Technical information
Technische Information

100490 Parteck® ODT

Content

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1. General

Parteck® ODT is a superior directly compressible excipient for fast disintegrating oral preparations. These solid dosage forms rapidly disintegrate on contact with saliva, thus eliminating the need for water and the difficulties some consumers have with swallowing tablets. This fast disintegration is a prerequisite for rapid dissolution of the active ingredients.

Parteck® is the brand name for a range of products under Merck's Functional Particle Engineering concept which allows us to offer specialty excipients with outstanding functionalities especially for the design of solid dosage forms. Further products in this context are **Parteck® delta M** (delta mannitol), **Parteck® M** (directly compressible mannitols), **Parteck® SI** (directly compressible sorbitols) and **Parteck® LUB** (various lubricants).

Parteck® ODT is produced using a unique spray and mixing technology which offers distinct advantages in direct compression to the pharmaceutical formulator. It is particularly developed to ensure a robust dosage form design of rapidly disintegrating drugs and to simplify their manufacturing as well.

2. Composition and CAS Numbers

Parteck® ODT is a combination of specifically spray-granulated D-mannitol and croscarmellose sodium. Croscarmellose sodium is the sodium salt of a cross-linked, partly *O*-(carboxymethylated) cellulose.[1]

All compounds within **Parteck® ODT** are conforming to the requirements of the relevant pharmacopeias.

D-Mannitol (Ph. Eur., BP, JP, USP, E 421)	CAS Registry	69-65-8
Croscarmellose sodium (NF, Ph. Eur., JP)	CAS Registry	74811-65-7

3. Appearance and Properties

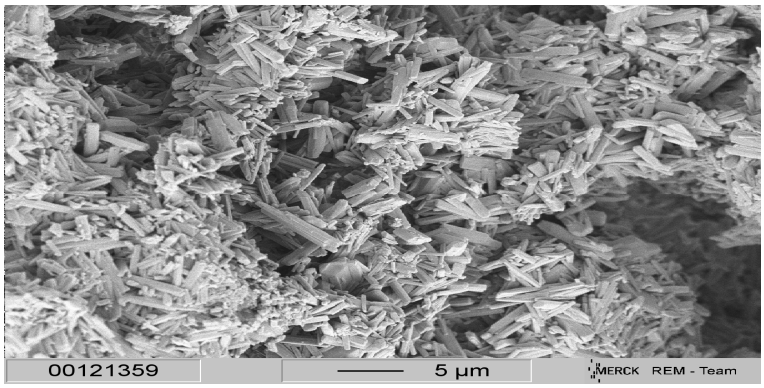
Parteck® ODT is a white, colorless, free-flowing and low hygroscopic powder showing unique particle morphology and properties.

• Bulk density	0.55 – 0.65 g/ml
• Tapped density	0.70 – 0.80 g/ml
• Mean particle size distribution (measured by laser diffraction, D 0.50)	70 – 120 µm
• Angle of repose	33 – 38°
• pH value (of a 5% aqueous solution, partially dissolved)	5.0 – 7.0
• BET surface area (measured by nitrogen adsorption)	2.4 – 3.5 m^2/g

The typical technical data above serve to generally characterize the excipient. These values are not meant as specifications and they do not have binding character. The product specification is available separately, on request.

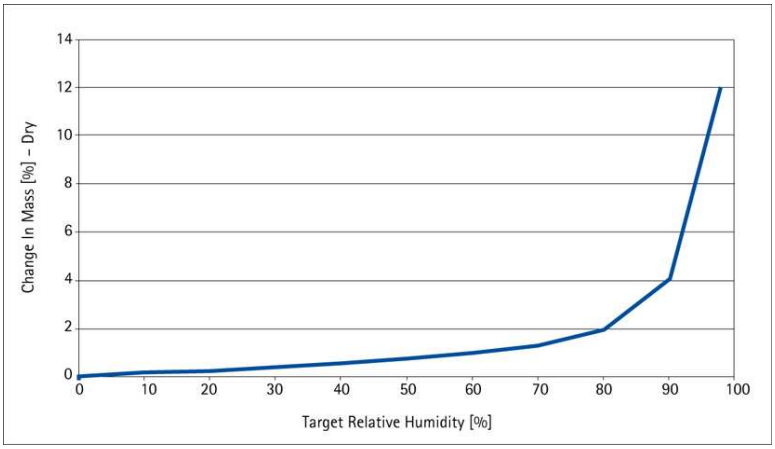
[1] USP 24-NF 19

SEM 1. Morphology of **Parteck® ODT** powder (magnification 2000x)



Compression with **Parteck® ODT** minimizes the wear and tear of the tabletting equipment since **Parteck® ODT**, due to its open filamentous particle structure, allows tablets to be compacted at quite low compression forces.

