2024

THE WHOLE WORLD OF LACTOSE

BUSINESS UNIT EXCIPIENTS

Gurkan Altunok

Sep 2024

BRIEFLY MEGGLE

01

OUR COMPANY

Business Unit Excipients

FOUNDING YEAR

1887 as cheese dairy

HEADQUARTER

Wasserburg am Inn

EMPLOYEES

About 2,500 worldwide

COMPANY NAME

Since 2020 MEGGLE Group GmbH

OUR PHILOSOPHY

tradition • innovation • quality • success

We feel committed to our roots, but still want to grow further with a strong MEGGLE brand.

We are constantly expanding our national and international competitiveness: with an attractive range of high-quality products and services.

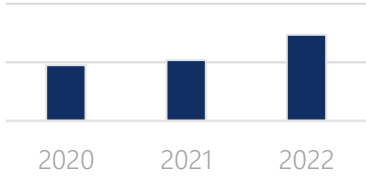
We are MEGGLE!

CONSOLIDATED KEY FIGURES

OF THE MEGGLE GROUP 2020 - 2022

SALES REVENUE in Mio., 2022

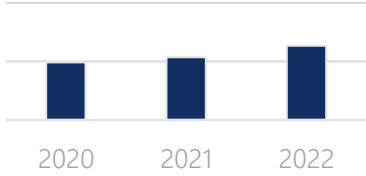
EUR 1,467



2020: EUR 951
2021: EUR 1,038

TOTAL ASSETS in Mio., 2022

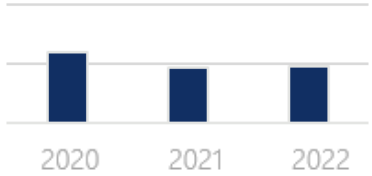
EUR 633



2020: EUR 491
2021: EUR 536

EMPLOYEES Ø 2022

2,485



2020: 2,600
2021: 2,467

Business Unit Excipients

MEGGLE Group GmbH

RAW MATERIAL-SOURCES UND -PROCESSING

FIGURES OF 2022

LOCATION: WASSERBURG AM INN

263 Mio. kg
raw milk

76 Mio. kg
cream

10.000 t
vegetable fats

46 Mio. kg
skimmed milk/whole milk

95.000 t
whey (dry matter*)

*Converted to whey with 6% dry matter = 1.5 billion litres of whey

OUR BUSINESS UNITS

Consumer Products	Business Division Consumer Products
Contract Manufacturing	Business Division Ingredients
Excipients	
Feed Ingredients	
Food Ingredients	

QUALITY MANAGEMENT

CERTIFICATIONS

BUSINESS DIVISION INGREDIENTS

LOCATION: WASSERBURG AM INN

MEGGLE

Business Unit Excipients

Excipients

EXCiPACT-Certification, IPEC PQC (GMP-Guideline for pharmaceutical excipients)

Feed Ingredients

Q+S-System (DE), GMP+ Standard

Food Ingredients

IFS (International Featured Standards Food – GFSI), EU-Bio (834/2007: DE Öko-003)

Contract Manufacturing

Feed Additives-FAMIQS, EU-Bio (834/2007: DE Öko-003)

Further line and production standards

Kosher, Halal, VLOG (GVO-free), RSPO (Rountable of Sustainable Palm Oil)

