited for directly compressed and dry granulated formulations (roller compaction, slugging).

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.

Our new state-of-the-art, pharma-dedicated production facility in Le Sueur, MN complies with cGMP according to the Joint IPEC-PQG Good Manufacturing Practices Guide for Pharmaceutical Excipients and USP General Information Chapter <1078>.
The Le Sueur facility demonstrates lactose production capabilities, including milling and roller-drying.

Additionally, MEGGLE is a member of IPEC (International Pharmaceutical Excipients Council).

MEGGLE invests considerably in raw material resource sustainability, production standards, efficiency and is actively engaged in environmental protection. Lactose meeting pharmaceutical standards is our first priority.

Application

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

- Low dose DC formulations
- Dry granulation (Roller compaction, slugging)
- Capsule filling

BENEFITS

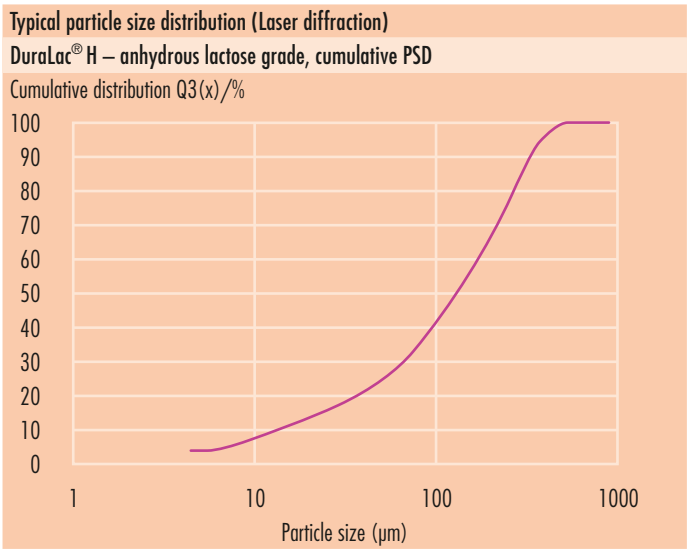
DuraLac® H

- Excellent compactability
- 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 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 DuraLac® H particle size distribution specification.



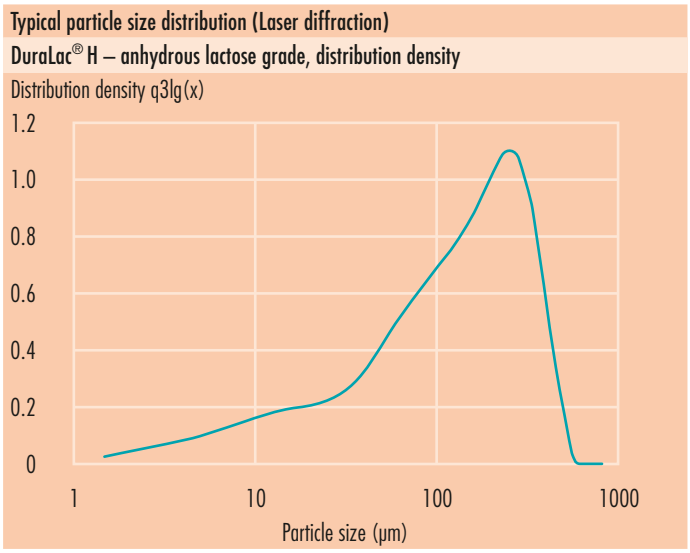


Figure 2: Typical cumulative PSD and distribution density of MEGGLE's DuraLac® H. Analyzed by Sympatec®/Helos & Rodos particle size analyzer.

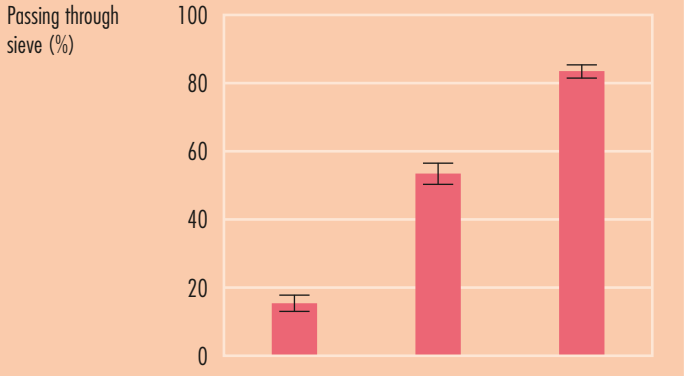
Sieve data – anhydrous lactose		
	Lactose type	DuraLac® H
		specified/typical
Particle size distribution	< 45 µm	NMT 20 %/16 %
Method:	< 150 µm	40 – 65 %/54 %
Air jet sieving	< 250 µm	NLT 80 %/83 %

Figure 3: Specified PSDs for MEGGLE's anhydrous lactose grade by air jet sieve 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: Particle size distribution batch-to-batch consistency of DuraLac® H by air jet sieving. 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.

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.

