Omyapharm

A newly developed structured mineral as multifunctional excipient

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Company Profile

Omya is a **leading global producer** of calcium carbonate and a **worldwide distributor** of specialty additives, premium services and solutions.

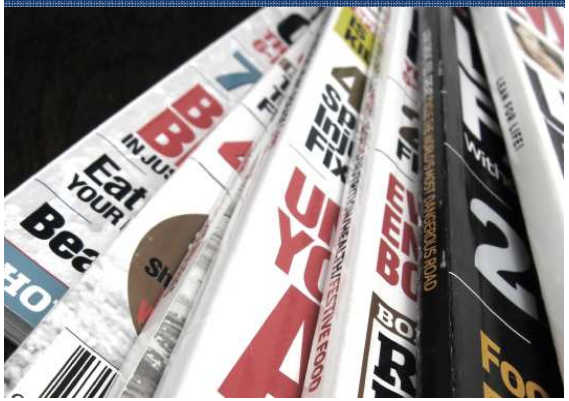
In the segment of consumer goods, Omya provides **innovative solutions** based on high purity natural **minerals and complementary ingredients** meeting the most stringent regulatory and quality standards.

Key Facts & Figures

- Corporate head office in **Oftringen**, Switzerland
- **8,000 employees**
- **175 plants** in over **50 countries**
- Turnover of **CHF 3.5 billion**
- Ownership of mineral deposits for the next **100 years** of business
- Most plants are **ISO** 9001 / **ISO** 14001 certified
- **Pioneer** in ISO 14001 for quarries
- In business for **130 years**
- **Privately-owned** Swiss based Corporation

Our Markets

Printing & Writing



Construction

Technical Polymer Applications

Packaging

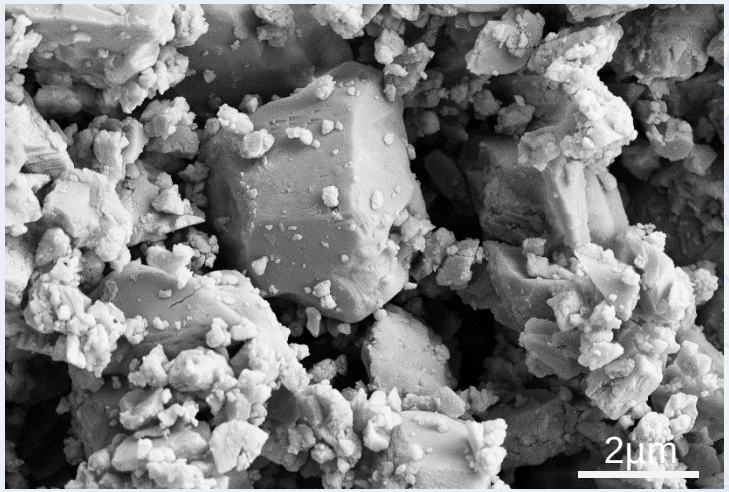
Consumer Goods

Agriculture & Forestry

Water & Energy

Pharmaceuticals- Natural Calcium Carbonate

Omyapure 35 OG

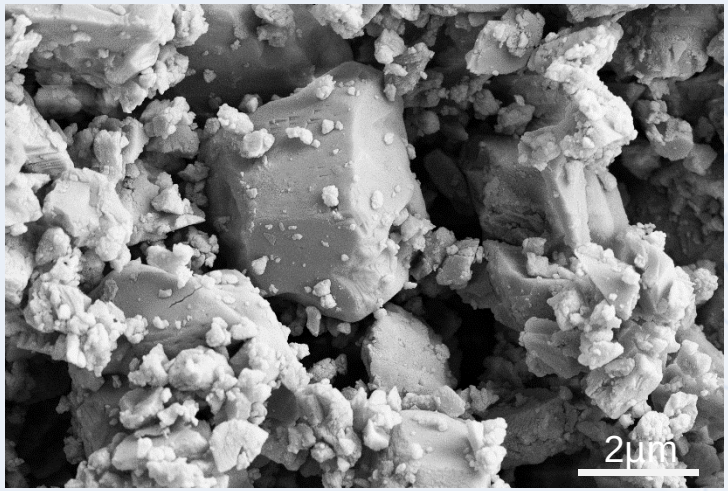


First producer of **natural calcium carbonate** to achieve the certificate of suitability **(CEP/CoS)** in accordance with the EP as an **API** (EDQM)

- **Active ingredient** in antacids
- **Natural source** of calcium in osteoporosis treatment and mineral supplements