Figure 1. Dynamic vapor sorption isotherm for **Parteck® ODT** at 25 °C



Parteck® ODT exhibits low hygroscopicity, a typical and well-known characteristic of mannitol. Below 80% relative humidity at 25 °C the moisture sorption of **Parteck® ODT** is below 2%. Due to its low hygroscopic behavior, it is eminently suitable for moisture-sensitive active ingredients.

4. Direct Compression Properties

Parteck® ODT placebo formulation

Parteck® ODT, Merck KGaA, Cat. No. 100490	495 mg	99%
Parteck® LUB MST Magnesium stearate, Merck KGaA, Cat. No. 100663	5 mg	1%

Parteck® LUB MST Magnesium stearate is sieved through a 250 µm sieve onto the Parteck® ODT and than blended for 10 minutes in a drum hoop mixer (J. Engelsmann AG, Germany). After that, the tabletting mixture is compressed on a Korsch EK 0 single punch instrumented tablet press and on a Korsch PH 230/14 high speed rotary press with a total tablet weight of 500 mg into 11 mm tablets, flat, facetted at 52 rpm.

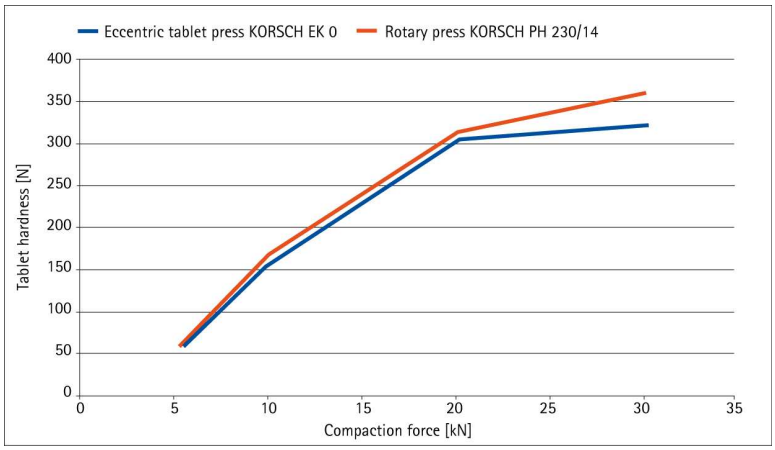
Tablet hardness is measured with an Erweka TBH 30 MD and the Ph. Eur./USP disintegration test method with automatic detection is applied in 800 ml of demineralized water at 37 °C.

Table 1. Physical data for **Parteck® ODT** placebo tablets ex rotary press

Compaction force [kN]	5	10	20	30
Tablet thickness [mm]	5.1	4.5	4.1	3.9
Tablet weight [mg]	495.3	496.4	495.4	496.1
Weight variation [% RSD[1]]	0.47	0.46	0.35	0.41
Tablet hardness [N]	59	168	313	360
Hardness variation [% RSD[1]]	8.31	9.94	18.67	14.81
Disintegration[2] [s]	56 – 106	64 – 120	74 – 104	126 – 142
Friability[3] [%]	0.34	0.06	0.03	0.06