MEGGLE CERTIFICATIONS

Quality Management

DIN EN ISO 9001

Since 1994

Environmental Management

DIN EN ISO 14001

Since 2001

Occupational Health and Safety

DIN EN ISO 45001

Since 2019

Energy management

DIN EN ISO 50001

Since 2013

For GMP and GDP

EXCiPACT international excipients certification

Since July 2014

MEGGLE

Business Unit Excipients

SUSTAINABILITY MANAGEMENT SYSTEMS

STANDARDS, CERTIFICATIONS, RATINGS

MEGGLE

Business Unit Excipients

Sustainability Management System

GRI Empowering Sustainable Decisions

Interner Nachhaltig-keitsbericht jährlich

Öffentl. Nachhaltig-keitsbericht alle vier Jahre

ISO standards

DIN ISO 9001

DIN ISO 14001

DIN ISO 22000

DIN ISO 45001

DIN ISO 50001

Independent evaluation of individual locations

SILVER ecovadis 2019 CSR Rating

CDP DISCLOSURE INSIGHT ACTION

Sedex

Standards in defined areas

CERTIFIED SUSTAINABLE PALM OIL RSPO

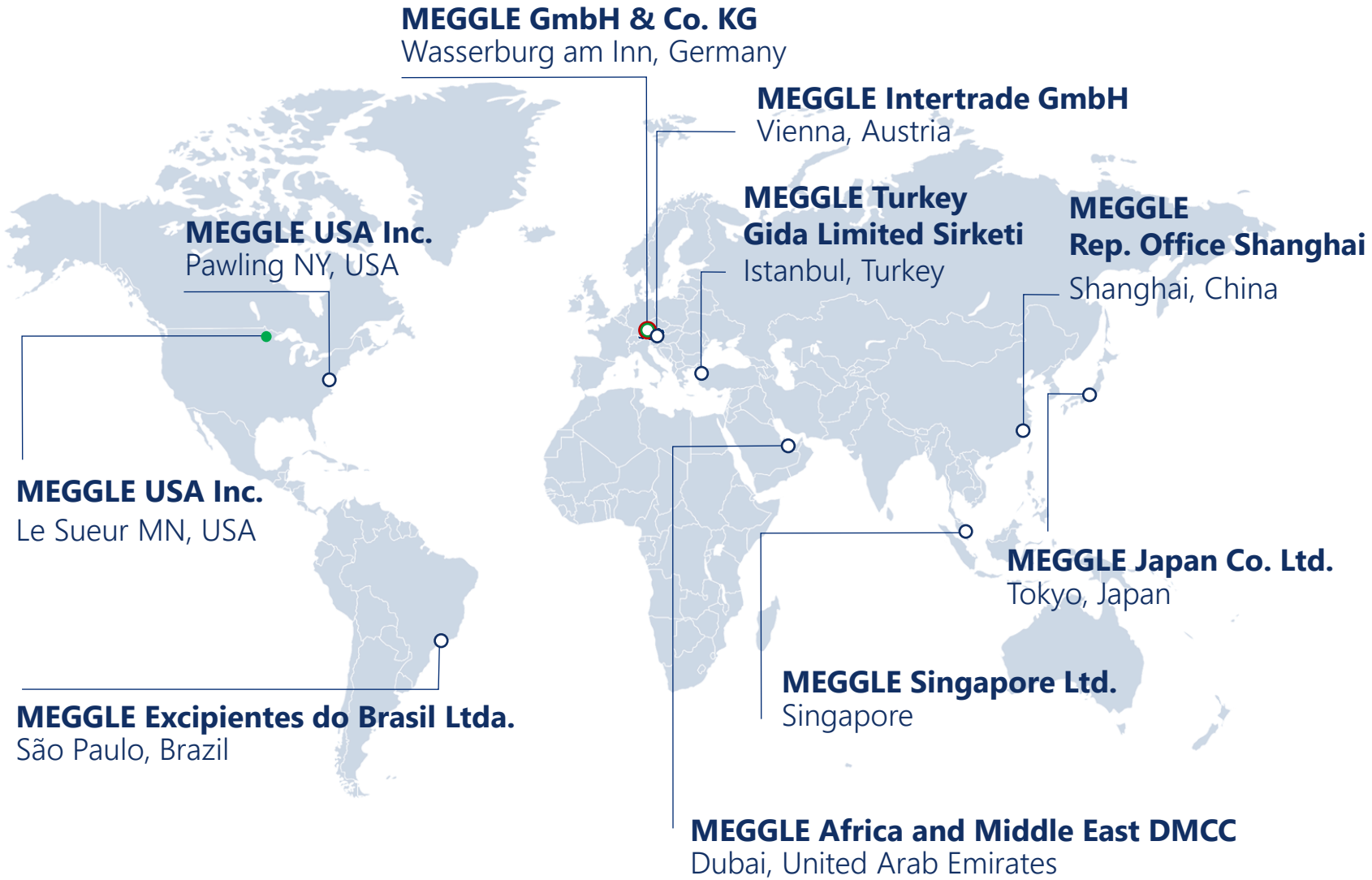
VLOG Lebensmittel ohne Gentechnik

Öko-VO EG Nr. 834/2007 Nr. 889/2008

Examples and projects on all activities in the field of sustainability of MEGGLE Group GmbH at www.meggle.com

