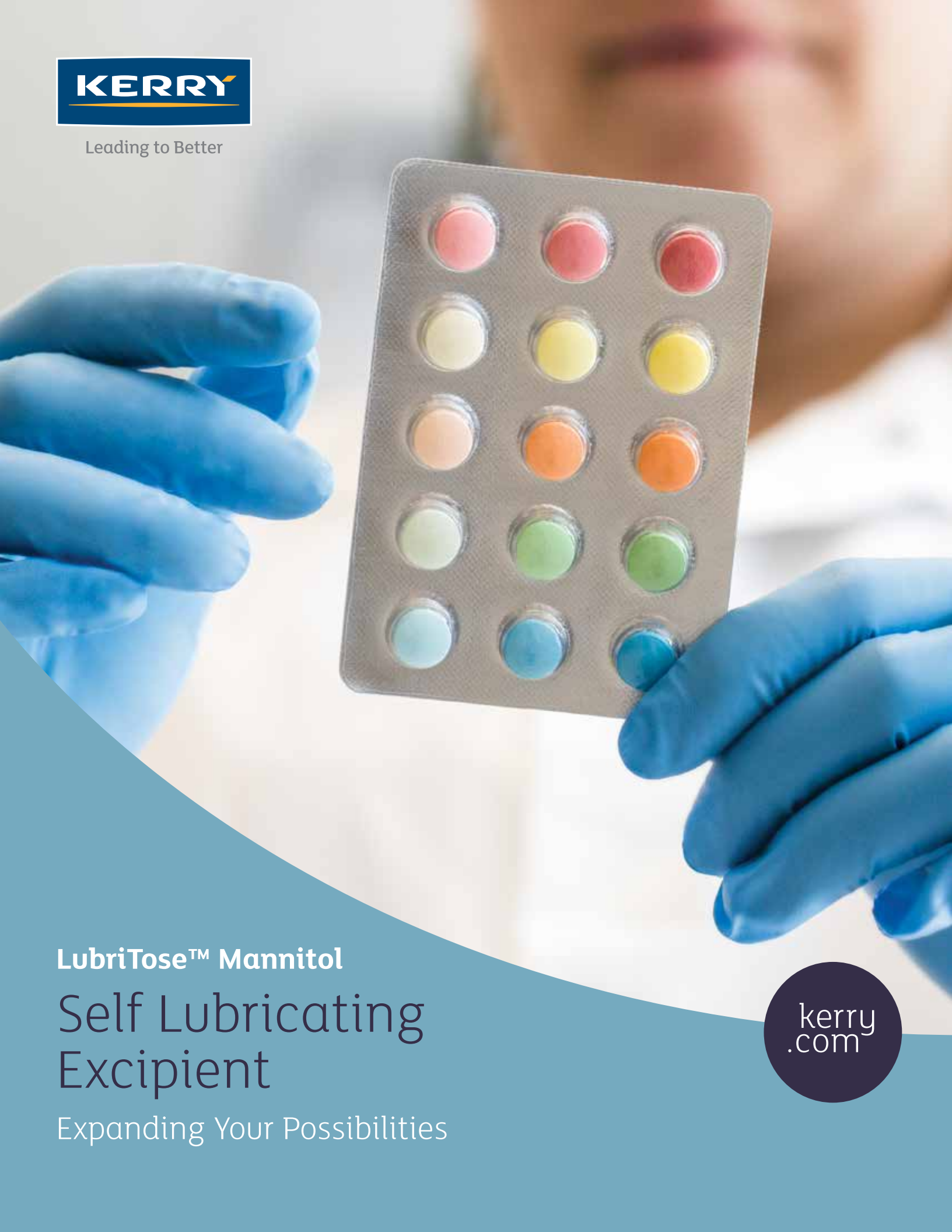




Leading to Better



LubriTose™ Mannitol
Self Lubricating
Excipient
Expanding Your Possibilities



LubriTose™ Mannitol

Mannitol is a commonly used excipient when used in an oral solid dose. It can provide non-cariogenic, and pleasant organoleptic properties to many chewable or ODT dose forms. The spray dried version of mannitol in particular offers the OSD formulator some very useful benefits when used in a direct compression manufacturing environment, due to its chemical stability and good flow properties.