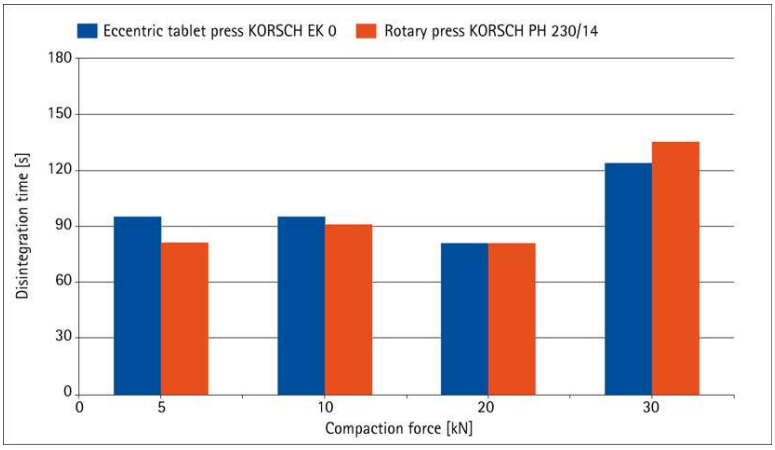
[1] Relative standard deviation
[2] Problems with tablets adhering to the disks result in prolonged disintegration times
[3] Friability acc. to the Ph. Eur./USP test method

Figure 2. **Parteck® ODT** placebo compression profile (single punch vs. rotary press)



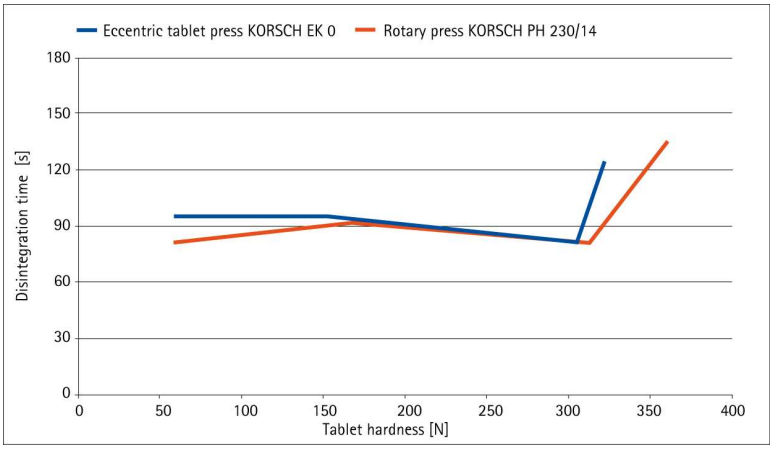
Good tablet quality can be achieved with very low compaction forces.

Figure 3. Influence of compaction force on disintegration time (single punch vs. rotary press)



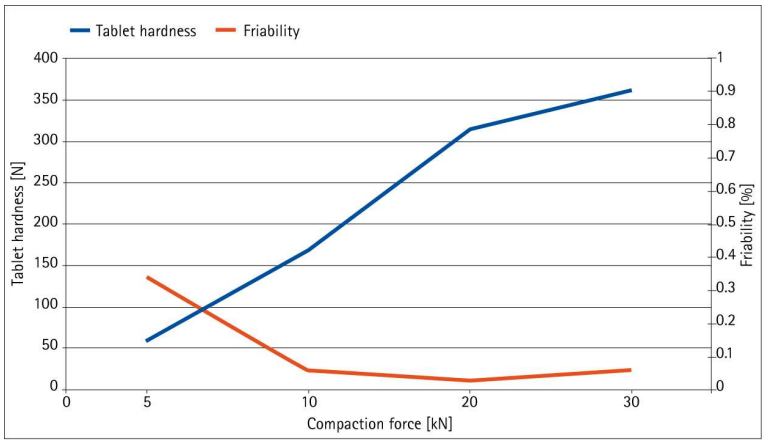
Fast tablet disintegration time even with high compaction forces.

Figure 4. Effect of tablet hardness on disintegration time (single punch vs. rotary press)



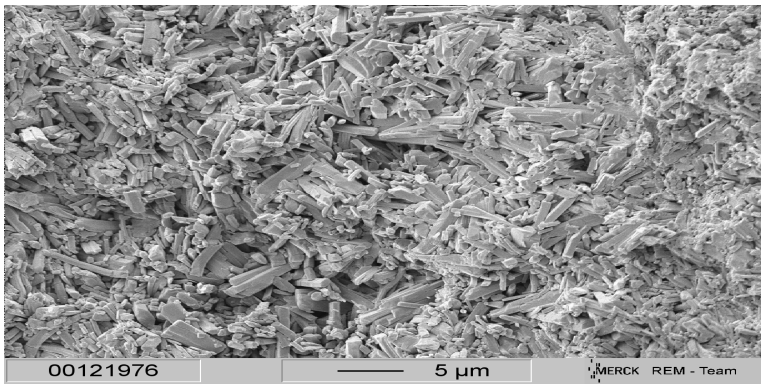
Increased physical stability of the tablets does not compromise disintegration time up to a tablet hardness of around 300 N.