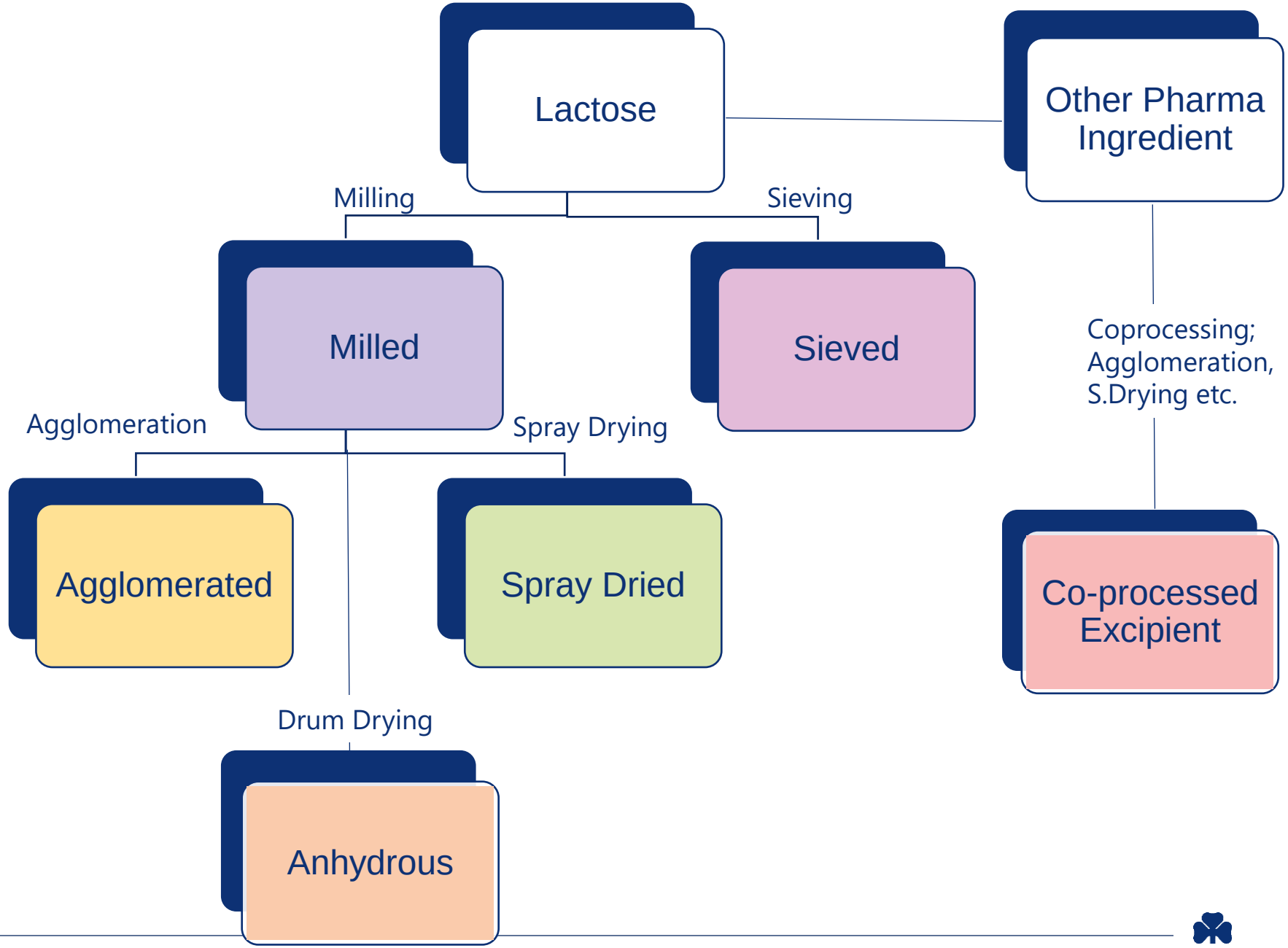
INGREDIENTS

- MEGGLE Group GmbH
- Sales
- Production



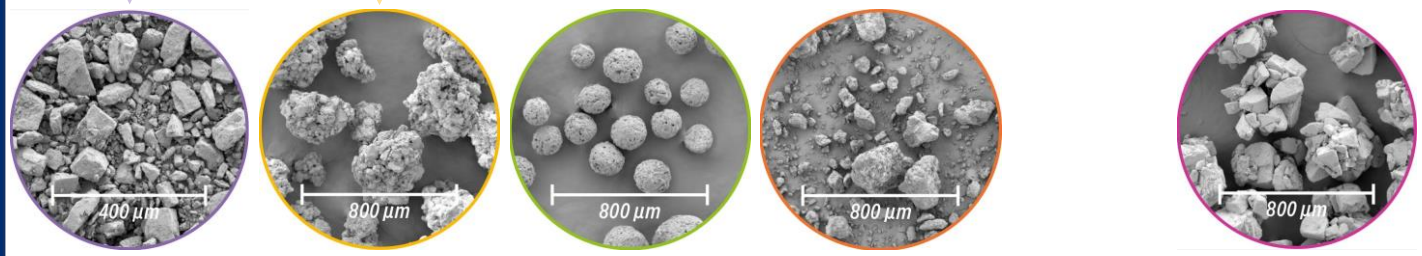
LACTOSE TYPES

PROCESS WISE



PRODUCT OVERVIEW

Tableting					Powder preparations	Dry powder inhalation	
Granulation	Direct compression						
milled	agglomerated	spray-dried	anhydrous	co-processed	sieved	sieved	milled
GranuLac® 70	Tablettose® 70	FlowLac® 90	DuraLac® H	Cellactose® 80	PrismaLac® 40	InhaLac® 70	InhaLac® 140
GranuLac® 80	Tablettose® 80	FlowLac® 100		MicroceLac® 100	CapsuLac® 60	InhaLac® 120	InhaLac® 145
GranuLac® 140	Tablettose® 100			StarLac®	SacheLac® 80	InhaLac® 160	InhaLac® 150
GranuLac® 200				CombiLac®	SpheroLac® 100	InhaLac® 230	InhaLac® 180
GranuLac® 230				sustained release		InhaLac® 251	InhaLac® 300
SorboLac® 400				RetaLac®			InhaLac® 400
							micronized
							InhaLac® 500



PRODUCT PORTFOLIO

02

PRODUCT OVERVIEW

Tableting					Powder preparations	Dry powder inhalation	
Granulation	Direct compression						
milled	agglomerated	spray-dried	anhydrous	co-processed	sieved	sieved	milled
GranuLac® 70	Tablettose® 70	FlowLac® 90	DuraLac® H	Cellactose® 80	PrismaLac® 40	InhaLac® 70	InhaLac® 140
GranuLac® 80	Tablettose® 80	FlowLac® 100		MicroceLac® 100	CapsuLac® 60	InhaLac® 120	InhaLac® 145
GranuLac® 140	Tablettose® 100			StarLac®	SacheLac® 80	InhaLac® 160	InhaLac® 150
GranuLac® 200				CombiLac®	SpheroLac® 100	InhaLac® 230	InhaLac® 180
GranuLac® 230				sustained release		InhaLac® 251	InhaLac® 300
SorboLac® 400				RetaLac®			InhaLac® 400
							micronized
							InhaLac® 500

PRODUCT OVERVIEW

POWDER PREPARATIONS

POWDER PREPARATIONS

SIEVED LACTOSE

Sieved Lactose

MEGGLE´s sieved lactose grades for powder preparations

SIEVED LACTOSE

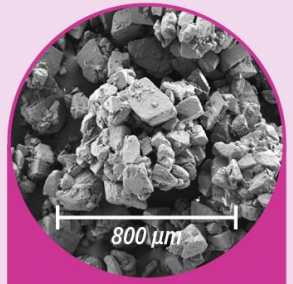
for powder preparations

BENEFITS:

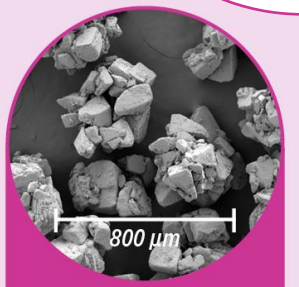
- Excellent flowability
- High batch-to-batch consistency
- Narrow particel size distribution
- High storage stability

APPLICATION:

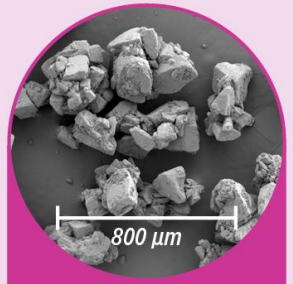
- High Speed Capsule and Sachet Filling
- Powder Blends & Premixes
- Triturations



