Omya Consumer Goods
omya.com

Pharmaceutical Oral Dosage Forms

Enlighten your formulation

THINKING OF TOMORROW

Active Pharmaceutical Ingredient

Natural Calcium Carbonate

Omya offers certified high purity, Natural Calcium Carbonate – a source of highly bioavailable calcium, specially designed for pharmaceutical applications.

Omya Natural Calcium Carbonate is suitable for solid and liquid oral dosage forms in pharma applications. Two product ranges are available: Omyapure® and Omya-Cal®.

Benefits

- *High purity*
- *Compliant with Pharmacopeia*
- *GMP*

APPLICATIONS:

Osteoporosis treatment

Antacids

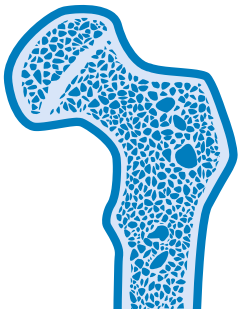
PRODUCTS:

Omyapure®

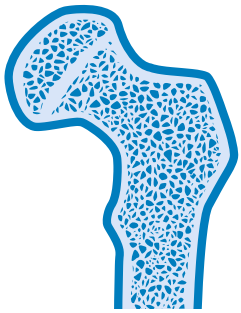
Omya-Cal®

Osteoporosis treatment

Human bone contains 99% of the total body calcium. Strong bones are the result of a good balance between the formation and resorption of bone mass. Bone calcium balance is neutral in healthy young adults. The resorption of old bone is equal to the formation of new bone. Osteoporosis occurs when the process is out of balance and often appears during normal aging or pregnancy.



Osteoporotic bone



Remineralized bone + Ca^{2+}

"It is estimated that an osteoporotic fracture occurs every 3 seconds." [1]

In order to prevent and treat osteoporosis, availability of Ca^{2+} in blood plasma is of high importance to facilitate the incorporation of the calcium mineral into the bones. Calcium Carbonate is insoluble at neutral pH but soluble in the acidic environment of the stomach. Upon reaction with hydrochloric acid, calcium ions are released and absorbed in the small intestine.

Calcium Carbonate provides similar oral calcium absorption to that of other calcium salts.[2]

Ref.1. International Osteoporosis Foundation
Ref.2. Weaver, Connie M., International Dairy Journal: Solubility and Absorbability of Calcium Salts 8 (1998), 443-449.

Omyapure® 35 - OG
Omyapharm® 500 - OG

Omya distribution products: Vitamin D_3, Vitamin K_2

Swallowable tablet formulation

Ingredients	Content %	Content per tablet (mg)	Active content per tablet (mg)
Omyapure® 35 - OG (Natural Calcium Carbonate)	50	400	400
Vitamin K2 4500 ppm	1.9	15.2	0.0675
Vitamin D3 100000 IU/g	0.4	3.2	0.0077
Omyapharm® 500 - OG	46.9	397	
Croscarmellose sodium	0.5	4	
Magnesium stearate	0.2	2	
Total	100	821.4	

Procedure

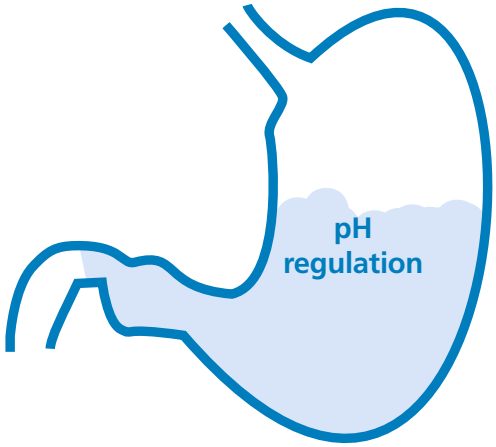
Mix all active ingredients together with Omyapharm® 500 - OG in the turbula mixer for 10 minutes. Granulate the blend by roller compaction. Then, add crosscarmellose sodium and mix again in the turbula mixer for 5 minutes. Finally, add magnesium stearate to the blend and mix for additional 5 minutes. Tablet the final blend.

Equipment	
Mixer	Turbula® - T 10 F
Roller compactor	Fitzpatrick CCS220
Tablet press	Fette1200i
Hardness tester	Pharmatron MultiTest 50
Friability tester	Erweka TAR 120
Disintegration tester	Pharmatron Disitest 50

Tablet characteristics	
Compaction force (kN)	6.8
Ejection force (N)	350
Tablet dimensions (diameter x height) (mm)	13 x 3.5
Tablet weight (mg)	800
Hardness (N)	90
Friability (%)	0.24
Disintegration time (s)	25

Antacids

Antacids are frequently used to neutralize gastric acid excess, providing relief against heartburn.
They do not prevent gastric acid overproduction but help to neutralize acid secretions.



Omyapure® and Omya-Cal® comply with most stringent quality requirements.

One of the most used alkaline APIs in antacid formulations is Calcium Carbonate. It acts as a buffer by reacting with the hydrochloric acid in the stomach as follows:

$$CaCO_3 + 2\ HCl \rightarrow CaCl_2 + CO_2 + H_2O$$

Omyapure® and Omya-Cal® are suitable for liquid and solid dosage forms. In suspensions, the low particle size of Omyapure® and Omya-Cal® ensures physical stability. In tablets, a wet granulation step is required prior to tableting.

Omyapure® 35 - OG
Chewable tablet formulation

No	Ingredients	% (w/w)	Content per tablet (mg)
1	**Natural Calcium Carbonate (Omyapure® 35 - OG)**	48.5	511.19
2	**PVP K-90**	3.50	36.89
3	**Mannitol DC**	29.3	308.82
4	**Sorbitol DC**	15	158.10
5	**Orange flavour**	2	21.08
6	**FD&C Yellow #6**	0.1	1.05
7	**Sucralose**	0.1	1.05
8	**Magnesium stearate**	1.50	15.81
	Total	100	1054

Procedure

Granulate Omyapure® 35 - OG with PVP K-90 in a fluid bed equipment (top-spraying). Blend the granulated Calcium Carbonate with mannitol DC, sorbitol DC, orange flavour and sucralose in the turbula mixer for 10 minutes. Then, add magnesium stearate and FD&C yellow #6 to the mixture and blend for additional 5 minutes. Tablet the final blend in a rotary tablet press.