Figure 5. Tablet hardness and friability as a function of compaction force ex rotary press



Friability over a broad hardness range is exceedingly low, as the diagram clearly shows. Even at a very low compaction force – e.g. 5 kN – friability of less than 0.4% can be achieved. This excellent characteristic of **Parteck® ODT** allows the manufacture of extremely rugged tablets.

SEM 2. Morphology of a **Parteck® ODT** tablet breaking edge (compaction force 11 kN, magnification 2000x)



The filamentous particle structure of **Parteck® ODT** is still present after the compression procedure. The unique particle structure and greatly increased surface area of **Parteck® ODT** facilitate extremely fast disintegration of even very hard tablets.

5. Sensitivity of Parteck® ODT Against Lubricants

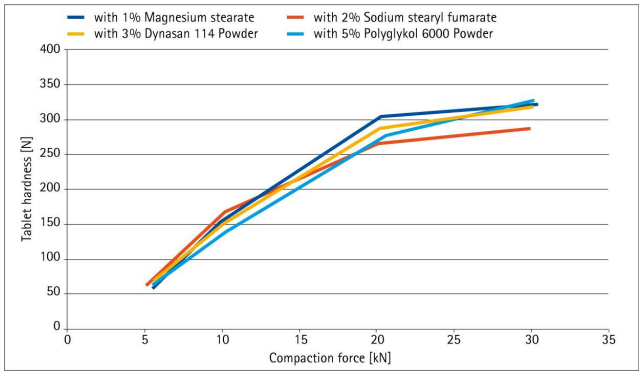
Parteck® ODT formulations with several lubricants

Parteck® ODT, Merck KGaA, Cat. No. 100490	495 mg	99%
Parteck® LUB MST Magnesium stearate, Merck KGaA, Cat. No. 100663	5 mg	1%
Parteck® ODT, Merck KGaA, Cat. No. 100490	490 mg	98%
PRUV™ Sodium stearyl fumarate, JRS Pharma GmbH & Co. KG	10 mg	2%
Parteck® ODT, Merck KGaA, Cat. No. 100490	485 mg	97%
Dynasan® 114 Powder, Sasol Germany GmbH	15 mg	3%
Parteck® ODT, Merck KGaA, Cat. No. 100490	475 mg	95%
Polyglykol® 6000 Powder, Clariant GmbH	25 mg	5%

For each formulation the different lubricants are sieved through a 250 µm sieve onto the Parteck® ODT and then blended for 5 minutes in a Turbula® shaker-mixer. After that, the tabletting mixtures are compressed on a Korsch EK 0 single punch instrumented tablet press (52 rpm, 11 mm diameter punch, flat, facetted) into tablets with a total tablet weight of 500 mg.

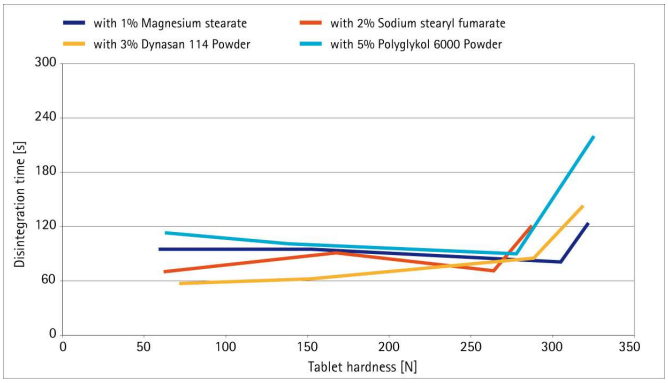
Tablet hardness is measured with an Erweka TBH 30 MD and the Ph. Eur./USP disintegration test method with automatic detection is applied in 800 ml of demineralized water at 37 °C.