PrismaLac® 40



CapsuLac® 60



SacheLac® 80

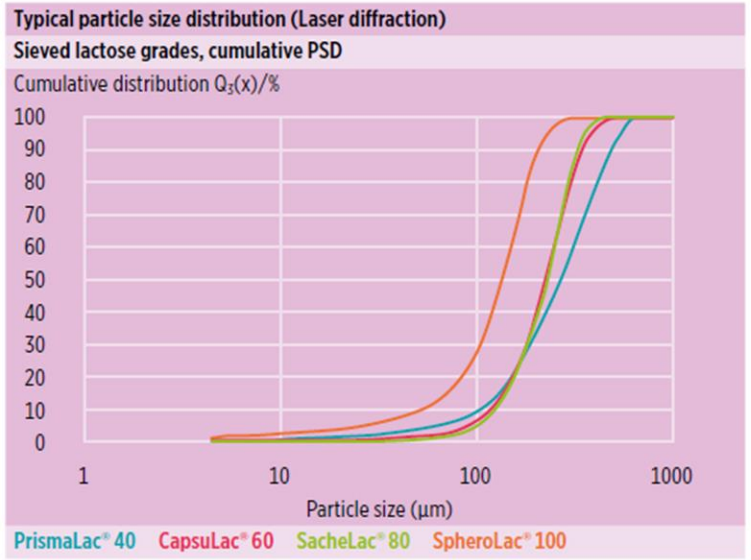
SpheroLac® 100

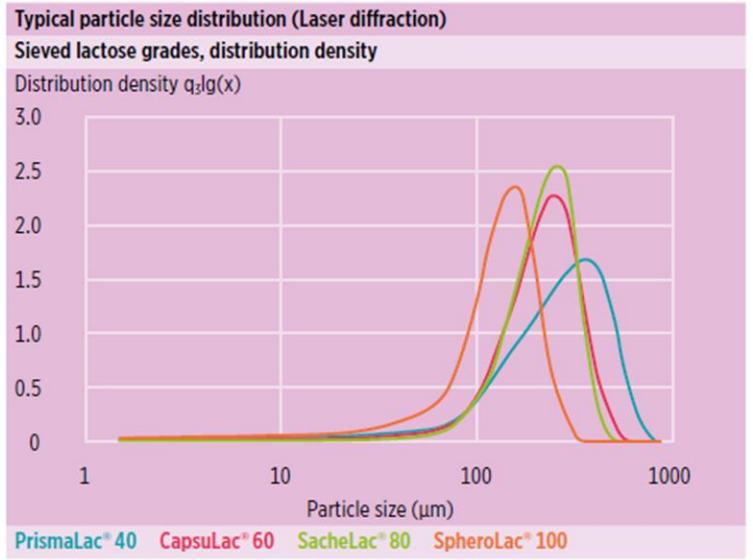
POWDER PREPARATIONS

SIEVED LACTOSE

Particle Size Distribution

& Specific Surface Area





Sieve data – sieved lactose (German-origin)

	Lactose type	PrismaLac® 40	CapsuLac® 60	SacheLac® 80	SpheroLac® 100
		specified/typical	specified/typical	specified/typical	specified/typical
Particle size distribution	< 63 µm				NMT 20 %/ 9 %
Method:	< 100 µm		NMT 10 %/ 3 %	NMT 20 %/ 3 %	
Mechanical sieve shaker	< 150 µm		/ 9 %		/ 70 %
	< 200 µm	NMT 10 %/ 4 %			NLT 75 %/ 97 %
	< 250 µm		40–70 %/50 %	/51 %	/100 %
	< 400 µm		NLT 90 %/99 %	NLT 98 %/99 %	
	< 500 µm	/ 58 %			
	< 630 µm	/ 88 %	NLT 97 %		
	< 800 µm	NLT 97 %/100 %			

Specific surface area determination by BET

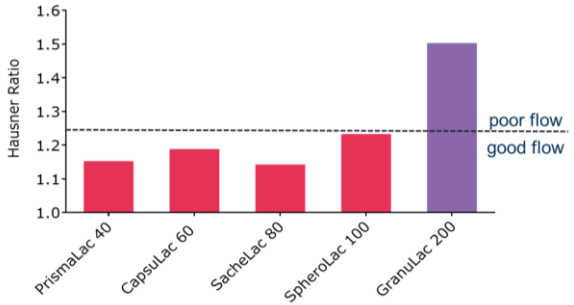
	(m^2/g)
Sieved	
PrismaLac® 40	0.20
CapsuLac® 60	0.13
SacheLac® 80	0.13
SpheroLac® 100	0.22

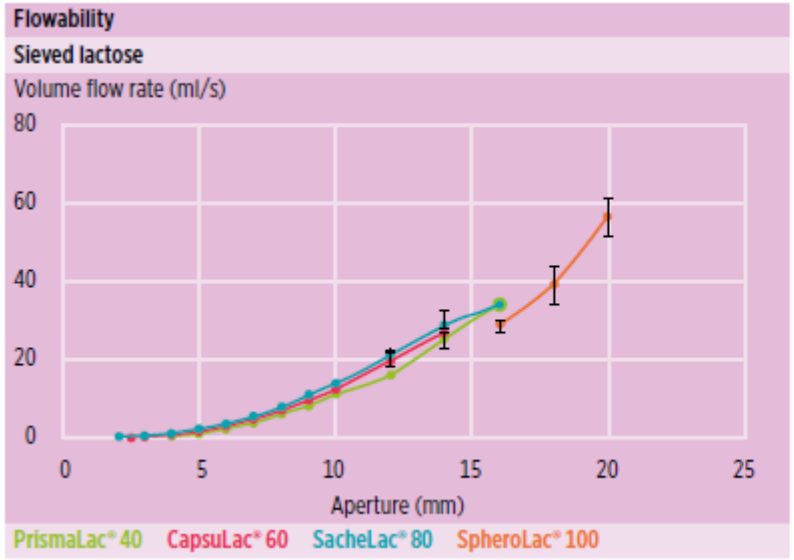
POWDER PREPARATIONS

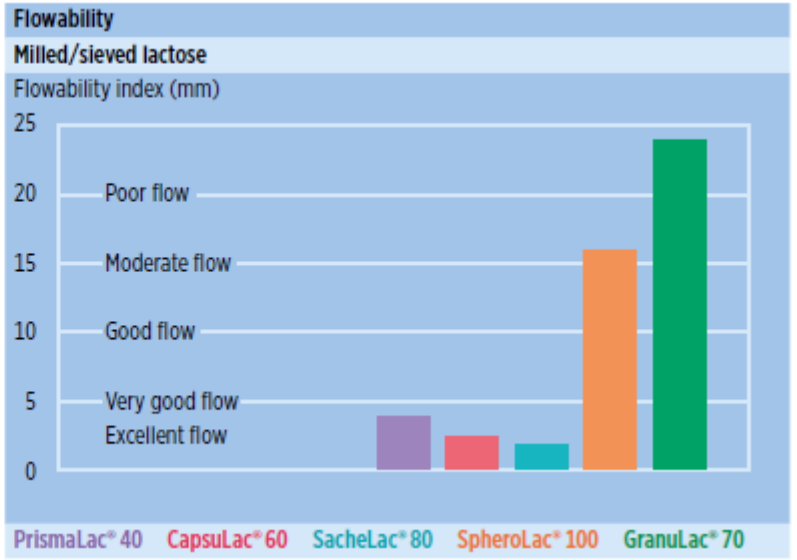
SIEVED LACTOSE

Powder Flow

Flowability	Angle of repose (°)	Density bulk (g/l)	Density tapped (g/l)	Hausner ratio	Carr's index (%)
Sieved					
PrismaLac® 40	34	440	540	1.23	19
CapsuLac® 60	33	570	700	1.23	19
SacheLac® 80	32	570	710	1.25	20
SpheroLac® 100	38	690	870	1.26	21