Equipment	
Mixer	Turbula® - T 10 F
Roller compactor	Fitzpatrick CCS220
Tablet press	Fette1200i
Hardness tester	Pharmatron MultiTest 50
Friability tester	Erweka TAR 120
Fluid bed	Glatt GPCG2 Top spray 6L

Tablet characteristics	
Compaction force (kN)	8.8
Ejection force (N)	251
Tablet dimensions (diameter x height) (mm)	13 x 5.78
Tablet weight (mg)	1054
Hardness (N)	82
Friability (%)	0.03

Excipients for solid oral dosage forms

Omya offers two different product ranges

Highly Structured Minerals

Omyapharm®

Water dispersible tablets & ODTs
Carrier
Dry granulation
Wet granulation

Natural Calcium Carbonate

Omyapure®
Omya-Cal®

Wet granulation

Omyapharm® is a multifunctional excipient based on Omya proprietary technology and suitable for a wide range of applications. It is a co-processed excipient consisting of Calcium Carbonate and tribasic calcium phosphate.

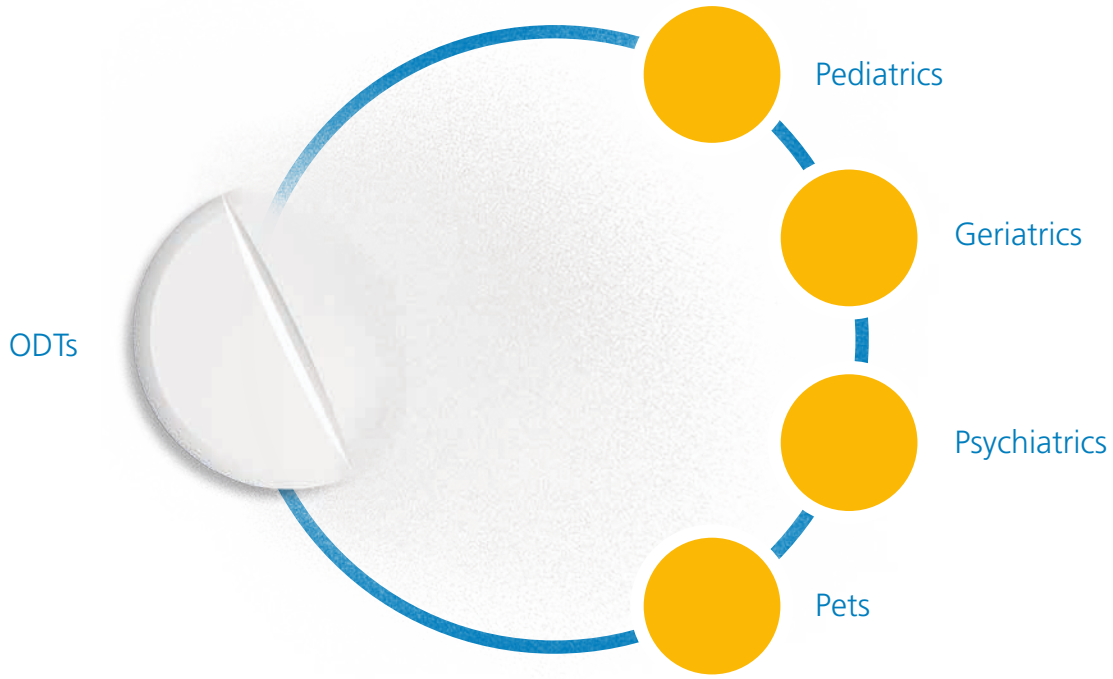
All Omyapharm® ingredients are monographed and Generally Recognised as Safe (GRAS).

PHARMACEUTICAL FORMS:

- *Chewable tablets*
- *Water dispersible tablets*
- *ODTs*
- *Granules*
- *Capsules*

Water dispersible tablets and ODTs

ODTs (Orally Dispersible Tablets) are innovative drug delivery systems used to improve patient compliance. ODTs are designed to disintegrate rapidly on contact with saliva, thus eliminating the need to chew the tablet, swallow an intact tablet, or take the tablet with liquids.



ODTs are a preferred dosage form when patient compliance is a challenge such as geriatric, psychiatric and paediatric patients.

In addition, they have become increasingly atractive for product life cycle management and marketing purposes.

Omya has developed Omyapharm®, an innovative direct compressible excipient for ODTs.

Orally dispersible tablets have received ever-increasing demand during the last decade

Benefits

- *Excellent compactability*
- *Fast disintegration time*
- *Fast drug release*
- *ODT disintegration time independent of hardness*

Excellent compactability

Thanks to the external lamellae and highly porous structure, Omyapharm® allows high compactability.
As shown in the comparative compaction profile in Figure 1, Omyapharm® is more compactable than ready-to-use ODT platforms.

Granules containing Omyapharm® and a superdisintegrant showed superior compactability properties than ready-to-use ODT platforms available in the market