Figure 6. Influence of the lubricant on tablet hardness



The formulation with sodium stearyl fumarate as lubricant shows a tablet hardness that is marginally lower than with the other lubricants at higher compaction forces, but that is still at a high level.

Figure 7. Influence of the lubricant on disintegration time



There is no significant influence on the disintegration behavior of **Parteck® ODT** observed by using different lubricants within a broad tablet hardness range.

6. Drug Formulations with Parteck® ODT by Direct Compression

Parteck® ODT formulation with 250 mg acetaminophen (sample No. 1)

Parteck® ODT, Merck KGaA, Cat. No. 100490	700 mg	70%
Paracetamol Acetaminophen, Merck KGaA, Cat. No. 817040	250 mg	25%
Dynasan® 118 micro fine, Sasol Germany GmbH	40 mg	4%
Silicon dioxide highly dispersed, Merck KGaA, Cat. No. 113126	10 mg	1%

Parteck® ODT, acetaminophen and silicon dioxide highly dispersed are blended for 5 minutes and passed through a 1.0 mm sieve. Afterwards, Dynasan® 118 micro fine is sieved through a 250 µm sieve onto the mixture and then again all components are blended for 5 minutes in a Turbula® shaker-mixer. In the next step, the tabletting mixture is compressed on a Korsch EK 0 single punch instrumented tablet press (52 rpm, 15 mm diameter punch, flat, facetted) into tablets with a total tablet weight of 1000 mg.

Tablet hardness is measured with an Erweka TBH 30 MD and the Ph. Eur./USP disintegration test method with automatic detection is applied in 800 ml of demineralized water at 37 °C.

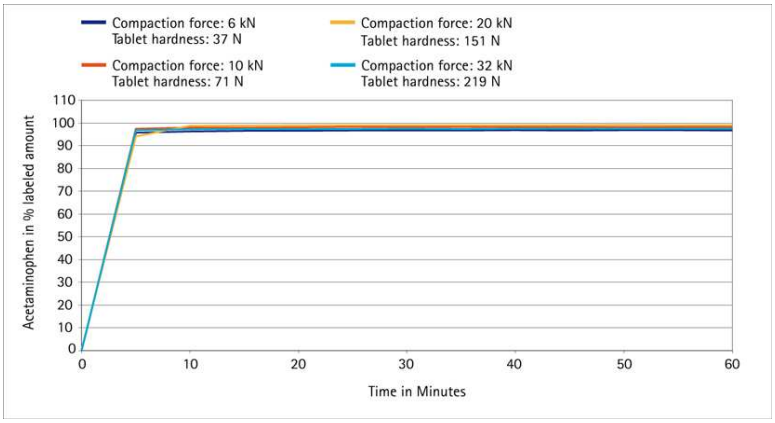
Table 2. Physical data for acetaminophen tablets based on **Parteck® ODT**

Compaction force [kN]	6	10	20	32
Tablet thickness [mm]	6.0	5.5	5.0	4.7
Tablet weight [mg]	997.2	992.0	992.8	989.7
Weight variation [% RSD[1]]	0.29	0.30	0.49	0.41
Tablet hardness [N]	37	71	151	219
Hardness variation [% RSD[1]]	13.90	8.75	15.33	19.97
Disintegration[2] [s]	56 – 70	48 – 58	44 – 56	50 – 104
Friability[3] [%]	3.04	0.79	0.31	0.15

[1] Relative standard deviation
[2] Problems with tablets adhering to the disks result in prolonged disintegration times
[3] Friability acc. to the Ph. Eur./USP test method

Figure 8. In-vitro acetaminophen release from **Parteck® ODT**-based tablets

Dissolution procedure: USP Apparatus 2 (Paddle Apparatus), 900 ml phosphate buffer, pH 5.8, 37 °C, 50 rpm, detection wavelength 243 nm



In all case studies more than 90% of the labeled amount of acetaminophen is dissolved from **Parteck® ODT**-based tablets after 5 minutes. There is virtually no influence on the in-vitro dissolution behavior observed by increasing tablet hardness and compaction forces.