Omyapharm- Functionalized Calcium Carbonate

Omyapure 35 OG



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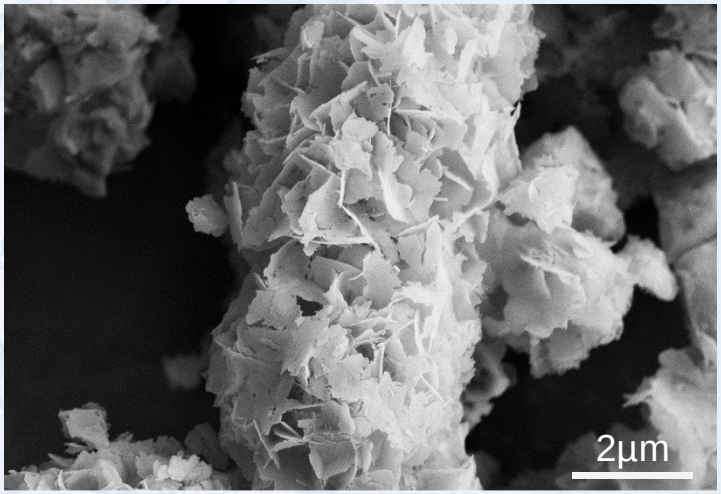
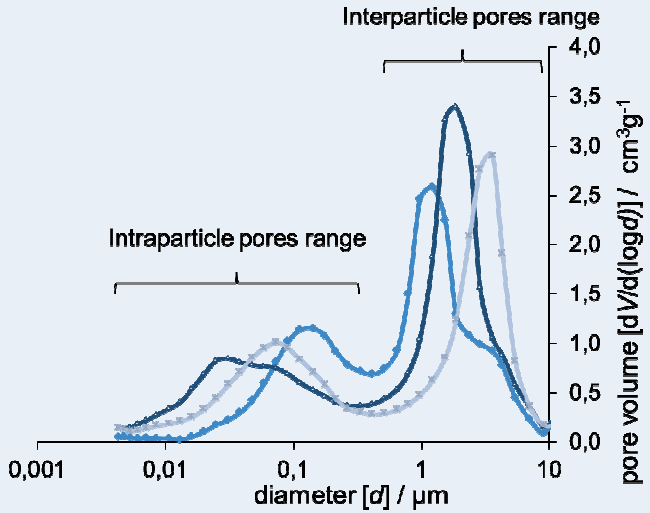
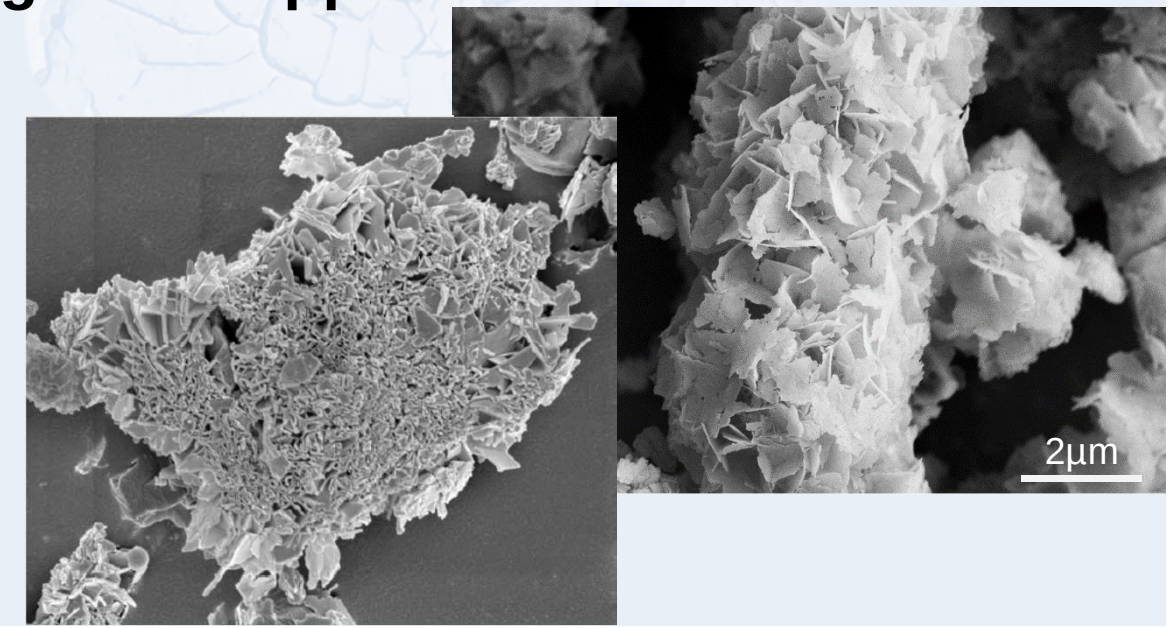


- Recrystallization process
- Final product mixture of monographed minerals
  - Calcium carbonate
  - Hydroxylapatite

Omyapharm Functionalized Calcium Carbonate

- **Discrete particles (no agglomerate)**
- **Lamellar structure**
- **High porosity**
- **High specific surface area**
- **PSD, SSA, pore size range and surface chemistry can be tailored according to the application**



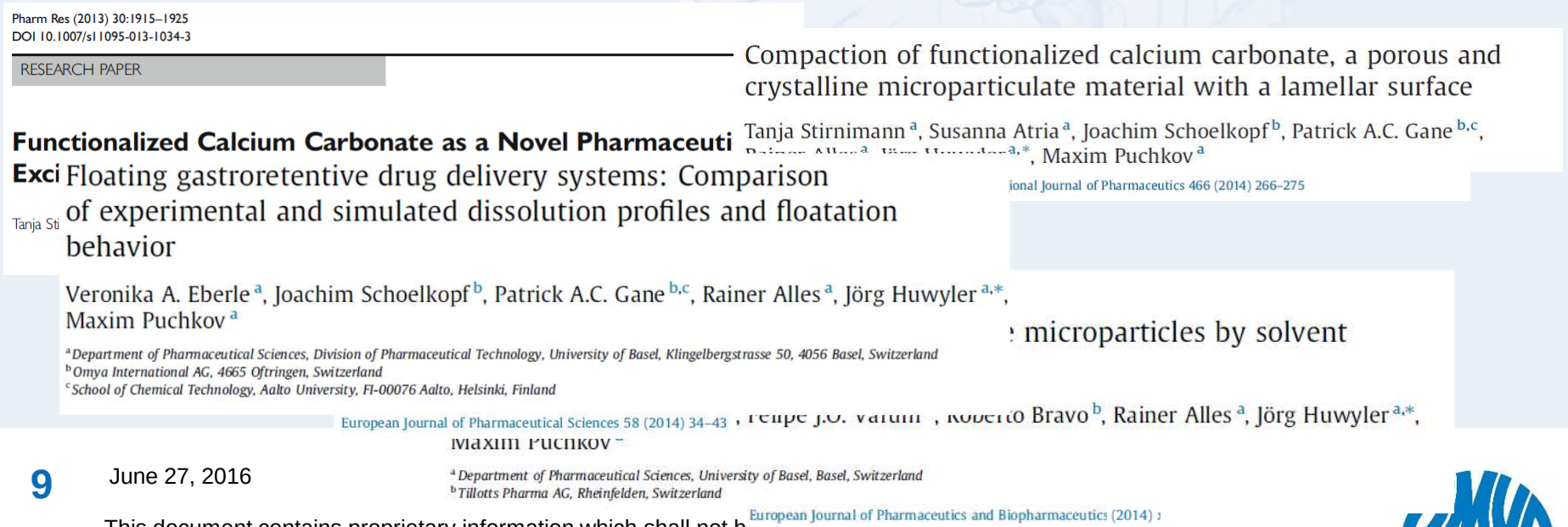


Omyapharm 500-OG

- **Particle Size Distribution D50 7.0 ±3.0 µm**
- **Specific Surface Area 53.0 ± 5.0 m2/g**
- **Porosity ~80%**
- **Co-processed excipient**
  - **Monographed starting material**
  - **Final product composite of monographed mineral**
  - **No significant chemical change during production**

Omyapharm 500-OG as an excipient: feasibility studies

- **University of Basel, Switzerland, Department of Pharmaceutical Science, Division of Pharmaceutical Technology, Prof. Jörg Huwyler.**
  - **3 PhD students: Dr. Tanja Stirnimann**
    Dr. Veronika Eberle
    Dr. Daniel Preisig
    Leonie Wagner-Hattler
    Roger Roth



Pharm Res (2013) 30:1915–1925
DOI 10.1007/s11095-013-1034-3

RESEARCH PAPER

Functionalized Calcium Carbonate as a Novel Pharmaceuti
Exci
Tanja Sti

Floating gastroretentive drug delivery systems: Comparison of experimental and simulated dissolution profiles and floatation behavior

Veronika A. Eberle [a], Joachim Schoelkopf [b], Patrick A.C. Gane [b,c], Rainer Alles [a], Jörg Huwyler [a,*], Maxim Puchkov [a]