Technical facts*

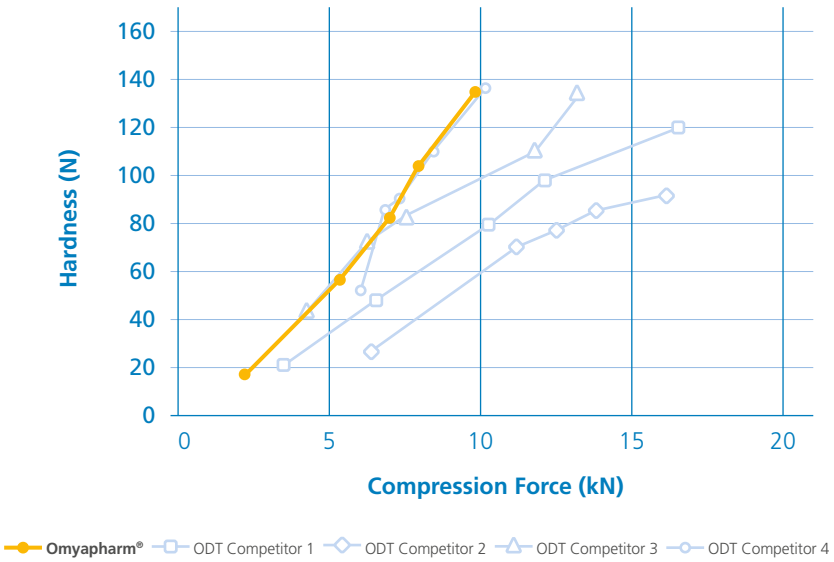
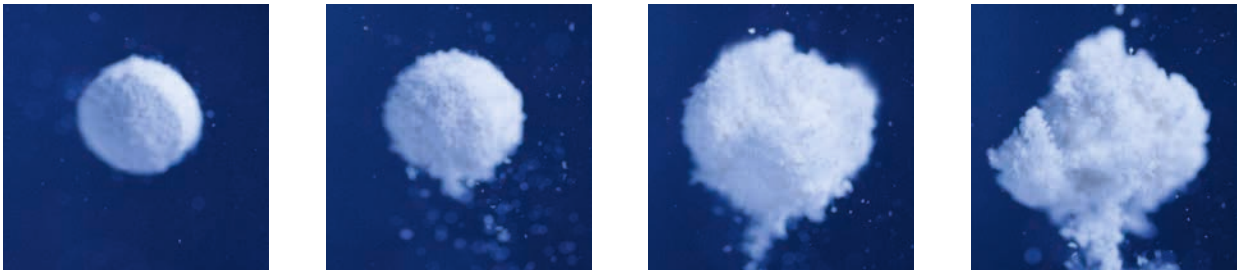


Figure 1: *Compaction profile (compression force vs hardness) of caffeine-containing ODTs*

Omyapharm®-based formulations show a linear increase in tablet hardness with increasing compression forces. When using Omyapharm®, lower compression forces are needed to reach the desired tablet hardness.

**Comparative studies performed at Omya pharma application laboratory*

Fast disintegration time



Fast disintegration is a key performance attribute of ODTs. Omyapharm® enables very fast disintegration times due to the preserved high porosity.

ODTs manufactured from Omyapharm® completely disintegrate within 5 seconds

Technical facts*

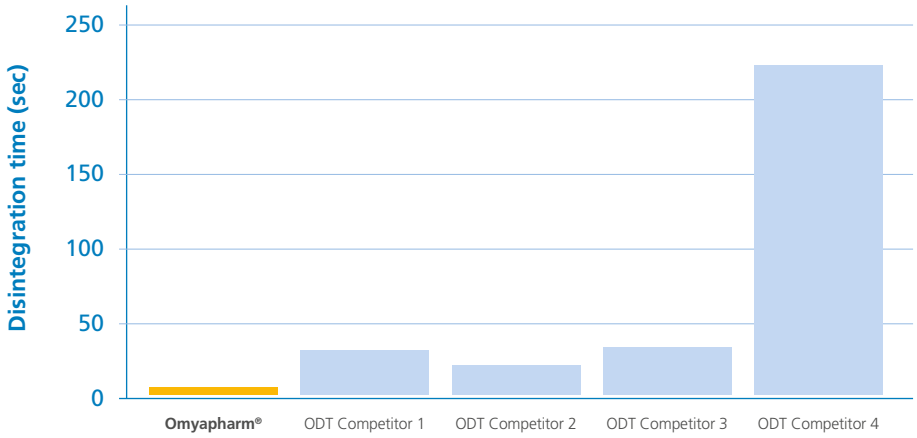


Figure 2: *Disintegration time of caffeine-containing ODTs*

ODTs formulated with Omyapharm® disintegrate twice as fast as a market reference

**Comparative studies performed at Omya pharma application laboratory*

ODT disintegration time is independent of tablet hardness

The robustness of an ODT platform allows a constant disintegration time across a wide range of tablet hardnesses. The disintegration time for Omyapharm®-based formulations remains short, despite a large hardness range, as shown in figure 3.

Omyapharm® in ODTs means hardness and fast disintegration

Technical facts*

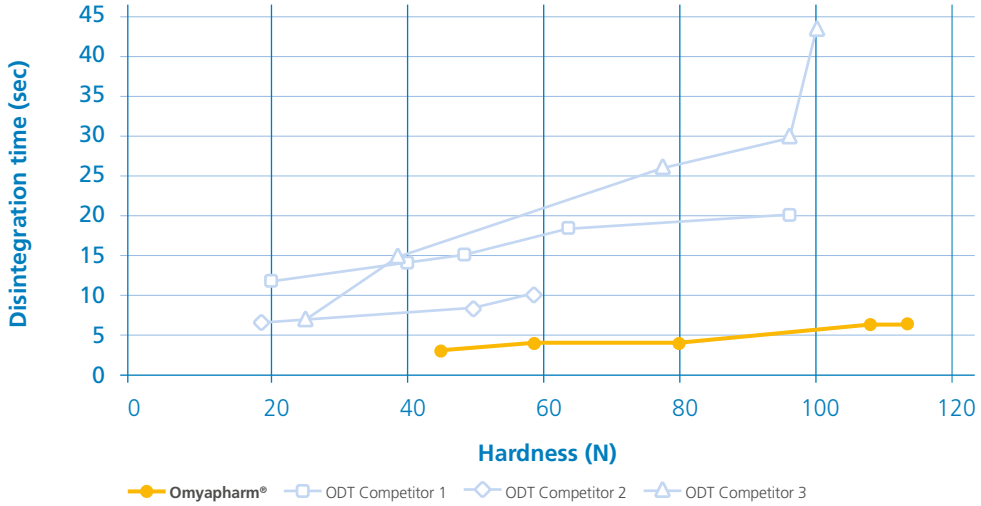


Figure 3: *ODT disintegration time as a function of the tablet hardness*

Fast drug release

In ODTs short disintegration times must be correlated to fast drug release. This is important to ensure the timely onset of the expected therapeutic effect. Omyapharm® formulation releases 100% of the caffeine contained in the ODTs within only 2 minutes, indicating a good correlation between the disintegration time and the release of the drug.