PRODUCT OVERVIEW

DIRECT COMPRESSION

BUSINESS UNIT
EXCIPIENTS

PRODUCT OVERVIEW

Agglomerated Lactose

Agglomerated Lactose

MEGGLE´s agglomerated lactose for Direct Compression Tablettose

AGGLOMERATED LACTOSE

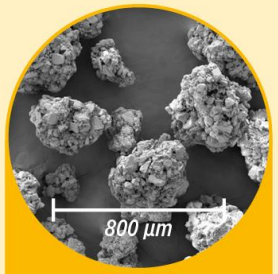
for direct compression

BENEFITS:

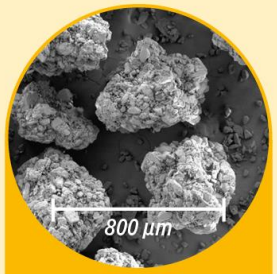
- Good flowability
- Good compactibility
- Low moisture content
- Low hygroscopicity
- Excellent stability
- Superior blending characteristics
- Fast disintegration times

APPLICATION:

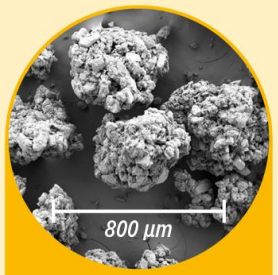
- Direct compression
- Continuous applications
- Capsule and sachet filling
- Effervescent tablets
- Artificial sweetener tablets



Tablettose® 70



Tablettose® 80



Tablettose® 100

BUSINESS UNIT
EXCIPIENTS

PRODUCT OVERVIEW

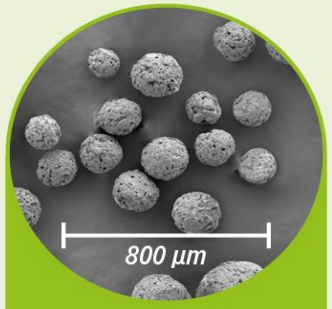
Spray-dried Lactose

Spray-dried Lactose

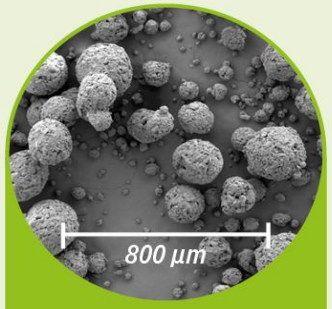
MEGGLE´s spray-dried lactose for Direct Compression FlowLac

SPRAY-DRIED LACTOSE

for direct compression



FlowLac® 90



FlowLac® 100

BENEFITS:

- Superior flowability
- Best in class compactibility
- Very low strain rate sensitivity (high speed compression)
- Smooth surface → glossy tablets
- Fast disintegration times

APPLICATION:

- Direct compression
- Continuous applications
- Formulations with poorly flowing APIs
- Capsule and sachet filling

BUSINESS UNIT
EXCIPIENTS

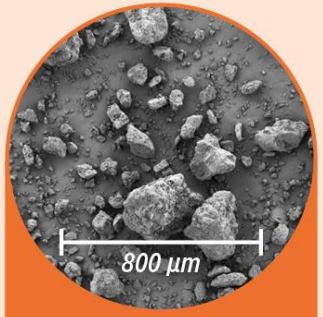
PRODUCT OVERVIEW

Anhydrous Lactose

Anhydrous Lactose

MEGGLE´s anhydrous lactose for Direct Compression DuraLac

ANHYDROUS LACTOSE
for direct compression



DuraLac® H

BENEFITS:
- Excellent compactibility
- Very good recompactability
- Disintegration independent of compaction pressure
- Low water content
- High storage stability

APPLICATION:
- Direct compression
- Capsule filling
- Dry granulation (roller compaction, slugging)

BUSINESS UNIT
EXCIPIENTS

PRODUCT OVERVIEW

Co-processed Excipients

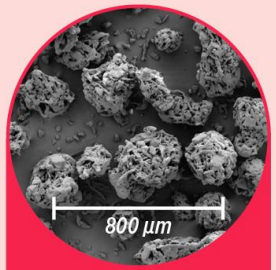
Co-processed Excipients

MEGGLE´s co-processed excipients for Direct Comperession

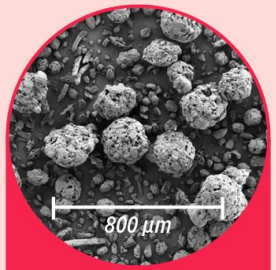
CO-PROCESSED EXCIPIENTS
for direct compression

BENEFITS:
- Direct compression
- High speed tableting
- Superior flow properties
- Reduction of process steps

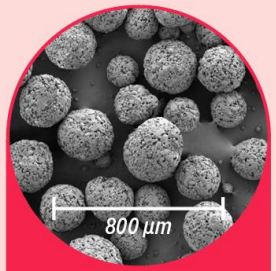
APPLICATION:
The DC solution for your challenges
- Higher drugload
- Continuous applications
- Fast disintegration
- Minimizing impact of lubricant and tablet hardness on drug release
- Excellent compactibility
- Fast and hardness independent disintegration



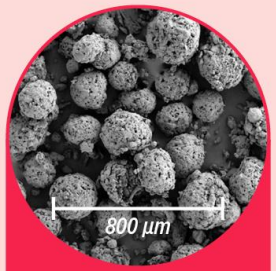
Cellactose® 80



MicroceLac® 100

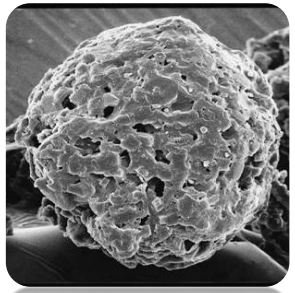


StarLac®



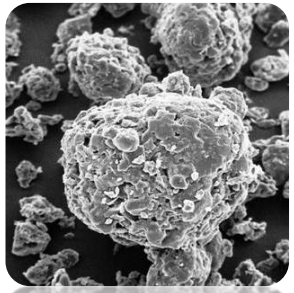
CombiLac®

Cellactose® 80
MicroceLac® 100
StarLac®
CombiLac®



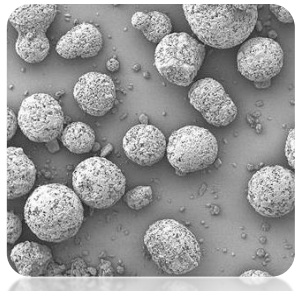
Cellactose® 80

- 75 % α–Lactose Monohydrate
- 25 % Powdered Cellulose
  - Ph.Eur./USP-NF/JP
  - Spray dried