[a] Department of Pharmaceutical Sciences, Division of Pharmaceutical Technology, University of Basel, Klingelbergstrasse 50, 4056 Basel, Switzerland
[b] Omya International AG, 4665 Oftringen, Switzerland
[c] School of Chemical Technology, Aalto University, FI-00076 Aalto, Helsinki, Finland

European Journal of Pharmaceutical Sciences 58 (2014) 34–43

Compaction of functionalized calcium carbonate, a porous and crystalline microparticulate material with a lamellar surface

Tanja Stirnimann [a], Susanna Atria [a], Joachim Schoelkopf [b], Patrick A.C. Gane [b,c], [a,*], Maxim Puchkov [a]

ional Journal of Pharmaceutics 466 (2014) 266–275

microparticles by solvent

Maxim Puchkov [a]

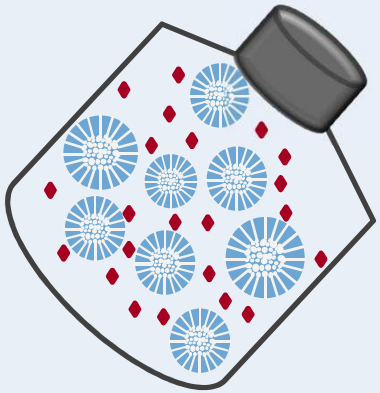
[a] Department of Pharmaceutical Sciences, University of Basel, Basel, Switzerland
[b] Tillotts Pharma AG, Rheinfelden, Switzerland

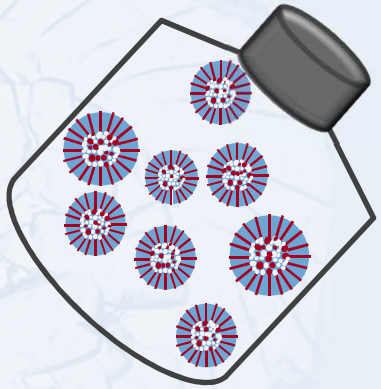
European Journal of Pharmaceutics and Biopharmaceutics (2014)

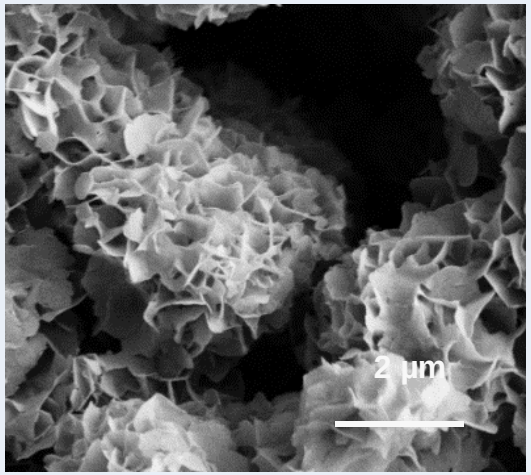
Omyapharm 500-OG as a porous API carrier

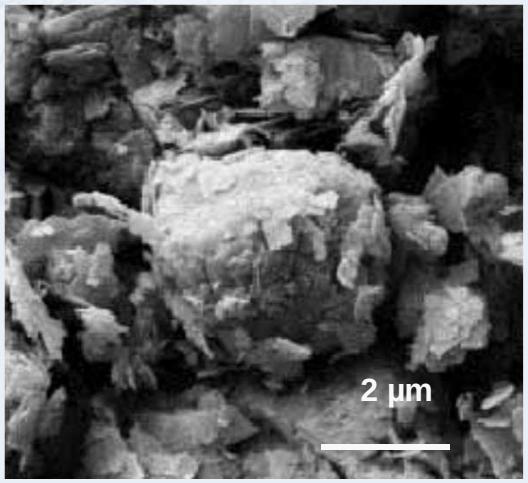
Loading method

Omyapharm + Drug → Omyapharm loaded with drug





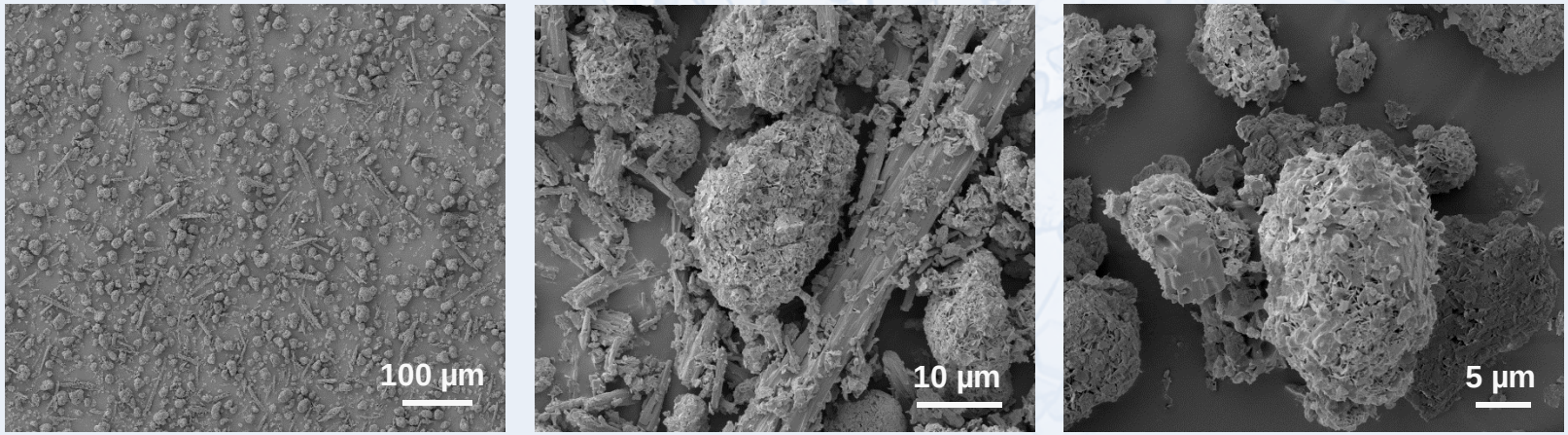




Case study: Omyapharm as a porous API carrier

Haid et al. Master thesis University of Basel (2013)

- **First screening low drug loads 15%, 20%, 25%wt.**
- **Second screening high drug load 40%wt.**
- **Screening of loading efficiency by imaging technology (SEM)**



High number of agglomerates and/or crystals outside Omyapharm particles

Case study: Omyapharm as a porous API carrier

Preisig et al. Eur J Pharm Biopharm (2014) 87:548-558

- **First screening**
  - **21 different APIs**
  - **Drug loads 15%, 20%, 25% w/w**