Technical facts*

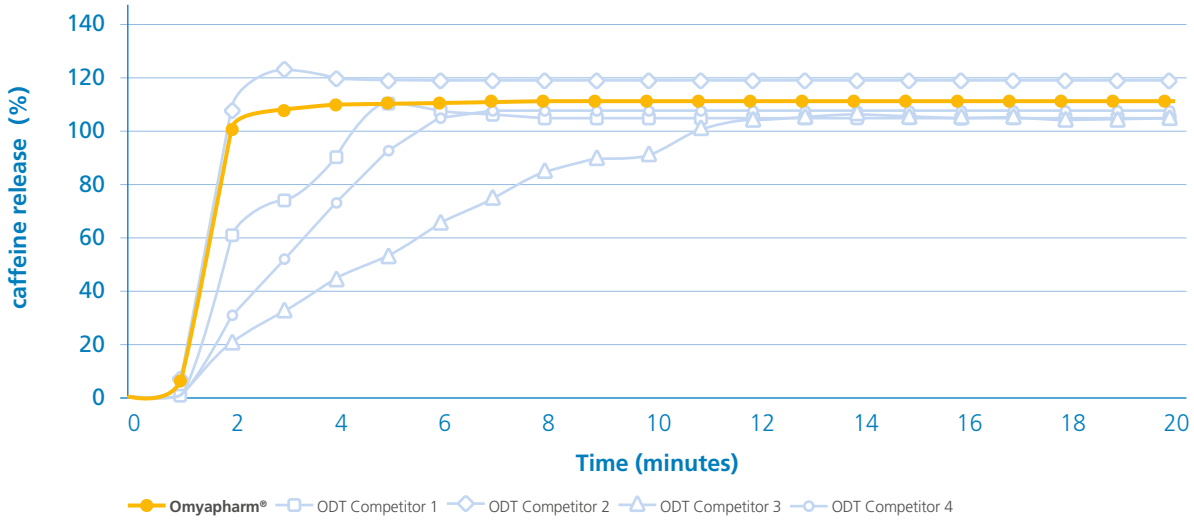


Figure 4: *Caffeine release from ODTs*

**Comparative studies performed at Omya pharma application laboratory*

Carrier

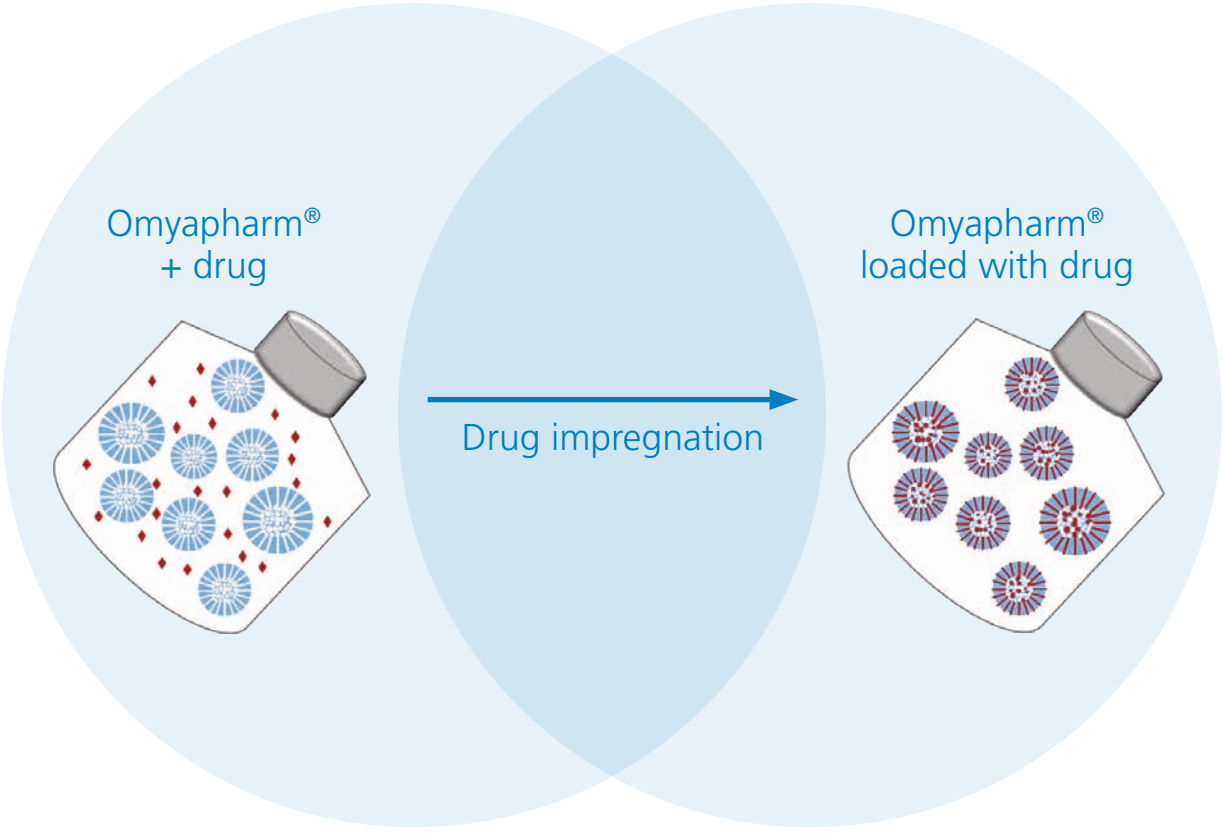
Solid dosage forms are the form of choice and preferred over liquid formulations due to ease of use, improved stability and robustness. Oil-based formulations are becoming increasingly important in pharma applications. For example, lipid-based formulations have drawn considerable attention as a way to increase bioavailability of poorly soluble actives.

Omyapharm® can be used to convert oils into compressible powders

Omyapharm® can be used as an efficient carrier to convert liquids and oils into compressible powders. For instance, oily drugs or drugs dissolved in lipids in SEEDS (self-emulsifying drug delivery systems) and SMEEDS (self-microemulsifying drug delivery systems) formulations can be converted into compressible powders with Omyapharm®.