Parteck® ODT formulation with 250 mg acetaminophen (sample No. 2)

Parteck® ODT, Merck KGaA, Cat. No. 100490	222.3 mg	44.46%
Compap PVP3® Acetaminophen, Mallinckrodt Inc.	257.7 mg	51.54%
PRUV™ Sodium stearyl fumarate, JRS Pharma GmbH & Co. KG	15 mg	3%
Silicon dioxide highly dispersed, Merck KGaA, Cat. No. 113126	5 mg	1%

Parteck® ODT, acetaminophen and silicon dioxide highly dispersed are blended for 5 minutes and passed through a 1.0 mm sieve. Afterwards, sodium stearyl fumarate is sieved through a 250 µm sieve onto the mixture and then again all components are blended for 5 minutes in a Turbula® shaker-mixer. In the next step, the tabletting mixture is compressed on a Korsch EK 0 single punch instrumented tablet press (52 rpm, 11 mm diameter punch, flat, facetted) into tablets with a total tablet weight of 500 mg.

Tablet hardness is measured with an Erweka TBH 30 MD and the Ph. Eur./USP disintegration test method with automatic detection is performed in 800 ml of demineralized water at 37 °C.

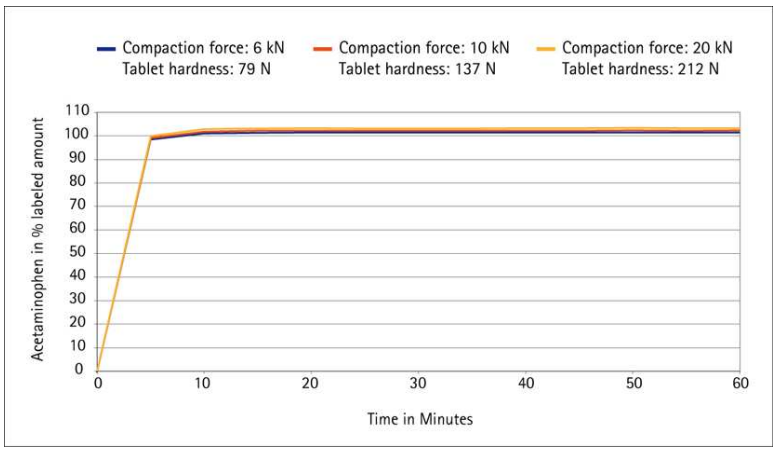
Table 3. Physical data for acetaminophen tablets based on **Parteck® ODT**

Compaction force [kN]	6	10	20
Tablet thickness [mm]	5.1	4.7	4.3
Tablet weight [mg]	497.5	498.2	499.7
Weight variation [% RSD[1]]	0.26	0.16	0.19
Tablet hardness [N]	79	137	212
Hardness variation [% RSD[1]]	6.86	8.66	4.98
Disintegration [s]	46 – 86	34 – 54	72 – 82
Friability[2] [%]	0.26	0.25	0.21

[1] Relative standard deviation
[2] Friability acc. to the Ph. Eur./USP test method

Figure 9. In-vitro acetaminophen release from **Parteck® ODT**-based tablets

Dissolution procedure: USP Apparatus 2 (Paddle Apparatus), 900 ml phosphate buffer, pH 5.8, 37 °C, 50 rpm, detection wavelength 243 nm



After 5 minutes nearly 99% of the labeled amount of acetaminophen is dissolved from the **Parteck® ODT**-based formulation by all three tested samples. In this case study there is also no observable influence of the tablet hardness and compaction forces on active substance release.

Parteck® ODT formulation with 250 mg calcium carbonate (100 mg calcium)

Parteck® ODT, Merck KGaA, Cat. No. 100490	434.9 mg	54.36%
Formaxx™ $CaCO_3$ 70, Merck KGaA, Cat. No. 114737	357.1 mg	44.64%
Parteck® LUB MST Magnesium stearate, Merck KGaA, Cat. No. 100663	8 mg	1%

Parteck® LUB MST Magnesium stearate is sieved through a 250 µm sieve onto the Parteck® ODT and Formaxx™ $CaCO_3$ 70. The components are blended for 5 minutes in a Turbula® shaker-mixer. After that, the tabletting mixture is compressed on a Korsch EK 0 single punch instrumented tablet press (52 rpm, 13 mm diameter punch, biconvex) into tablets with a total tablet weight of 800 mg.