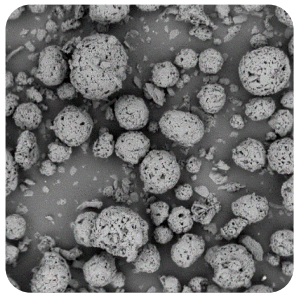
MicroceLac® 100

- 75 % α–Lactose Monohydrate
- 25 % Microcrystalline Cellulose
  - Ph.Eur./USP-NF/JP
  - Spray dried



StarLac®

- 85 % α–Lactose Monohydrate
- 15 % Corn starch



CombiLac®

- 70 % α–Lactose Monohydrate
- 20 % Microcrystalline Cellulose
- 10 % Corn starch

BUSINESS UNIT
EXCIPIENTS

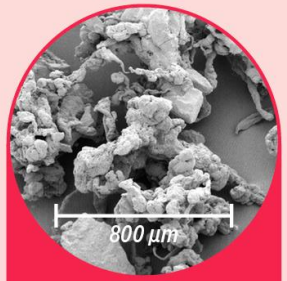
PRODUCT OVERVIEW

Co-processed Excipients

Co-processed Excipients
Sustained Release

MEGGLE´s co-processed excipients for Direct Comperession

Co-processed excipients for
SUSTAINED RELEASE
formulations



RetaLac®

BENEFITS:
- Direct compression of sustained release formulations
- Superior processibility compared to physical admixture
- High drug load capacity (up to 50 %)
- Meets compendial requirements
- Also available lactose-free

APPLICATION:
- Direct compression, also for multi unit and mini tablets
- Roller compaction
- Preparation of aqueous HPMC-formulations
- Spheronization, extrusion

SUMMARY

Benefits of the Different DC Excipients

Agglomerated Lactose

- Well established and robust standard for direct compression
- Interlocking enables lower risk of segregation
- Different grades available, e.g. Tablettose 70 with narrow particle size distribution for improved flowability

Anhydrous Lactose

- High compactability
- Perfectly suited for dry granulation (best re-compactability)
- Disintegration almost independent of compaction pressure

Spray Dried Lactose

- In case superior flowability or compactability is required
- Smooth, shiny tablet surface
- Also suitable for continuous manufacturing

Co-Processed
(Lactose with Cellulose/MCC and/or Starch)

- Combination with Cellulose/ MCC offers even higher loadability
- Good flowability
- Low capping tendency
- Combination with starch for even faster disintegration
- CPEs also ideal for continuous manufacturing

Different Grade (PSD) available → match according API properties (flow/ segregation) and required tablet strength

MITIGATION OF COMMON FORMULATION ISSUES

Tabletability

Improve tensile strength at moderate compression force

- Use lactose grade with smaller particle size
- Use spray dried lactose or co-processed excipients with MCC (ideal combination of brittle and plastic deformation)
- Add dry binder
- …

Weight Variability

Improve flowability/ permeability of blend

- Use lactose grade with larger particle size
- Decrease amount of fines, reduce span
- Use spherical particles (spray-dried or co-processed Excipients)
- Add colloidal silicon dioxide, lubricant
- …

Content Uniformity

Measures depend on type of segregation e.g.

- Match PSD/ density
- Enable mass flow
- Increase adherence to surface e.g. rougher surface Cellactose, Tablettose
- Trituration/ pre-blend for low dose
- …

Disintegration & Dissolution

- Reduce compression force / tensile strength
- CPE with starch
- Avoid over lubrication
- Adapt disintegrant (type / amount)

Increase Solubility of API

- Adjust particle size of API (micronize)
- Use salt or different polymorph
- Add solubilizer / solid dispersion

COMPARATIVE CHARACTERISTICS

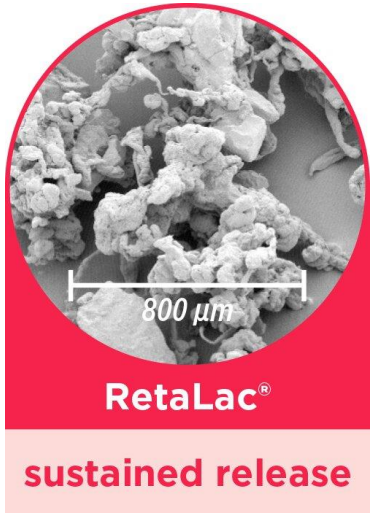
Co-Processed Excipients

Product	Dilution Potential	Flowability	Compressibility	Disintegration
Cellactose® 80	++	+(+)	++	+(+)
MicroceLac® 100	**+++**	++	**+++**	+(+)
StarLac®	+	**+++**	+	**+++**
CombiLac®	**++(+)**	**+++**	**++(+)**	**+++**