Benefits

- *Highly efficient & compactable carrier*
- *High oil absorption capacity*
- *Excellent compactability and low friability*



Highly efficient & compactable carrier

Thanks to its external lamellar structure and high internal porosity, Omyapharm® can be loaded with up to 50% w/w* with hydrophilic or hydrophobic substances.

** 50% w/w: 50 g of oil/drug plus 50 g of Omyapharm®*

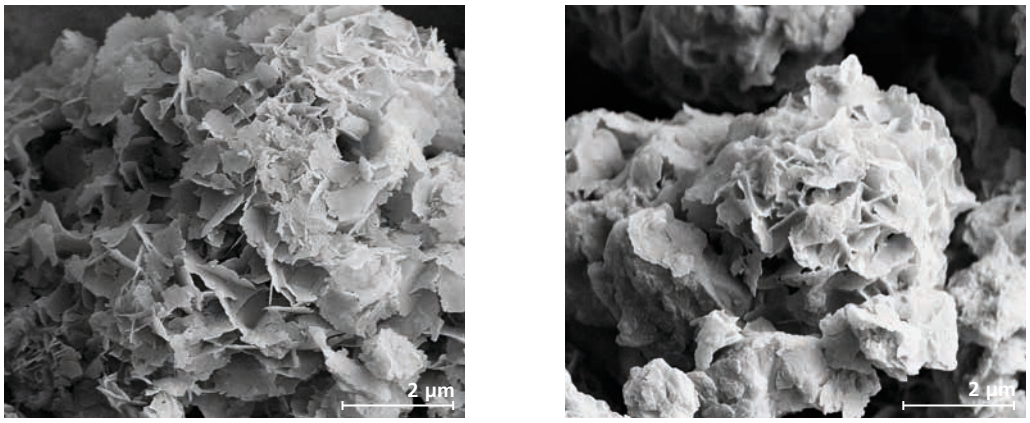
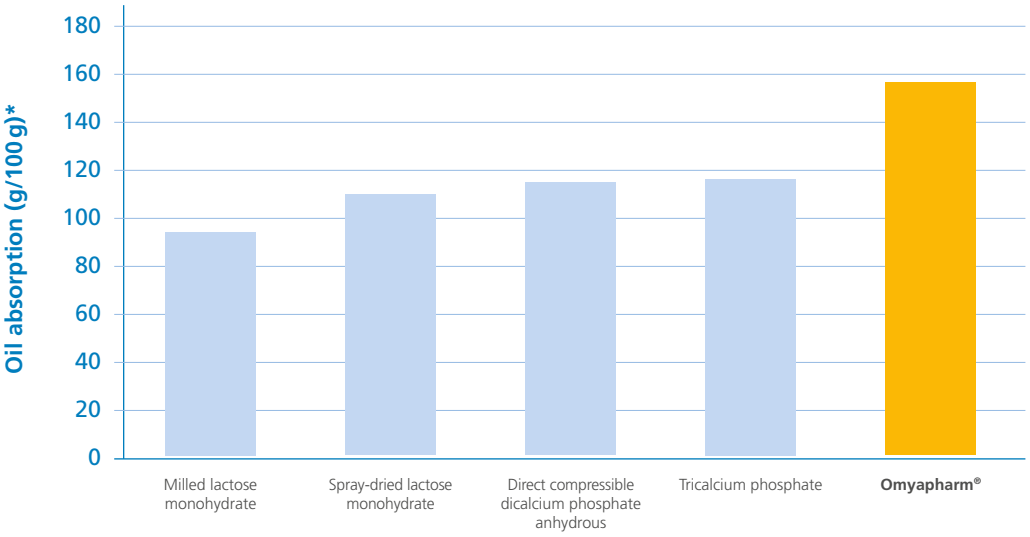


***Figure 5:** left: unloaded Omyapharm® carrier, right: loaded Omyapharm® carrier showing effective pore filling by the active*

High oil absorption capacity

As it can be seen in figure 6, Omyapharm® shows a higher absorption capacity than other common compressible ingredients, such as lactose and calcium phosphates.



*Brabender absorptometer to measure paraffin oil absorption

***Figure 6:** Oil absorption capacity of several excipients*

High Compactability and Low Friability

Dextrose formulations containing 10% of Omyapharm® loaded with oil can be directly compressed into tablets. These tablets show increased hardness and reduced friability when compared to tablets formulated with dextrose excipient alone.