Acetylsalicylic acid	Indometacin
Benzocaine	Lidocaine
Caffeine water free powder	Lidocaine hydrochloride
Carbamazepine	Lossartan potassium
Desipramine HCl	Metoprolol tartrate
Dextromethorphan hydrobromide	Nifedipine
Diclofenac sodium	Omeprazole magnesium
Duloxetine HCl	Phenacetin crystalline
Efavirenz	Phenylbutazone
Ibuprofen	Sulfathiazole
Ibuprofen pellets	Thioridazine

Case study: Omyapharm as a porous API carrier

Preisig et al. Eur J Pharm Biopharm (2014) 87:548-558

- **14 APIs could be successfully loaded up to 25%**

Acetylsalicylic acid	Indometacin
Benzocaine	**Lidocaine**
Caffeine water free powder	**Lidocaine hydrochloride**
Carbamazepine	**Lossartan potassium**
Desipramine HCl	**Metoprolol tartrate**
Dextromethorphan hydrobromide	**Nifedipine**
Diclofenac sodium	**Omeprazole**
Duloxetine HCl	Phenacetin crystalline
Efavirenz	Phenylbutazone
Ibuprofen	**Sulfathiazole**
Ibuprofen pellets	**Thioridazine**

Case study: Omyapharm as a porous API carrier

Preisig et al. Eur J Pharm Biopharm (2014) 87:548-558

- **Second screening**
  - **10 APIs could be successfully loaded up to 40%**

Acetylsalicylic acid	Indometacin
Benzocaine	Lidocaine
Caffeine water free powder	**Lidocaine hydrochloride**
Carbamazepine	**Lossartan potassium**
Desipramine HCl	**Metoprolol tartrate**
Dextromethorphan hydrobromide	**Nifedipine**
Diclofenac sodium	Omeprazole
Duloxetine HCl	Phenacetin crystalline
Efavirenz	Phenylbutazone
Ibuprofen	**Sulfathiazole**
Ibuprofen pellets	**Thioridazine**

Case study: Omyapharm as a porous API carrier

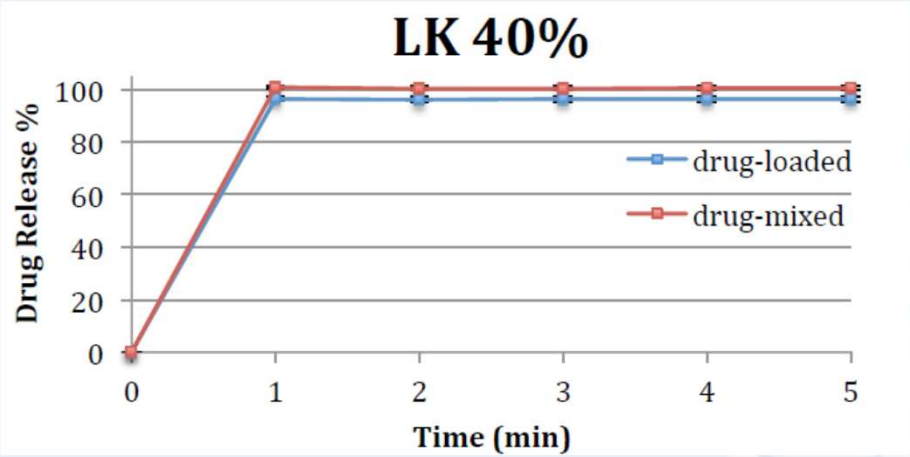
Preisig et al. Eur J Pharm Biopharm (2014) 87:548-558

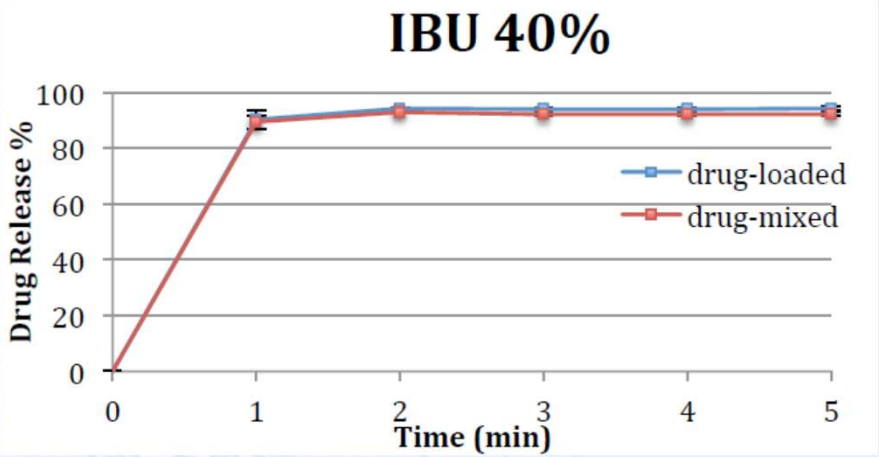
- **Third Screening**
  - **Nifedipine (NP), Ibuprofen (IBU) and Losartan Potassium (LK), were further investigated**
  - **Serial drug load: (25%-50% in steps of 5%)**
    - **SEM screening,**
    - **HPLC-UV to confirm screening**
    - **Pycnometry**
    - **BET surface area**
    - **Dissolution**
      - Enhanced dissolution?
    - **Differential scanning calorimetry**
      - Amorphous content?