Kerry introduced its LubriTose™ line of excipients that utilize a proprietary co-processing technique to incorporate GMS (Glyceryl Monostearate) in to the base excipient (typically Lactose, Microcrystalline Cellulose, or Mannitol) that essentially enables the entire formulation to become self lubricating, when used in combination with some API's.



The Study

The purpose of this study was to evaluate what other benefits co-processing with GMS could bring to spray dried mannitol. In this study, we used a version of Lubritose that was 96% Spray Dried Mannitol, and 4% GMS. Two different Spray Dried Mannitol suppliers were used in the study evaluations.

The study evaluated four parameters that are typically important to OSD formulators:

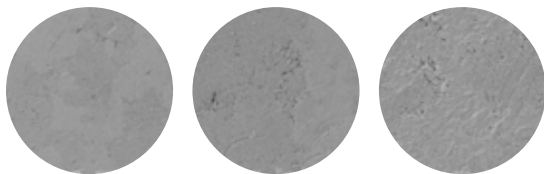
- Lubrication / ease of ejection
- Compressibility
- Tablet weight uniformity
- Tablet stability

Tablet Surface

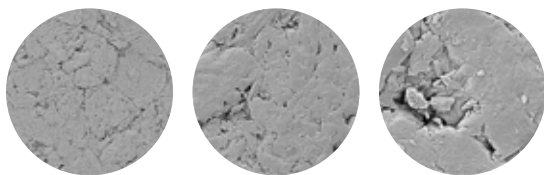
When the tablet surface is viewed using a SEM, it is readily apparent that the surface of the compressed tablet looks quite different. Our researchers wanted to know what impact this would have on the four parameters above.