Compactability

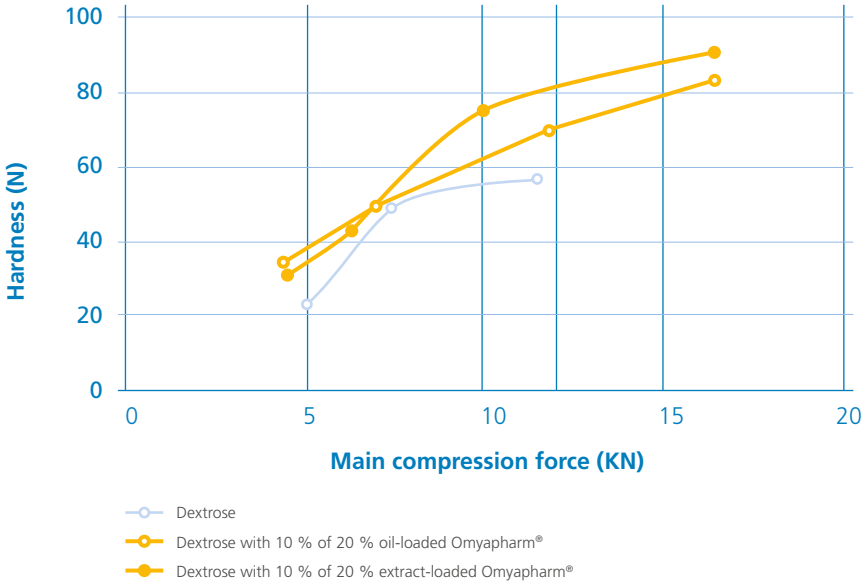


Figure 7: *Compaction profile of oil-containing tablets*

Friability

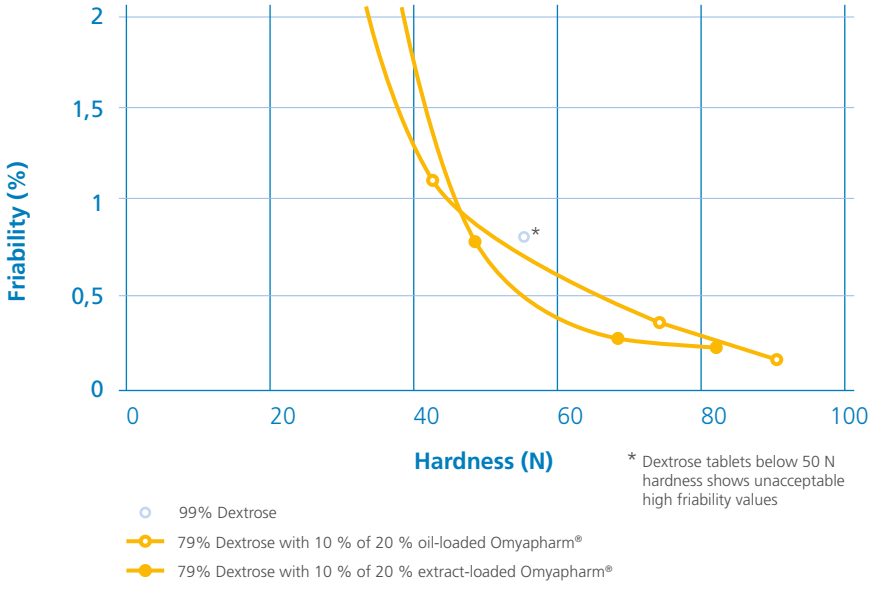


Figure 8: *Friability of oil-containing tablets*

Dry granulation

Dry granulation is the granulation method of choice for moisture or temperature sensitive APIs. In comparison to wet granulation, dry granulation is a faster and a more cost-effective process, which offers improved physical and chemical compatibility as well as easier scalability and technology transfer. Omyapharm® can be used in dry granulation as a highly efficient dry binder with excellent compaction properties.

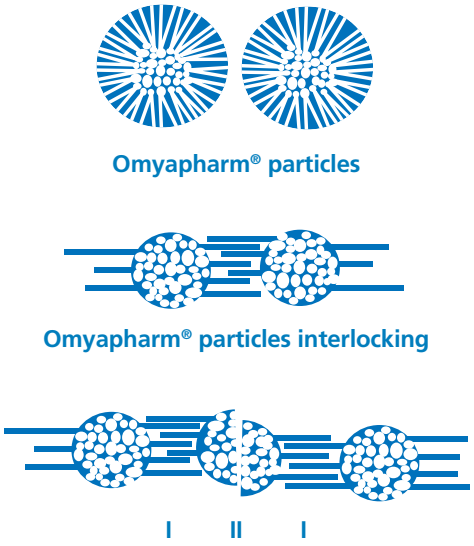


Figure 9: *Illustration of the compaction mechanism of Omyapharm® excipient*

Highly efficient binder

Omyapharm® has an unique morphology and physical structure. Its external lamellar structure provides many potential binding points for mechanical interlocking. Under low compression forces, Omyapharm® can be compacted into stable granules with preserved internal porosity.

Omyapharm® has a plastic-brittle behaviour as shown in figure 9. At low compression forces interlocking of lamellaes (I) results in interparticle bonding. At high compression forces, the particle fragments, creating new surfaces for interparticle bonding (II).

Benefits

- *Highly efficient binder*
- *Excellent compactability properties*
- *Retained high porosity*

Excellent recompactability properties

Omyapharm® shows excellent recompactability properties, much higher than microcrystalline cellulose (MCC) and lactose. As in figure 10, placebo tablets manufactured by dry granulation of Omyapharm® show excellent mechanical properties, with increased hardness compared to those of MCC and lactose.

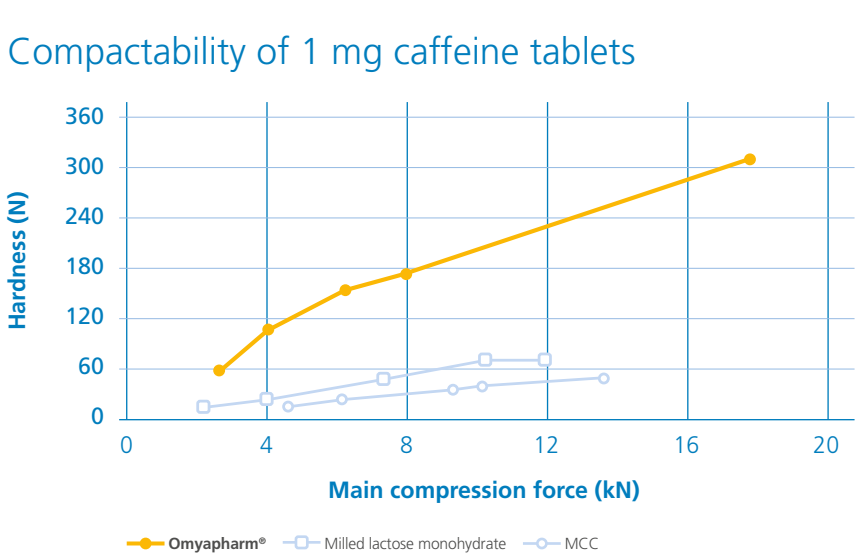


Figure 10: *Compaction profile (compression force vs hardness) of tablets obtained via dry granulation*

Wet granulation

Wet granulation is been extensively used in tablet manufacturing. It is the preferred process in the following cases:

· High-dose drug formulations with actives exhibiting poor flow and compactabilty

· Very potent low-dose drug formulations

Natural Calcium Carbonate is an efficient functional filler in wet granulation processes. As shown in figure 11, $CaCO_3$ can be used in tablet formulations in combination with other excipients such as MCC.