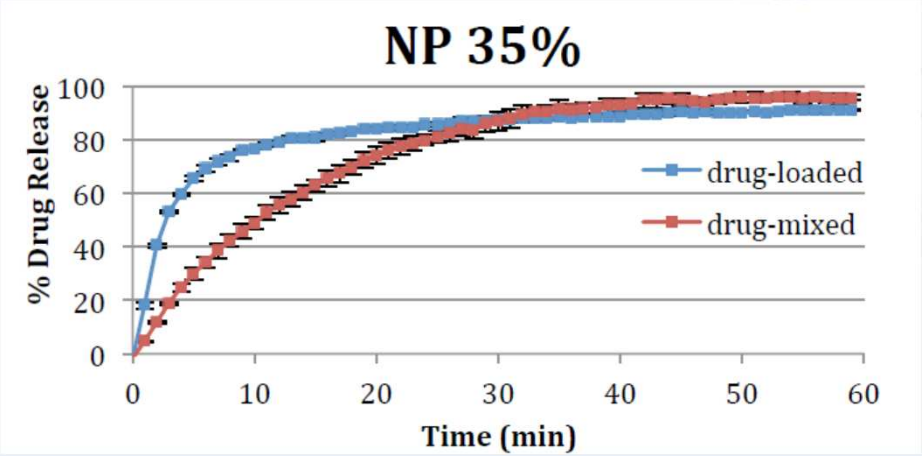
June 27, 2016

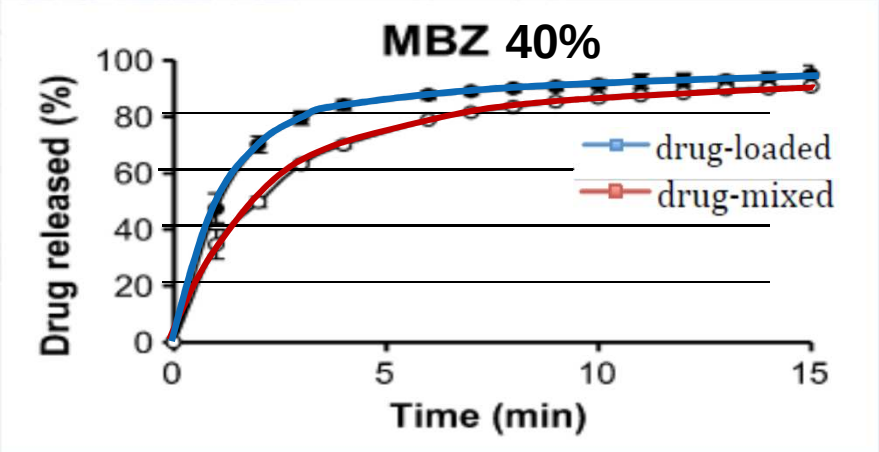
Case study: Omyapharm as a porous API carrier

Preisig et al. Eur J Pharm Biopharm (2014) 87:548-558





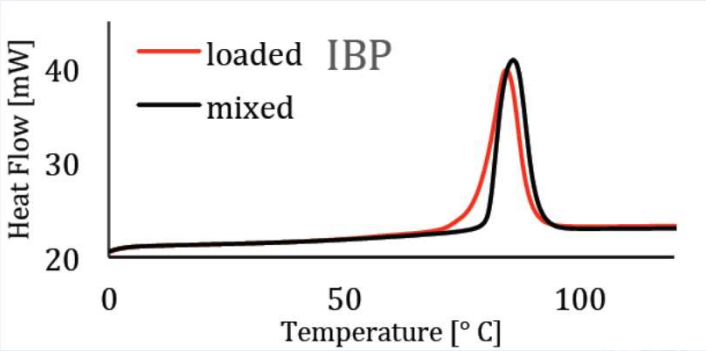


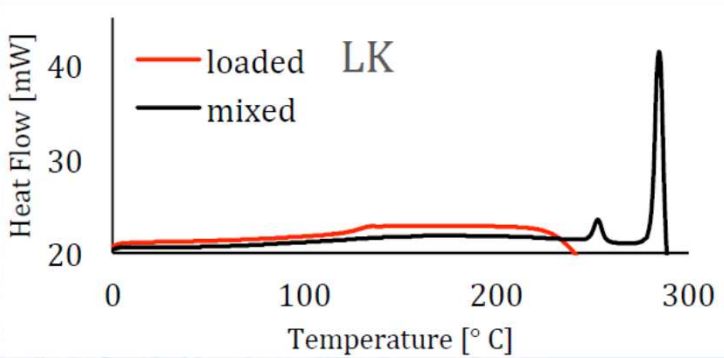


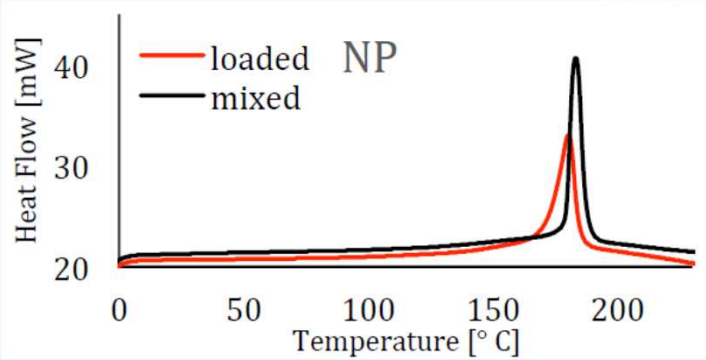
- **Omyapharm improves dissolution rate of Nifedipine and metronidazole benzoate**

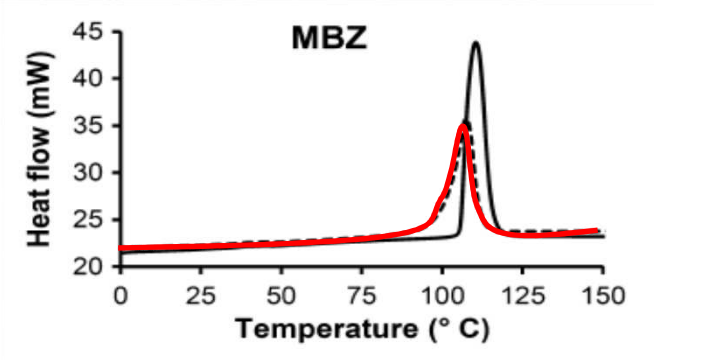
Case study: Omyapharm as a porous API carrier