Tablet SEMs

LubriTose™ Mannitol



Spray Dried Mannitol



200x

1000x

5000x

Powder SEMs

LubriTose™ Mannitol



Spray Dried Mannitol



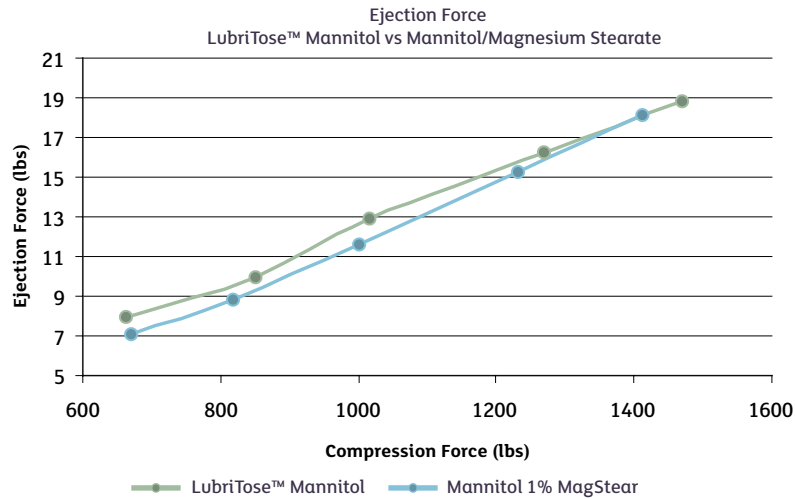
200x

1000x

5000x

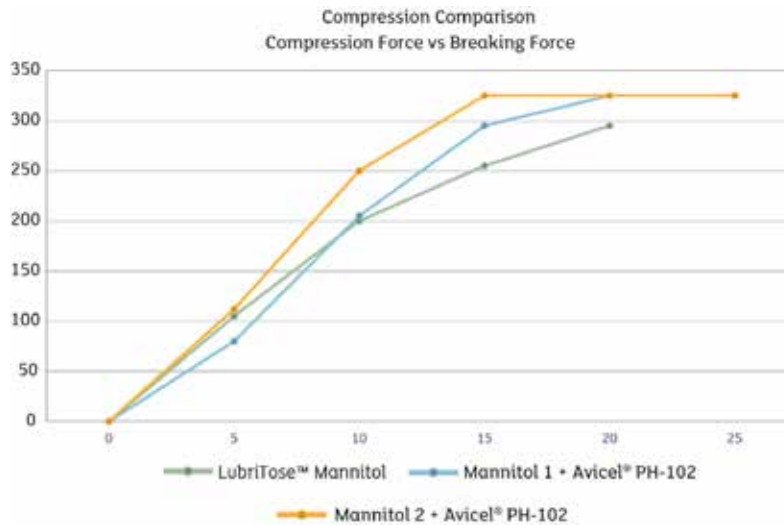
Lubrication Evaluation

As previously demonstrated in other research, the lubrication properties of the tablet as measured by the ejection force showed that the lubrication properties of the LubriTose™ Mannitol were the same as those using Spray Dried Mannitol with the addition of 1% magnesium stearate as external lubricant.



Compression Evaluation

The compression profile of LubriTose™ Mannitol was also shown to be superior to Spray Dried Mannitol. Even when comparing neat LubriTose™ Mannitol to 50/50 blends of Spray Dried Mannitol together with Microcrystalline Cellulose, the compression forces were similar.



Tablet Weight Uniformity

Tablet weight uniformity was measured over a range compression forces. At each compression force studied, the weight variation was less than that of Spray Dried Mannitol with Microcrystalline Cellulose, even after 20 days at accelerated storage conditions.

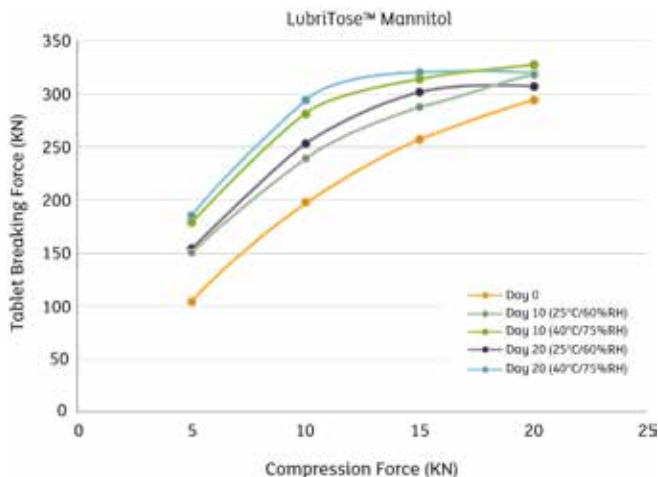
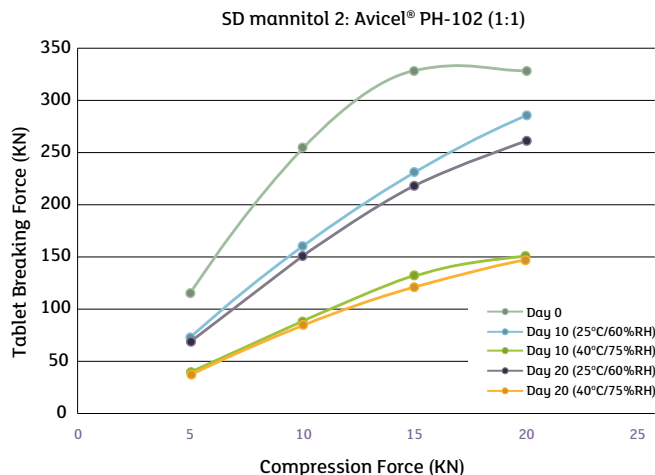
	Condition	Compression Force (KN)			
		10	15	20	25
LubriTose™ Mannitol	Day 0	501.8 ± 1.32	499.8 ± 1.32	502.6 ± 1.26	502.9 ± 1.60
	25°C/60% RH				
	Day 10	502.2 ± 0.63	501.0 ± 1.63	502.4 ± 1.07	502.2 ± 1.03
	Day 20	502.0 ± 1.25	500.4 ± 1.43	502.1 ± 1.91	501.7 ± 0.82
	40°C/75% RH				
	Day 10	502.4 ± 0.84	501.1 ± 0.88	502.3 ± 0.82	501.9 ± 0.99
	Day 20	500.7 ± 2.06	500.7 ± 0.95	501.9 ± 0.88	502.2 ± 1.23