Compactability

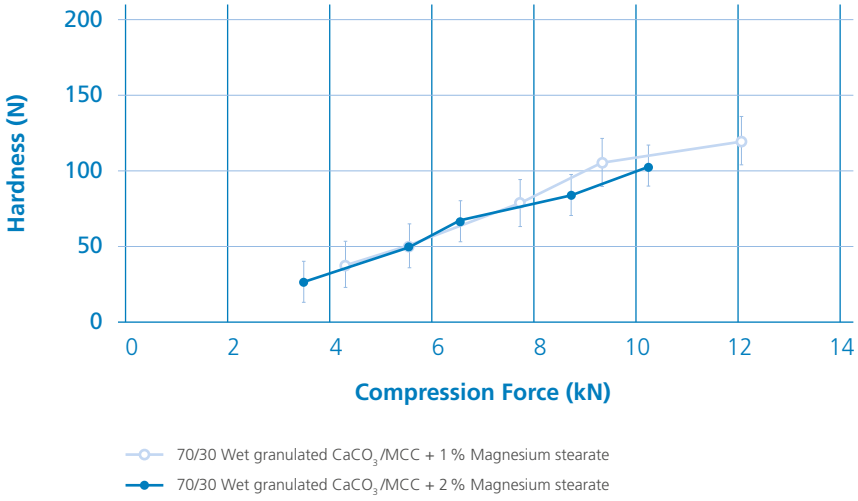


Figure 11: *Compaction profile of wet-granulated Calcium Carbonate & microcrystalline cellullose tablets*

Benefits

- *Lactose-free*
- *Gluten-free*
- *Suitable for diabetics*
- *Low reactive impurities level*
- *Compatibility with a wide range of excipients and actives*

Dry binder for direct compression

Omyapharm® is a highly efficient dry binder. As little as 5% can significantly improve direct compression manufacturing process.

Compactability 20 mg piroxicam tablets

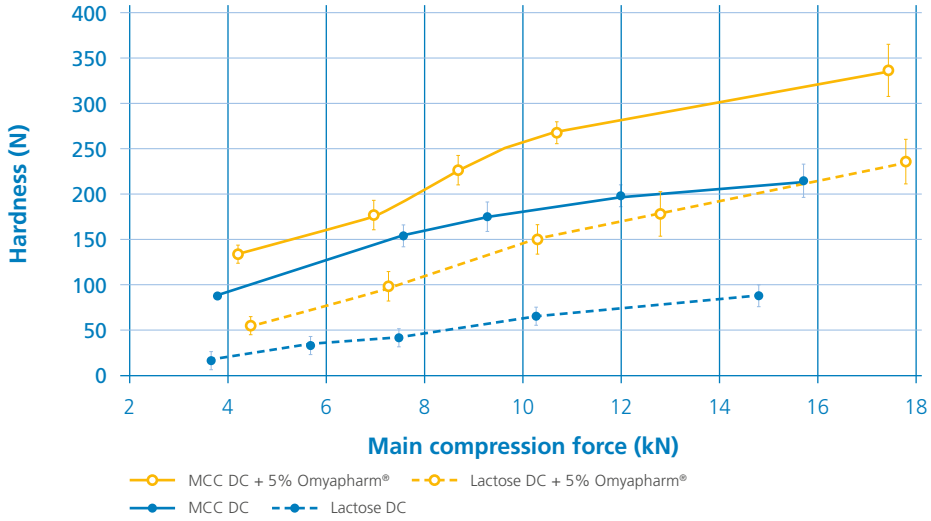
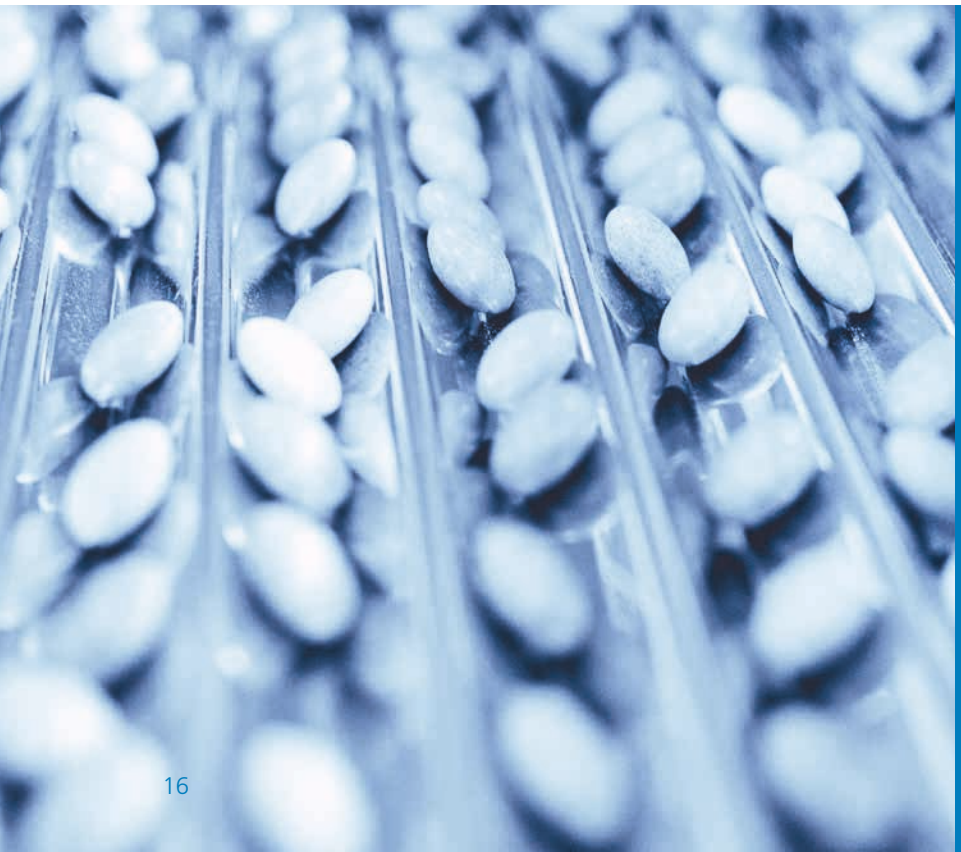