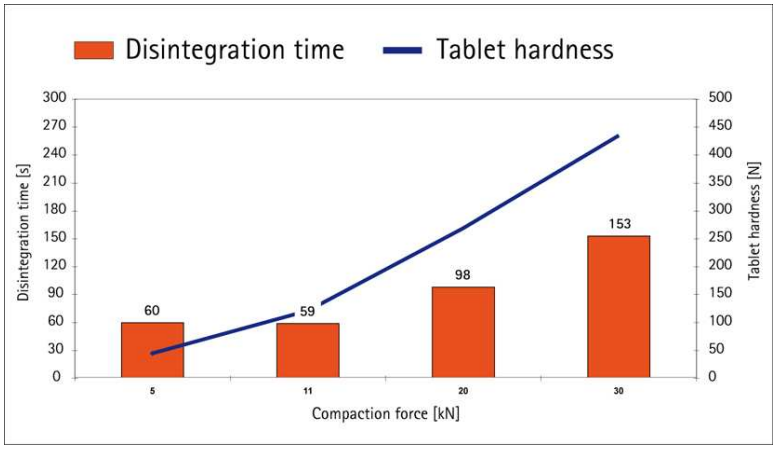
Tablet hardness is measured by Erweka TBH 30 MD and the Ph. Eur./USP disintegration test method with automatic detection is performed in 800 ml of demineralized water at 37 °C.

Table 4. Physical data for calcium carbonate tablets based on **Parteck® ODT**

Compaction force [kN]	5	11	20	30
Tablet thickness [mm]	6.2	5.8	5.3	5.1
Tablet weight [mg]	795.5	797.9	802.7	804.3
Weight variation [% RSD[1]]	0.27	0.35	0.52	0.31
Tablet hardness [N]	45	121	269	435
Hardness variation [% RSD[1]]	3.30	4.68	9.49	13.69
Disintegration [s]	38 – 78	48 – 74	90 – 116	142 – 172
Friability[2] [%]	1.04	0.32	0.16	0.14

[1] Relative standard deviation
[2] Friability acc. to the Ph. Eur./USP test method

Figure 10. Influence of compaction force on disintegration time and tablet hardness



There is nearly no negative influence observed on the disintegration behavior of calcium carbonate tablets based on **Parteck® ODT** up to a compaction force of 30 kN.

Parteck® ODT formulation with 200 mg ibuprofen

Parteck® ODT, Merck KGaA, Cat. No. 100490	290 mg	58%
Ibuprofen 38 micron, BASF SE	200 mg	40%
Silicon dioxide highly dispersed, Merck KGaA, Cat. No. 113126	5 mg	1%
Parteck® LUB MST Magnesium stearate, Merck KGaA, Cat. No. 100663	5 mg	1%

Parteck® ODT, ibuprofen and silicon dioxide highly dispersed are blended for 5 minutes and passed through a 1.0 mm sieve. Afterwards, Parteck® LUB MST magnesium stearate is sieved through a 250 µm sieve onto the mixture and then again all components are blended for 5 minutes in a Turbula® shaker-mixer. In the next step, the tabletting mixture is compressed on a Korsch EK 0 single punch instrumented tablet press (52 rpm, 11 mm diameter punch, flat, facetted) into tablets with a total tablet weight of 500 mg.

Tablet hardness is measured using an Erweka TBH 30 MD and the Ph. Eur./USP disintegration test method with automatic detection is applied in 800 ml of demineralized water at 37 °C.