Sorption isotherm (Dynamic vapor sorption at 20 °C)
DuraLac® H

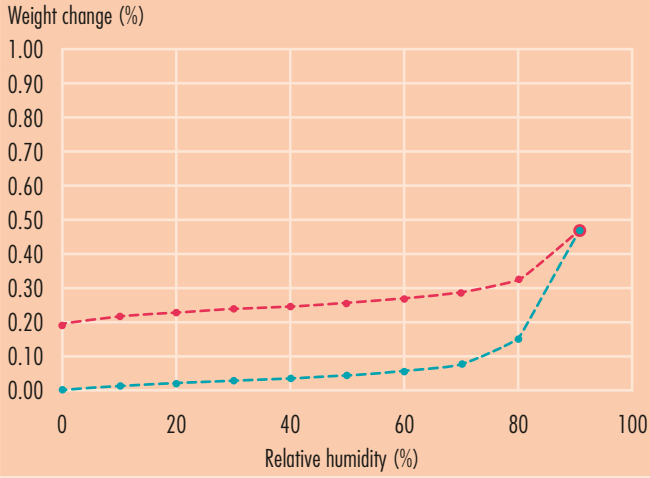


Figure 5: Sorption-desorption isotherm of DuraLac® H.

Scanning electron micrograph (SEM)

Lactose monohydrate and anhydrous lactose exhibit different morphology. Where lactose monohydrate products are defined typically by monoclinic sphenoidal, "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.

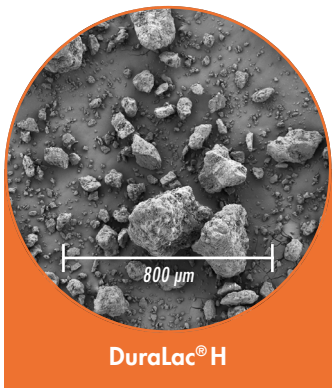


Figure 6: SEM image of MEGGLE´s anhydrous lactose grade DuraLac® H.

Functional related characteristics

Powder flow

It is well-known that particle size and shape influence powder flowability. Particles less 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 alone. Due to its shape, the anhydrous lactose flowability is moderate, but improves significantly with lubricant and/or glidant addition.

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 8** shows typical flowability indices for DuraLac® H, indicating the moderate flowability possessed by anhydrous grades.

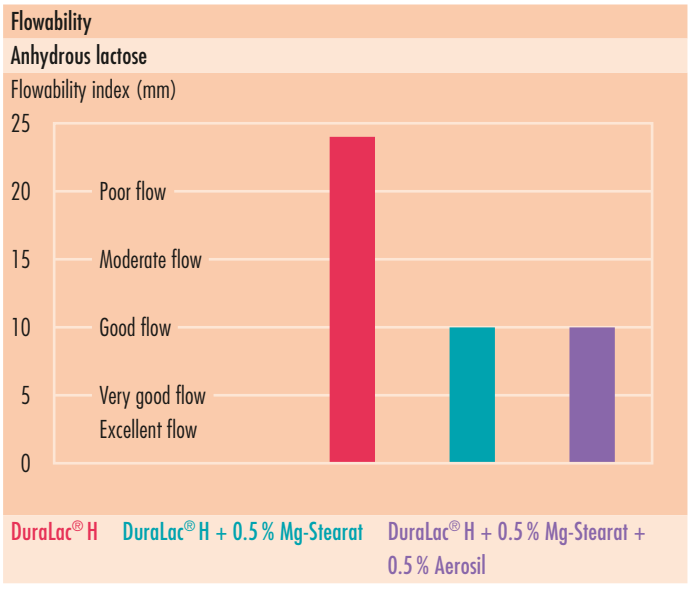


Figure 7: Flowability index of DuraLac® H in pure, lubricated and lubricated+glidant added form.

Flowability
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: Typical powder technological flowability values for DuraLac® H.

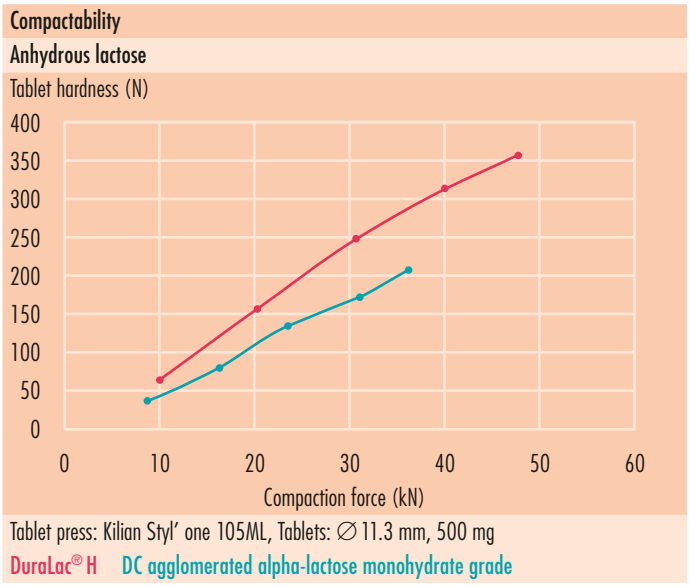


Figure 9: Force-hardness profile of DuraLac® H compared to DC agglomerated alpha-lactose monohydrate.

Compactability

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 greater tablet hardness compared to DC agglomerated alpha-lactose monohydrate.

Packaging and shelf life

DuraLac® H

	Size	Material	Shelf life
DuraLac® H	25 kg	Corrugated carton box with an aluminium laminated inliner	24 months

Figure 10: Packaging and shelf life of MEGGLE´s DuraLac®.

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.

MEGGLE App:

MEGGLE Consultant

MEGGLE Group Wasserburg
BG Excipients & Technology
Megglestrasse 6–12
83512 Wasserburg
Germany

Phone +49 8071 73 476
Fax +49 8071 73 320
service.pharma@meggle.de
www.meggle-pharma.com

US 02-06-2014 Sai