Preisig et al. Eur J Pharm Biopharm (2014) 87:548-558







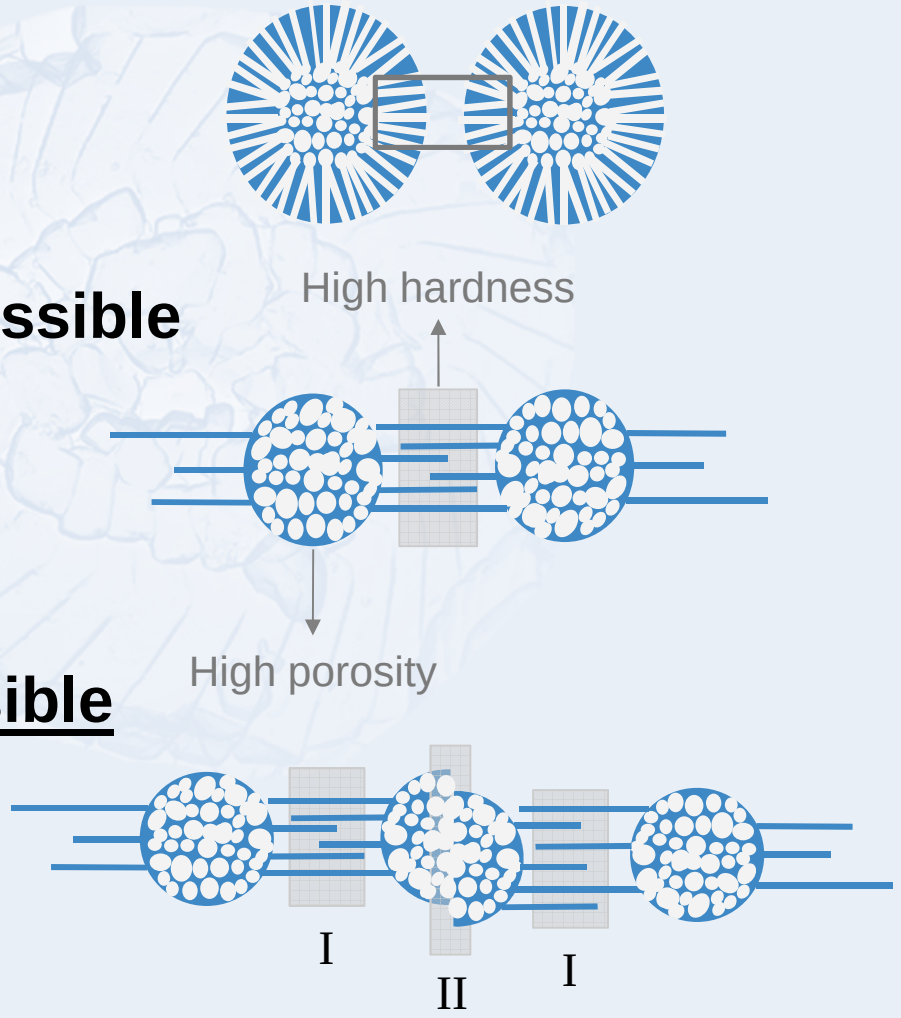


- **Improvement in dissolution rate does not correlate with amorphous drug content**
- **Increased surface area improves the dissolution rate**

Omypharm compressibility properties

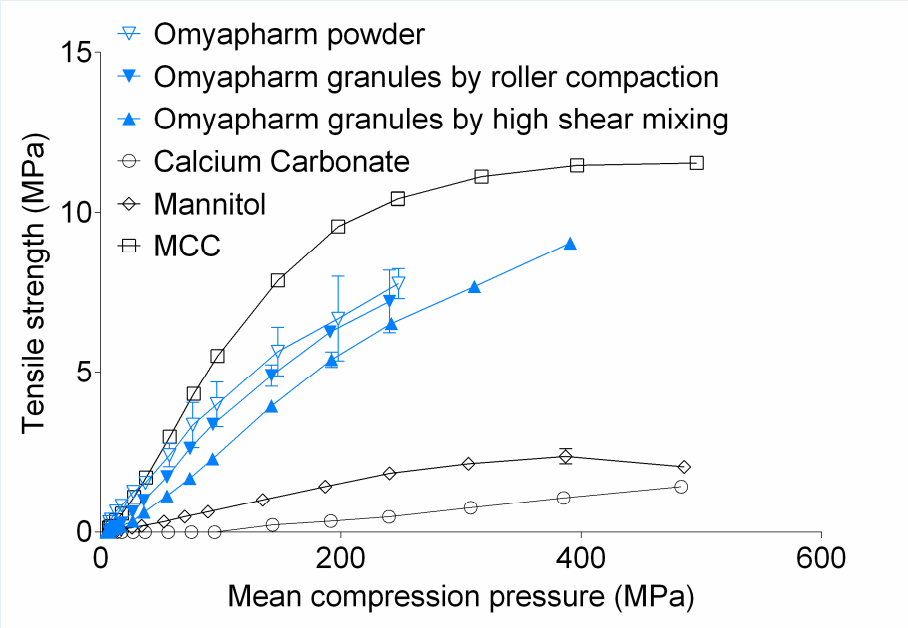
Dry granulation

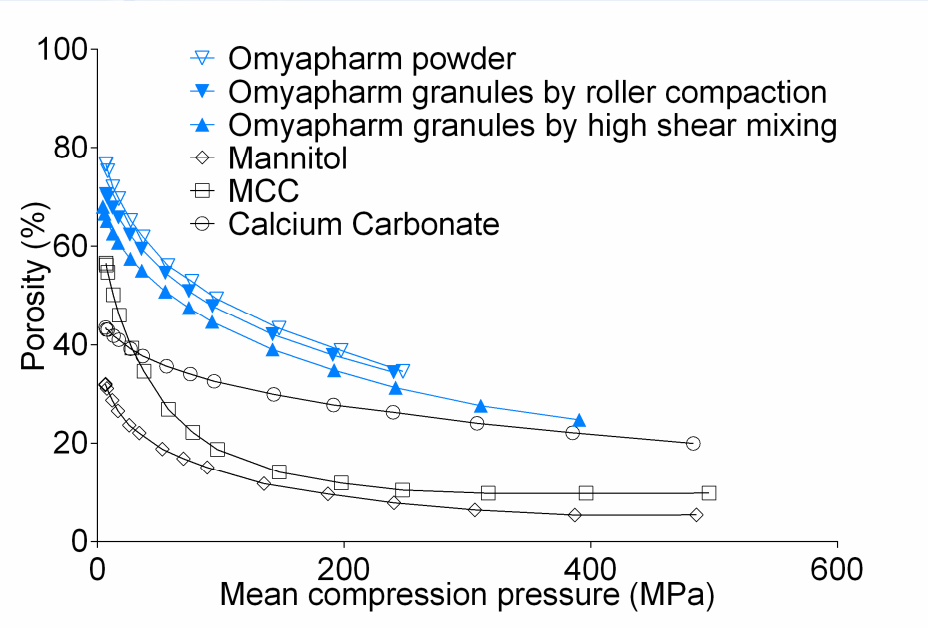
- **Roller compactor**
- **Omyapharm direct compressible into granules**
- **Porosity is preserved**
- **Omyapharm is a <u>compressible porous carrier</u>**