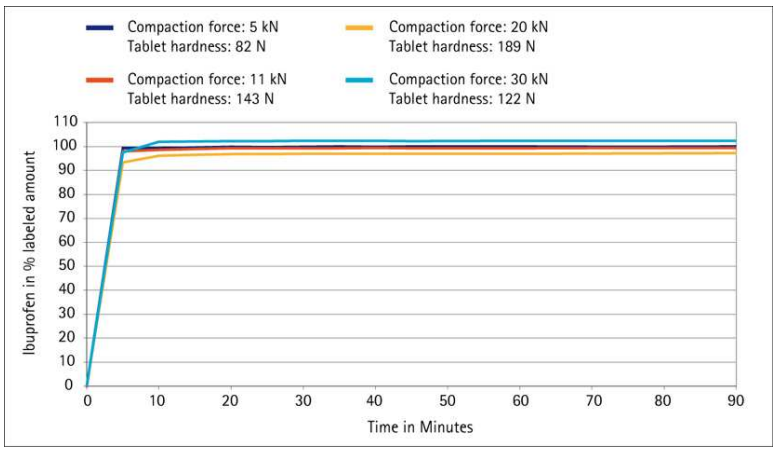
Table 5. Physical data for ibuprofen tablets based on **Parteck® ODT**

Compaction force [kN]	5	11	20	30
Tablet thickness [mm]	5.2	4.9	4.7	4.6
Tablet weight [mg]	500.4	502.1	509.6	510.3
Weight variation [% RSD[1]]	0.38	0.36	0.54	0.53
Tablet hardness [N]	82	143	189	122
Hardness variation [% RSD[1]]	8.73	10.88	12.30	16.56
Disintegration [s]	40 – 72	68 – 74	148 – 164	190 – 216
Friability[2] [%]	0.28	0.29	0.38	0.74

[1] Relative standard deviation
[2] Friability acc. to the Ph. Eur./USP test method

Figure 11. In-vitro ibuprofen release from **Parteck® ODT**-based tablets

Dissolution procedure: USP Apparatus 2 (Paddle Apparatus), 900 ml phosphate buffer, pH 7.2, 37 °C, 50 rpm, detection wavelength 221 nm



After 10 minutes all of the ibuprofen has been released. There is no significant **Parteck® ODT** influence observed on the ibuprofen dissolution behavior, not even by increasing tablet hardness and compaction forces.

7. General Formulation with Parteck® ODT

Parteck® ODT allows the designing of a robust dosage form in an easy and cost-efficient way, irrespective of the drug substance grade, tablet weight and tablet size.

The following approximate simple formulation should give good results for a variety of drugs:

Active ingredient	4 – 50%
Parteck® ODT	30 – 80%
Colloidal silicon dioxide	0.2 – 1.0%
Magnesium stearate	0.25 – 1.0%
Alternative lubricant:	
Sodium stearyl fumarate	0.5 – 2.0%

If the active ingredient has a very strong unpleasant taste, which is not covered by the taste-masking performance of Parteck® ODT, additional flavor(s) and/or sweetening agents may be added to the formulation.

8. Main Benefits of Parteck® ODT

- **Direct compressibility:** facilitates formulation work and reduces production costs
- **High compactibility even at low compression forces:** reduces stress on tabletting presses and tooling
- **Exceptionally strong tablet hardness possible associated with reduced capping tendency:** simplifies formulation work and handling – improves product quality
- **Fast disintegration and dissolution performance of the resulting tablets over a broad compression and hardness range:** ensures production safety and product quality
- **Smooth mouth feel and a pleasant taste:** improves patient compliance
- **No license agreement or payment required:** saves time

9. Specification

The currently valid specification can be retrieved from the website: www.merck4pharma.com

10. Storage and Shelf Life

Storage in tightly closed packs protected from moisture. The storage temperature should be kept around 25 °C. Minimum 2 years shelf life when stored in unopened original packs in this way.

11. Packaging and Ordering Information

100490 Parteck® ODT	1 kg	PE bottle with a screw cap	Order No. 1.00490.1000
100490 Parteck® ODT	25 kg	PE bag in carton box	Order No. 1.00490.9025

12. Safety Data Sheet

The currently valid safety data sheet can be retrieved from the website: www.merck4pharma.com

13. Legal Disclaimer

We provide information and advice to our customers on application technologies and regulatory matters to the best of our knowledge and ability, but without obligation or liability. Existing laws and regulations are to be observed in all cases by our customers. This also applies in respect to any rights of third parties. Our information and advice do not relieve our customers of their own responsibility for checking the suitability of our products for the envisaged purpose.

Latest update: August 25, 2009