Figure 12: *5% of Omyapharm® significantly improved the compactability of MCC and lactose-based direct compressible filler-binders*



Omyapharm® as a dry binder in direct compression processes can:

- *Improve compactability*
- *Reduce disintegration time*
- *Lower ejection forces*
- *Lower friability*

Disintegration 20 mg piroxicam tablets

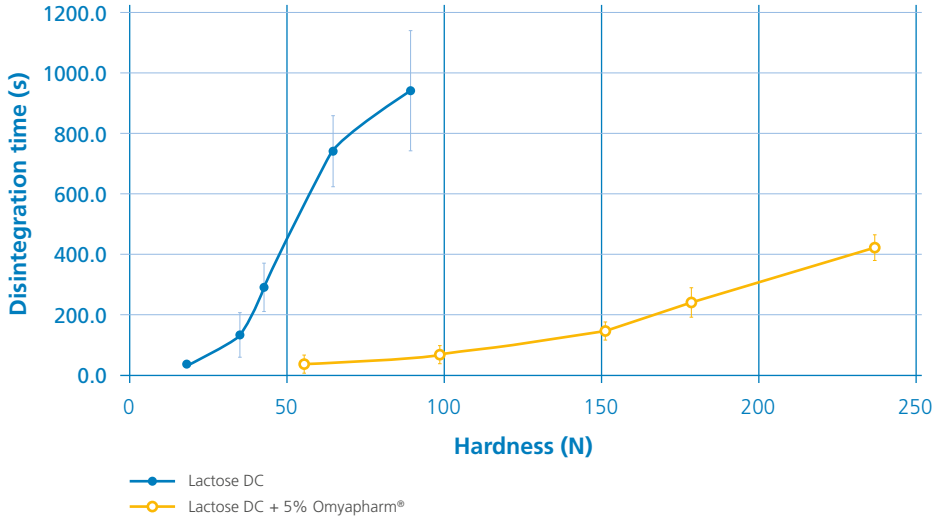


Figure 13: *5% of Omyapharm® significantly decreased the disintegration time of equal hardness tablets using a lactose-based direct compressible filler-binder. The addition of Omyapharm® to the formulation reduced dependency of disintegration time on hardness*

The addition of Omyapharm® can reduce the amount of lubricant and disintegrate needed. Additionally, due to the lower compression forces required, it can reduce machine wearability and may contribute to the chemical stability of actives, by lowering temperature during tableting.

Friability 20 mg piroxicam tablets

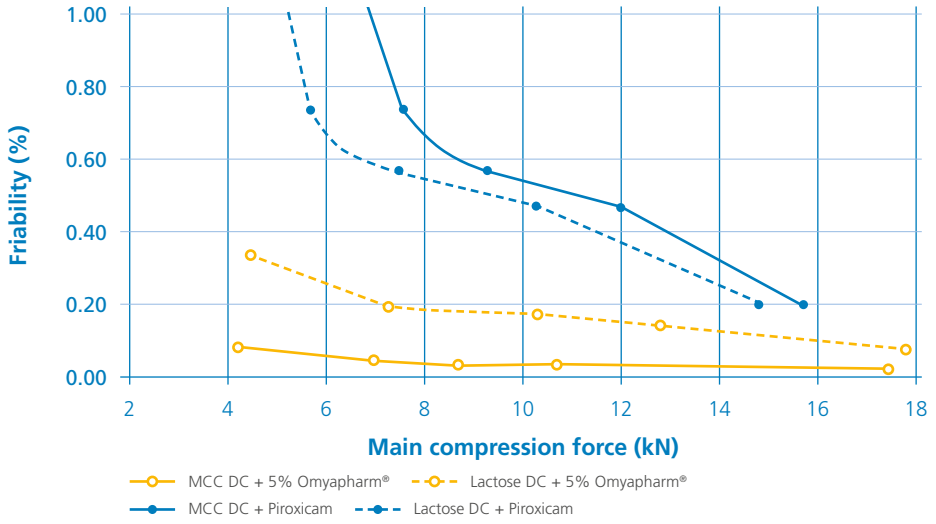


Figure 14: *5% of Omyapharm® increased the mechanical stability of formulations containing a MCC or a lactose-based direct compressible filler-binder*

Expertise and state-of-the-art facilities for dedicated customer support

Our team of experts advises on customer product formulations and continously develop new mineral solutions for pharma applications.
In our state-of the-art pharma laboratory in Switzerland (Oftringen) we are ready to support you with your projects.

Developing pharma innovative solutions for our customers

Product Recommendation

High-purity Natural Calcium Carbonate

	Omyapure® 35 - OG	Omya-Cal® USP-4 - AZ	Omya-Cal® USP-10 - AZ	Omya-Cal® USP/EP-15 - AZ
Applications				
Osteoporosis treatment	√	√	√	√
Antacid	√	√	√	√
Regulatory & Quality Status				
Pharmacopeia compliance	EP/USP/JP	USP	USP	EP/USP
Manufacturing standards	cGMP/ ICHQ7	cGMP/ ICHQ7	cGMP/ ICHQ7	cGMP/ ICHQ7
Regulatory submissions	CEP	DMF Type II	DMF Type II	DMF Type II
Product Characteristics				
Calcium Carbonate content	98.5 - 100.5%	98 - 100.5%	98 - 100.5%	98.5 - 100.5%
Median particle size (d50%)	3.0 µm	3.3 µm	12.0 µm	14.5 µm
Production site	Orgon (France)	Arizona (US)	Arizona (US)	Arizona (US)

Multifunctional Excipient – Omyapharm®

	Omyapharm® 500 - OG
Applications	
Wet granulation	√
Dry granulation	√
Hot-melt extrusion	√
Dry binder	√
Carrier	√
ODT formulation	√
Regulatory & Quality Status	
Manufacturing standards	EXCiPACT
Product Characteristics	
Product	Powder
Compactability	High
Production site	Orgon (France)

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THIS PAPER CONTAINS OMYA PIGMENTS

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