	Condition	Compression Force (KN)			
		10	15	20	25
SD Mannitol + Avicel® PH-102 (1:1)	Day 0	505.8 ± 2.44	504.3 ± 2.31	502.1 ± 3.31	500.2 ± 2.62
	25°C/60% RH				
	Day 10	505.7 ± 3.20	506.7 ± 2.45	501.1 ± 3.45	503.5 ± 2.32
	Day 20	506.5 ± 2.99	506.9 ± 2.18	501.1 ± 3.03	502.8 ± 1.55
	40°C/75% RH				
	Day 10	506.4 ± 2.80	506.6 ± 3.66	503.3 ± 2.36	501.5 ± 2.22
	Day 20	504.4 ± 4.06	504.8 ± 2.94	502.6 ± 2.27	499.2 ± 4.73

	Condition	Compression Force (KN)			
		10	15	20	25
SD Mannitol 2 + Avicel® PH-102 (1:1)	Day 0	499.2 ± 4.69	501.0 ± 2.21	503.1 ± 4.31	504.6 ± 2.80
	25°C/60% RH				
	Day 10	500.0 ± 5.40	503.6 ± 2.37	506.6 ± 2.32	509.2 ± 2.62
	Day 20	502.1 ± 4.70	502.9 ± 2.38	505.4 ± 3.06	512.3 ± 2.83
	40°C/75% RH				
	Day 10	500.1 ± 4.53	503.4 ± 2.67	505.3 ± 2.21	509.6 ± 2.76
	Day 20	498.4 ± 4.17	501.0 ± 2.36	503.4 ± 3.57	507.5 ± 5.32

Tablet Stability

The tablet stability was also dramatically improved, as the hardness of the tablet dropped significantly for the Spray Dried Mannitol + Microcrystalline Cellulose compared to LubriTose™ Mannitol.



Finished Tablet

Our researchers also found that the tablets produced with LubriTose™ Mannitol produced tablets with an elegant glossy finish, as shown below.



LubriTose™ Mannitol (DMF# 27343)

Ingredient	CAS Number
Spray Dried Mannitol (USP)	69-65-8
Glyceryl Monostearate (NF, JP)	123-94-4

Physical and Chemical Specification

Assay	Method Description	Limits
Appearance	Visual	White/Off-White Powder
Identification by FTIR	FTIR	Conforms
Mannitol Uniformity (%)	FTIR	94-97
Loss on Drying	USP <731>	<=2.0
Percent on 40 Mesh (%)	USP <786>, ROTAP	0-8
Percent on 100 Mesh (%)	USP <786>, ROTAP	10-30
Percent on 200 Mesh (%)	USP <786>, ROTAP	50-85

Microbiological Specifications

Assay	Method Description	Limits
Total Aerobic Microbial Count	UPS <61>, cfu/g	<=1000
Total Combined Mold and Yeast	UPS <61>, cfu/g	<=100

Packaging

200 lb Fiber drum with polyethylene liner

100 lb Fiber drum with polyethylene liner

25 kg box with polyethylene liner