Case study: Omypharm compressibility properties

Stirnimann et al. Int J Pharm (2014) 466:266-275



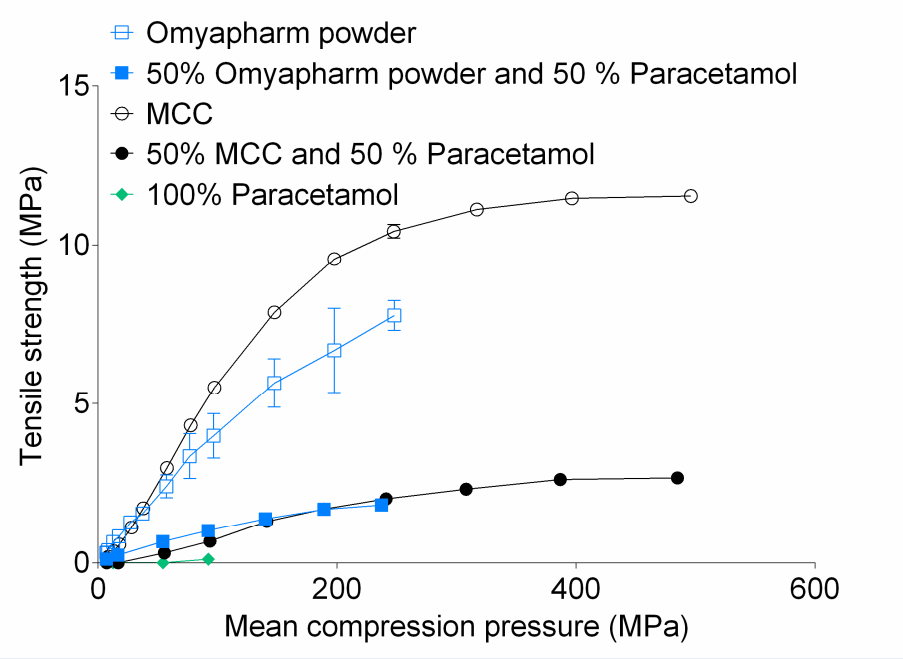


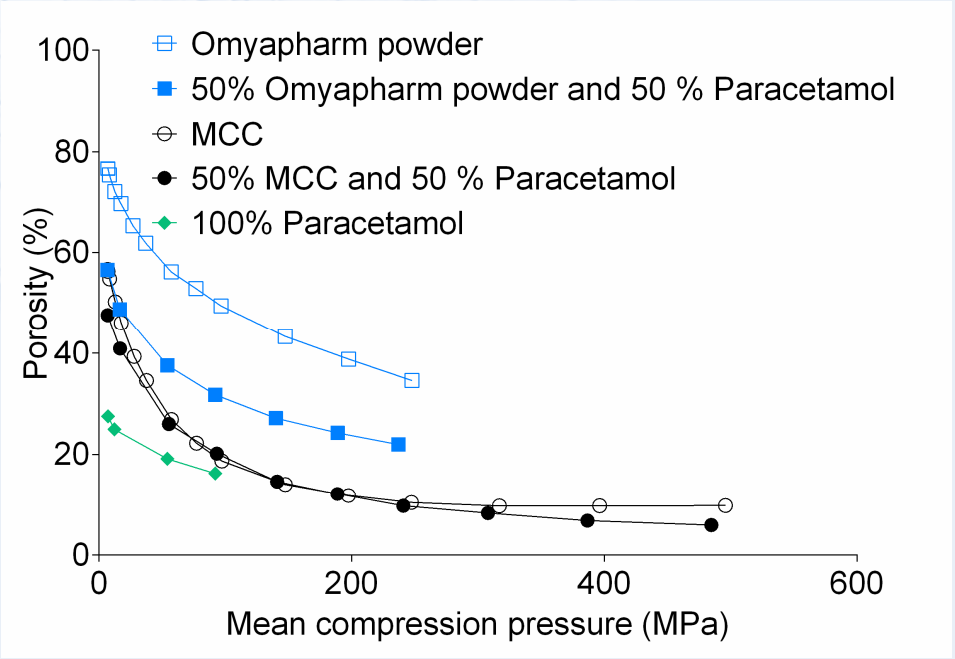
- **Tensile strength higher or comparable to other reference excipients**
- **Decrease in porosity due to increasing compression pressure less than other reference excipients**

Case study: Omypharm compressibility properties

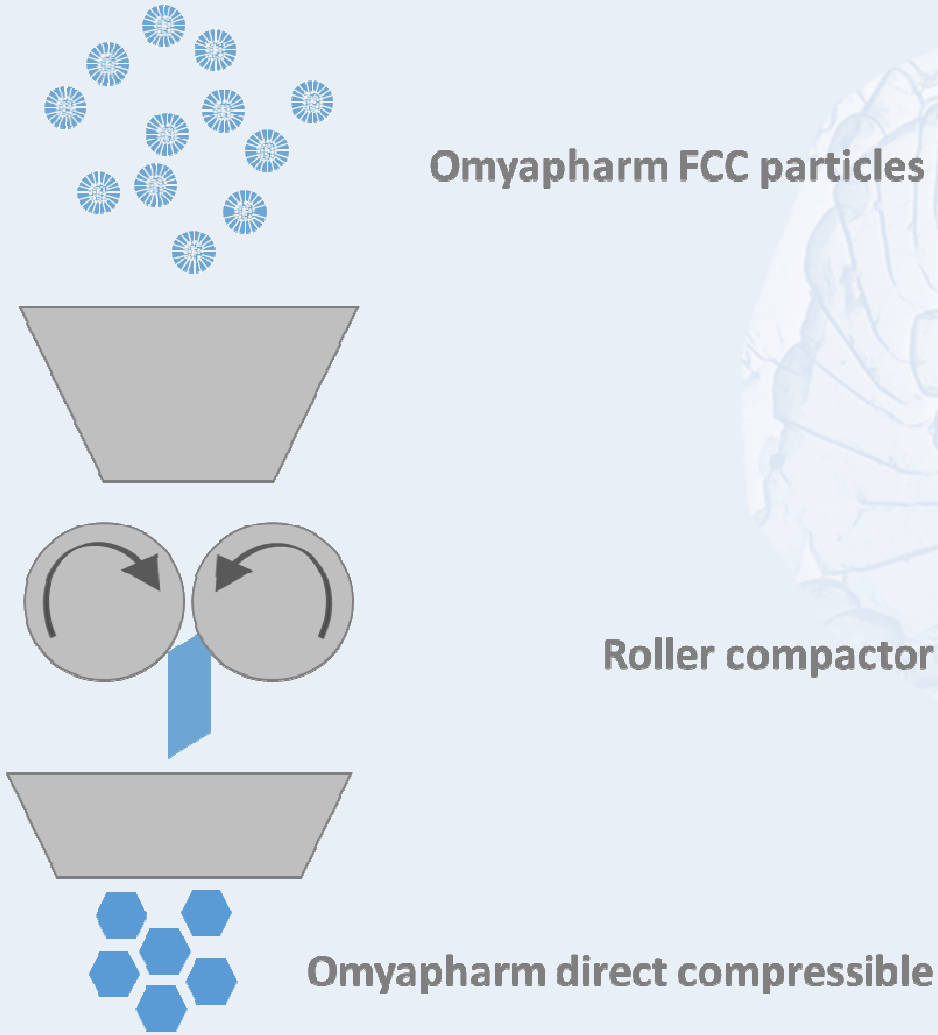
Stirnimann et al. Int J Pharm (2014) 466:266-275

- **Formulation with active pharmaceutical ingredient (API)**
  - **Tensile strenth is higher (especially at low compressive pressures) or comparable to reference material**
  - **Porosity decreases but is still higher compared to reference material**





Omyapharm 500-OG DC



- **Particle Size Distribution**
  - **D50 445 µm**
- **Specific surface area**
  - **54 m2/g**
- **Hausner factor**
  - **1.17**
- **Compressibility index**
  - **14.75%**

