Oral Dosage Forms

Enlighten your formulation
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:

Antacids
Osteoporosis treatment

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.

“It is estimated that an osteoporotic fracture occurs every 3 seconds.”¹

In order to prevent and treat osteoporosis, availability of Ca²⁺ 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

Omyapure® 35-OG
Omyapharm® 500-OG
Omya distribution products: Vitamin D₃, Vitamin K₂

Swallowable tablet formulation

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

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 croscarmellose 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

Ref. 1. International Osteoporosis Foundation
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.

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:

$$\text{CaCO}_3 + 2 \text{HCl} \rightarrow \text{CaCl}_2 + \text{CO}_2 + \text{H}_2\text{O}$$

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:

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

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

### 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. Table 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

Omyapharm® is a multifunctional excipient platform 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. Omyapharm® ODT platform contains additionally croscarmellose sodium as a superdisintegrant.

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

PHARMACEUTICAL FORMS:
- Chewable tablets
- Water dispersible tablets
- ODTs
- Granules
- Capsules
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.

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
Omyapharm® is an innovative direct compressible platform for ODTs.
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 the most compactable ODT platform.

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*Omyapharm® ODT platform shows superior compactability properties Vs. other excipients in the market.*

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Technical facts*

Omyapharm® ODT platform shows a linear increase in tablet hardness with increasing compression forces. When using Omyapharm® ODT platform, lower compression forces are needed to reach the desired tablet hardness.

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*Figure 1. Compaction profile (Compression force vs hardness) of caffeine-containing ODTs*
Fast disintegration is a key performance attribute of ODTs. Omyapharm® ODT platform enables very fast disintegration times due to the preserved high porosity.

**Technical facts***

*ODTs manufactured from Omyapharm® completely disintegrate within 5 seconds.*

![Figure 2. Disintegration time of caffeine-containing ODTs](image)

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

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*Technical facts*

Comparative studies performed at Omyapharma application laboratory.

Current marketed ODT platforms were compared to Omyapharm® ODT platform.
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.

Technical facts*

*Medium and high dose products available

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.

Technical facts*

Comparative studies performed at Omya pharma application laboratory. Current marketed ODT platforms were compared to Omyapharm® ODT platform.

Figure 4. Caffeine release from ODTs

Omyapharm® 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.
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.

The Omyapharm® excipient range 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

Omyapharm® loaded with drug

Drug impregnation

Omyapharm® + drug
Highly efficient & compactable carrier

Due to the high specific surface area and high internal porosity Omyapharm®, excipients 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®

High oil absorption capacity

As it can be seen in figure 6, Omyapharm® shows a higher absorption capacity than other common ingredients, such as sugars, cellulose or other inorganic excipients.

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

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

![Compactability Graph]

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

Friability

![Friability Graph]

**Figure 8.** Friability of oil-containing tablets

* Dextrose tablets below 50 N hardness show unacceptable high friability values
Dry granulation

Dry granulation is the granulation method of choice for moisture or temperature sensitive APIs. Dry granulation, in comparison to wet 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 as a highly efficient dry binder with excellent compaction properties.

Highly efficient binder

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

Omyapharm® shows a plastic-brittle behaviour as 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 re-compactability properties, much higher than microcrystalline cellulose (MCC). As in figure 10, placebo tablets manufactured by dry granulation of Omyapharm® show excellent mechanical properties, with increased hardness compared to those of MCC.

Re-Compactability

Figure 10. Recompactability (dry-granulation plus tableting) properties of Omyapharm® & microcrystalline cellulose excipient
Wet granulation

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

- High-dose drug formulations with actives exhibiting poor flow and compactability
- Very potent low-dose drug formulations

Natural Calcium Carbonate is an efficient functional filler in wet granulation processes. As shown in figure 11, CaCO₃ can be used in tablet formulations in combination with other excipients such as MCC.

**Benefits**

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

**Figure 11.** Compaction profile of wet-granulated calcium carbonate & microcrystalline cellulose tablets
Expertise and state-of-the-art facilities for dedicated customer support

Our team of experts advises on customer product formulations and continuously 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

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoporosis treatment</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Antacid</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

| Certifications                              |                   |                      |                       |                          |
| Pharmacopeia                                | EP/USP/IP         | USP                  | USP                   | EP/USP                   |
| GMP                                         | ICH Q7A           | ✓                    | ✓                     | ✓                        |

| Product Characteristics                      |                   |                      |                       |                          |
| Purity                                      | 99.50%            | >99%                 | >99%                  | >99%                     |
| Median particle size d(50)                  | 3.0 μm            | 3.3 μm               | 12.0 μm               | 14.5 μm                  |
| Production site                             | Orgon (France)    | Arizona (US)         | Arizona (US)          | Arizona (US)             |

Multifunctional Excipient Platform – Omyapharm®

<table>
<thead>
<tr>
<th>Applications</th>
<th>Omyapharm® 500-OG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wet granulation</td>
<td>✓</td>
</tr>
<tr>
<td>Dry granulation</td>
<td>✓</td>
</tr>
<tr>
<td>Hot-melt extrusion</td>
<td>✓</td>
</tr>
<tr>
<td>Direct compression</td>
<td>✓</td>
</tr>
<tr>
<td>Carrier</td>
<td>✓</td>
</tr>
<tr>
<td>Microencapsulation</td>
<td>✓</td>
</tr>
<tr>
<td>Fast disintegration</td>
<td></td>
</tr>
</tbody>
</table>

| Product Characteristics                      |                   |
| Product                                      | Powder            |
| Compressibility                             | Compressible      |
| Production site                             | Orgon (France)    |
Omya Consumer Goods

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