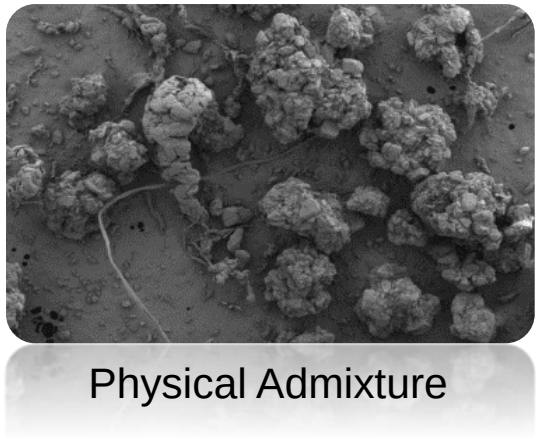
PRODUCT OVERVIEW

SUSTAINED RELEASE

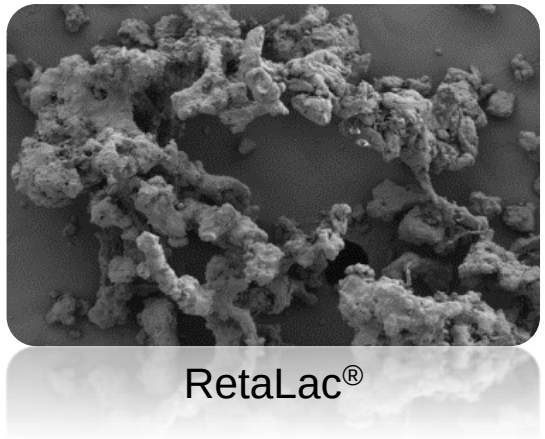
CO-PROCESSED EXCIPIENT RetaLac®



- 50 % α-Lactose Monohydrat [Ph.Eur./USP-NF/JP]
- 50 % HPMC [Ph.Eur./USP-NF/JP] 2208 type, ca. 4000 mPas (2 % aqueous solution)



Physical Admixture



RetaLac®

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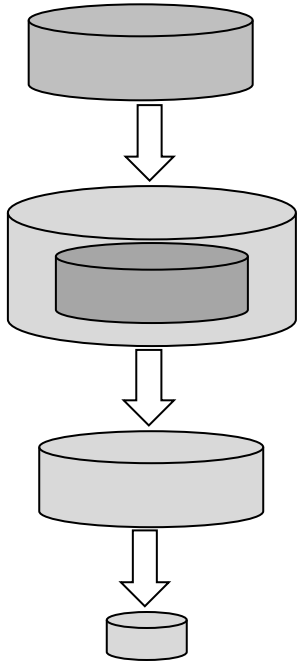
Hydrophilic Matrix System

API Release Mechanism

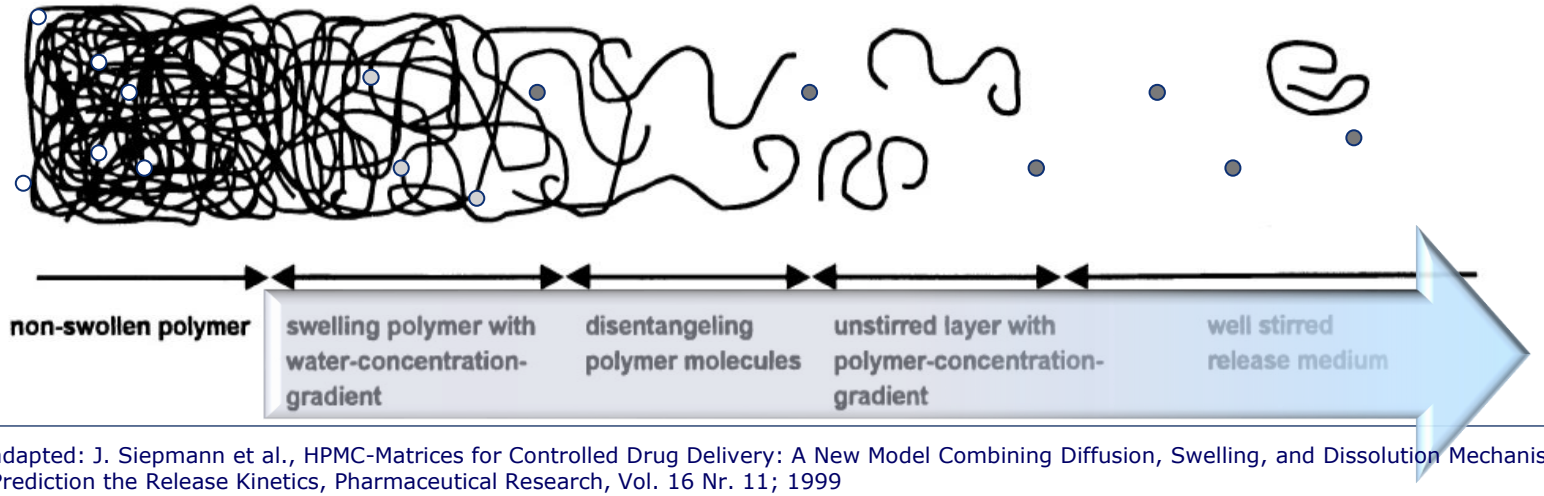


Administration of SR tablet

Hydrating, formation of gel layer, water penetration, expansion of gel layer
API release controlled by diffusion

Completed hydration,
API release controlled by erosion

Erosion of tablet



adapted: J. Siepmann et al., HPMC-Matrices for Controlled Drug Delivery: A New Model Combining Diffusion, Swelling, and Dissolution Mechanisms and Prediction the Release Kinetics, Pharmaceutical Research, Vol. 16 Nr. 11; 1999