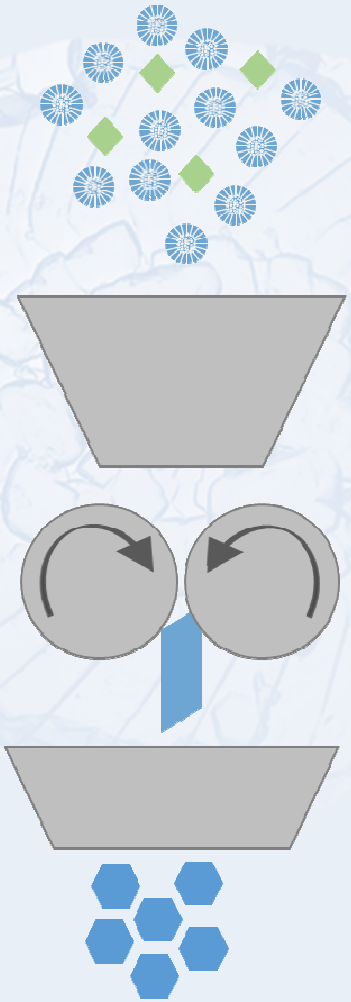
Application: Omypharm in orally dispersible tablets (ODTs)

- **Increased compliance in patients (geriatric/pediatric)**
- **Omyapharm tablets have high porosity AND high hardness**
  - **High drug load**
  - **Standard packaging**
  - **Easy manufacturing process**
  - **Taste masking/ good mouthfeeling**

Case study: Omypharm in orally dispersible tablets (ODTs)

Stirnimann et al. Int J Pharm (2014) 466:266-275

Easy manufacturing process



FCC particles
pre-mixed with disintegrant

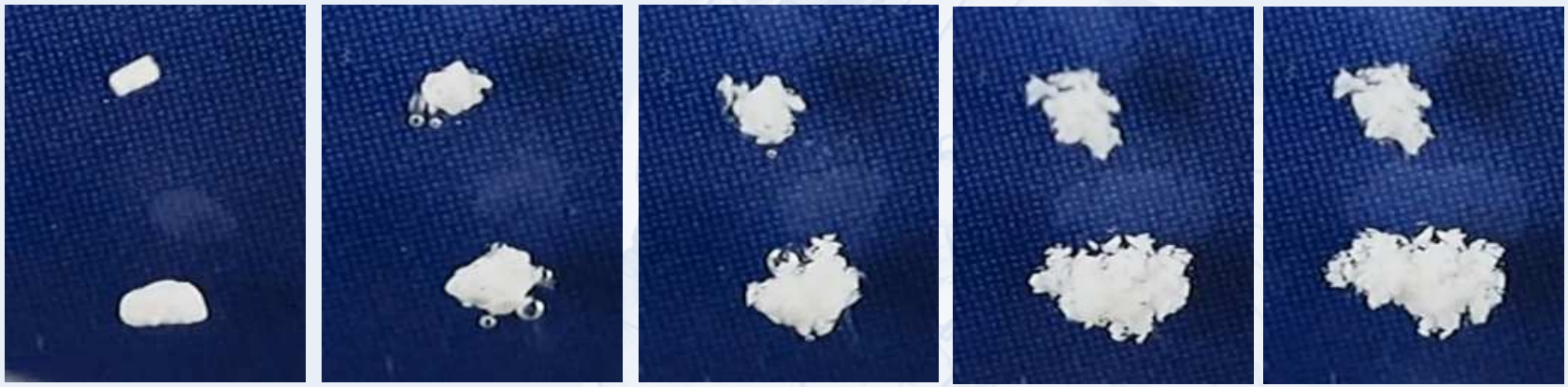
Roller compactor
(dry granulation)

Mill and sieve

FCC orally dispersible granules
Ready to mix with API and direct compressible into ODTs

Case study: Omypharm in orally dispersible tablets (ODTs)

Stirnimann et al. Int J Pharm (2014) 466:266-275



Disintegration time 2 seconds

Case study: Omypharm in orally dispersible tablets (ODTs)

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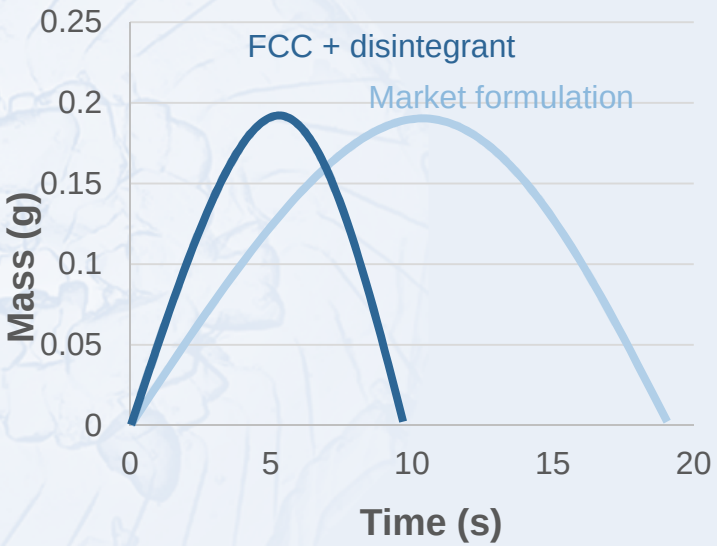
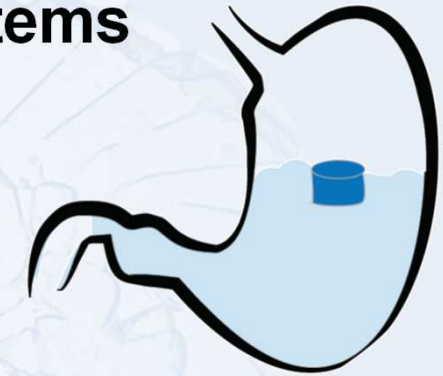


Further case studies with Omyapharm

- **Gastro-retentive drug delivery systems (Eberle *et al*. 2014 and 2015)**



- **Target delivery mucoadhesive particles (Preisig *et al*. 2015)**

Omyapharm main points

Omyapharm is a co-processed mineral excipient

Omyapharm is a multifuctional excipient that can be used in very diverse applications

Omyapharm is a highly suitable excipient to produce tablets with high hardness and high porosities (fast desintegrating granules, ODTs)

Omyapharm has high loading capability

Omyapharm can improve dissolution rate of certain APIs

Omyapharm has been registered for clinical trials in Switzerland as part of a pharmaceutical formulation

CPhI Award winner Innovation in APIs & Excipients

Omyapharm

Omyapharm outlook

- **2 new PhD students at University of Basel**
  - **Omyapharm potential in different applications**
- **Clinical trials with Floating drug delivery sytems (FDDS) in 2017**
- **Clinical trials in Switzerland with collaboration partners in industry in 2016**
- **Customer requests for ODT formulations with different APIs**

Phamaceutical formulation lab

Thank you for your attention

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