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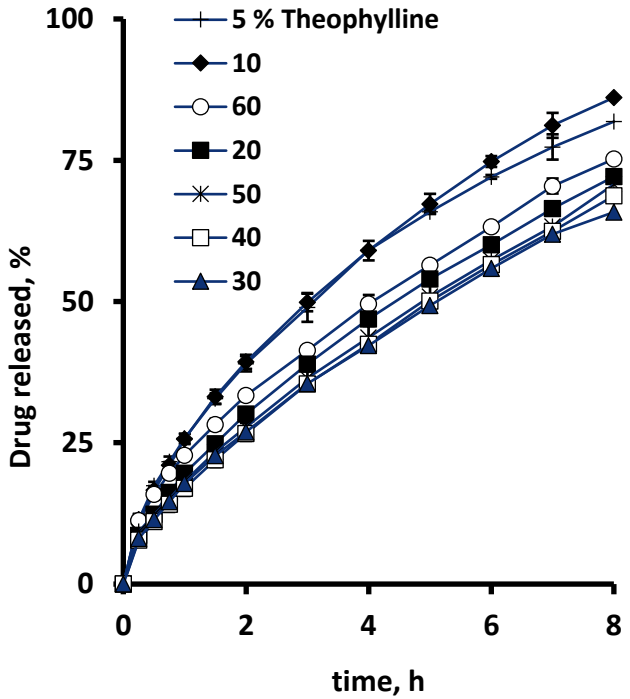
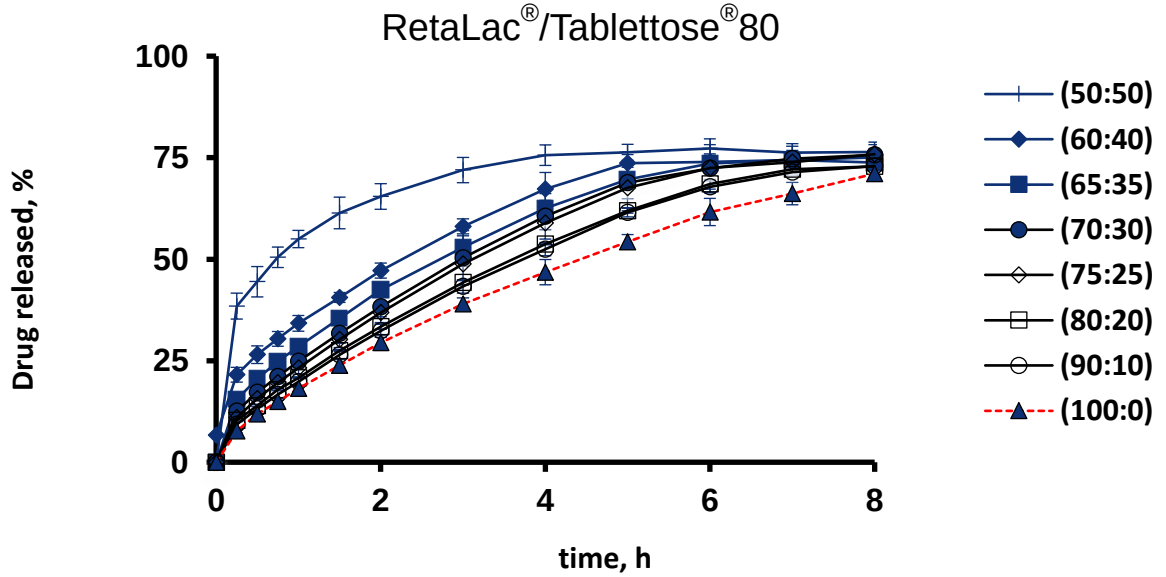
Drug Release Kinetics

Release rate of HPMC-based matrix tablets strongly depends on:

- Composition: API(s), polymer concentration(s), other excipients
- Device Design Parameters: Geometry of tablet (shape, size, volume vs. surface ratio); technology of preparation





RETALAC®

Summary

- **Characteristics/ Benefits**
  - Direct compression of sustained release formulations
  - Superior compactability compared to physical admixture
  - Structured surface
  - Defined and adjustable release profiles
  - Improves wettability of HPMC

- **Application**
  - Direct compression of modified release formulations (up to 60 % API)
  - Facilitates preparation of dispersions containing HPMC/ Lactose

CHALLENGES IN TRACE LEVEL METHOD

03

NITRITE METHODE LACTOSE

Update

- A **new analytical method** for trace level determination of nitrite in lactose has been developed and successfully validated in cooperation with Technical University Munich.
- Limit of Quantification (LOQ) 0.03 ppm (34 ppb)
- Limit of Detection (LOD) 0.01 ppm (11 ppb)
- At least 3 samples from every product group (sieved, milled, agglomerated, spray dried and anhydrous lactose as well as milled and sieved inhalation grade lactose) have been analyzed with the new method

  → All results are **below 0.01 ppm**
- Independent measurements of lactose samples with different methods (IC with post-column Griess Derivatization) confirmed that range of nitrite in our lactose is extremely low.
- The estimated nitrite content for the GranuLac sample used in this study was 0.002 ppm (2 ppb).

The measurements confirmed that our Pharma Grade Lactose products have an extremely low nitrite content - basically “nitrite free”.

FIRST RESULTS WITH NEW METHOD

Nitrite Content in our Lactose Products is Extremely Low

Product Group	Product Name	Nitrite Content	Number of Lots tested
Sieved Lactose	SpheroLac 100	< 0.01 ppm	3
Milled Lactose	GranuLac 200 GranuLac 200 US	< 0.01 ppm	5
Agglomerated Lactose	Tablettose 70 Tablettose 80 Tablettose 100	< 0.01 ppm	3
Spray Dried Lactose	FlowLac 90 FlowLac 100	< 0.01 ppm	6
Anhydrous Lactose	DuraLac H	< 0.01 ppm	3
Inhalation Grade Lactose sieved	InhaLac 120 InhaLac 230 InhaLac 251	< 0.01 ppm	3
Inhalation Grade Lactose milled	InhaLac 145 InhaLac 300 InhaLac 400	< 0.01 ppm	3

NITRITE IN LACTOSE

Common Methods and Potential Issues

Nitrites in Excipients
21st March 2024
Free registration

Key Message

- Commonly used IC methods, even if validated for low amounts of nitrite, might lead to “wrong” results for lactose due to **co-elution**.
- Recommendation: at least perform confirmatory test with lactose to avoid errors due to co-elution in selected method. This can be done by spiking lactose solution with different amounts of nitrite
- Our pharma grade lactose offer lowest amount of nitrite.
- Our lactose products offers a good solution to mitigate/ reduce risk of nitrosamine formation.
- In case of required reformulations, we are happy to offer support at our Innovation & Formulation Campus Munich

Matrix could impact results

→ **What method are you using for Nitrite Determination?**

→ **Verification for lactose (e.g. spiking test)?**

- Global Meeting 2024

THANK YOU!
ДЯКУЮ

Gürkan Altunok

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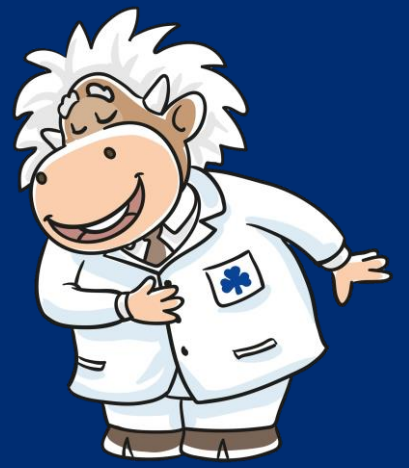

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