Jungbunzlauer

*From nature to ingredients®*

# facts

## Tableting properties of Trimagnesium Citrate Anhydrous GN

## Introduction

### Magnesium is important for the body

The mineral magnesium is essential to health. It is a cofactor in more than 300 enzymatic reactions and plays a role in regulating muscle function, maintaining a healthy heart rhythm, and strengthening bones and teeth. Furthermore it contributes to normal psychological functioning and helps to reduce tiredness and fatigue. There are a variety of approved health claims that can be used for foods and dietary supplements that contain magnesium.[1–3] The recommended daily intake level for magnesium is 375 mg/d in the European Union and 420 mg/d in the USA.

A variety of magnesium supplements can be found on the market, either on their own or in combination with vitamins, other minerals or botanicals. They come in the form of tablets, capsules, powders or liquids, in different dosages and from different magnesium sources. Magnesium is available as a number of salts, of which the most important ones for supplements are magnesium citrate, magnesium oxide and magnesium carbonate.[4] Among these, magnesium citrate is the only organic magnesium salt. Several studies indicate that organic mineral salts like magnesium citrate have better bioavailability than inorganic salts such as magnesium oxide.[5–7] Supplements with magnesium citrate are often premium products, ensuring good absorption in the body and good compatibility.

### Tablets with trimagnesium citrate

Tablets are still the most important application form for dietary supplements. They have many advantages, being simple and cheap to produce, easy to dose for the consumer and offering a long shelf life.

A high mineral content is crucial to keeping the tablets as small as possible. Of the organic magnesium salts, trimagnesium citrate anhydrous has the highest mineral content (16%) and is therefore preferred for the production of magnesium tablets.

However, trimagnesium citrate anhydrous is typically available as a fine powder, which can cause problems with processing due to dust formation. It can lead to large amounts of fines in the tablet press. To overcome this issue, Jungbunzlauer offers a granulated form of trimagnesium citrate anhydrous: Trimagnesium citrate anhydrous GN.

## An investigation into the benefits of granulated trimagnesium citrate

### Particle size distribution

Particle size distribution is a very important parameter for the tableting process. Lower fine content causes less issues and cleaning effort during production which improves process times and output. Figure 1 shows the particle size distribution analysis of two tested trimagnesium citrate anhydrous granulations.

Trimagnesium citrate anhydrous GN (TMC GN) is a granulated product and has significantly lower fines and a broader particle size distribution compared to the non-granulated trimagnesium citrate anhydrous fine (TMC fine).

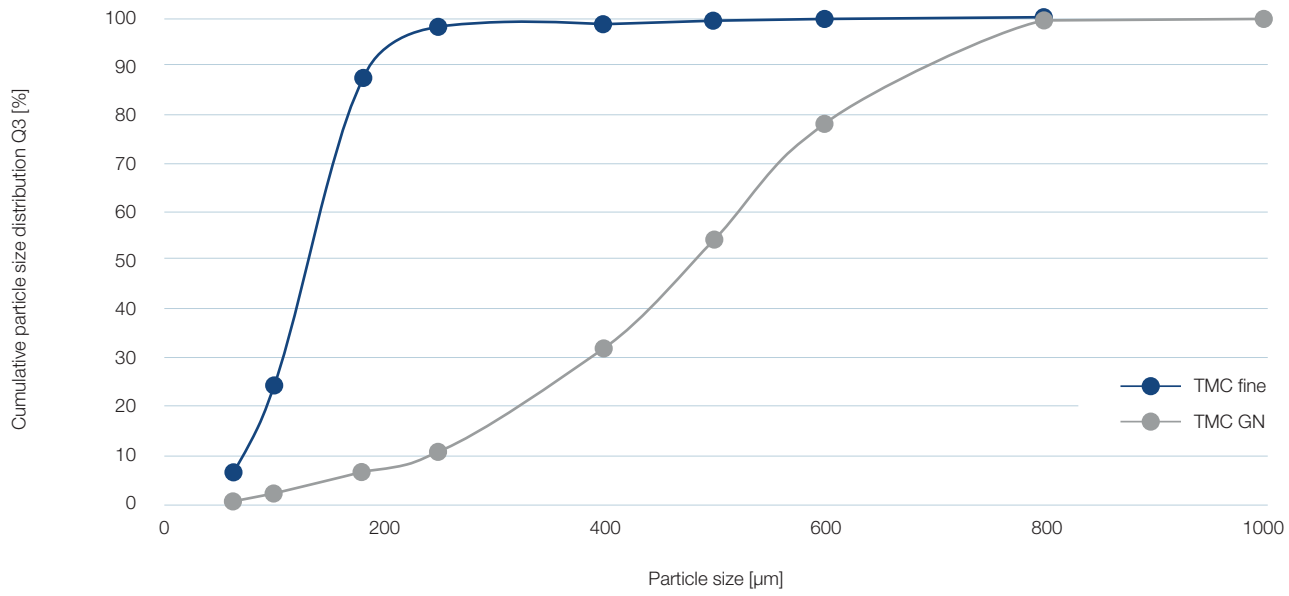


**Figure 1: Typical particle size distribution of trimagnesium citrate anhydrous fine (TMC fine) and trimagnesium citrate anhydrous GN (TMC GN), analysed by sieving**

As a granulated salt, trimagnesium citrate anhydrous GN shows enhanced flowability, which improves its overall processability compared to the non-granulated product.

### Tableting setup

Tablets were produced on a pneumo-hydraulic, single-punch tablet press from Röltgen (Flexitab XL). The diameter of the round, flat tablets was 18 mm and the filling depth was adjusted to a tablet kernel weight of 2.0 g. The pressure holding time was set to 20 milliseconds.

Different press forces from 30 kN to 60 kN were tested in this project to evaluate tablet hardness with different percentages of trimagnesium citrate anhydrous fine and GN.

### Tablet recipe for the pre-tests

Recipes with different percentages of trimagnesium citrate anhydrous fine and GN were used in pre-tests, as shown in table 1. These recipes were designed to test the influence of different percentage of trimagnesium citrate on the tensile strength of the tablets.

**Table 1: Recipes for pre-tests with different percentages of trimagnesium citrate anhydrous fine and trimagnesium citrate anhydrous GN**

| Ingredient [%] | R 1 | R 2 | R 3 | R 4 | R 5 |
|---|---|---|---|---|---|
| Trimagnesium Citrate Anhydrous fine/GN | 65.0 | 70.0 | 75.0 | 80.0 | 90.0 |
| Microcrystalline Cellulose 102 | 33.9 | 28.9 | 23.9 | 18.9 | 8.9 |
| Magnesium Stearate | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 |

## Hardness

Figure 2 shows the tensile strength of tablets with different percentages of trimagnesium citrate anhydrous GN. The tensile strength decreases as the content of trimagnesium citrate anhydrous in the tablets increases. The data shows that to achieve a tensile strength of 1.0 MPa the proportion of trimagnesium citrate anhydrous GN in the formulation must not exceed 70%. However, it is still possible to achieve almost 600 kPa with 90% trimagnesium citrate anhydrous GN using a compression force of 60 kN (236 MPa).

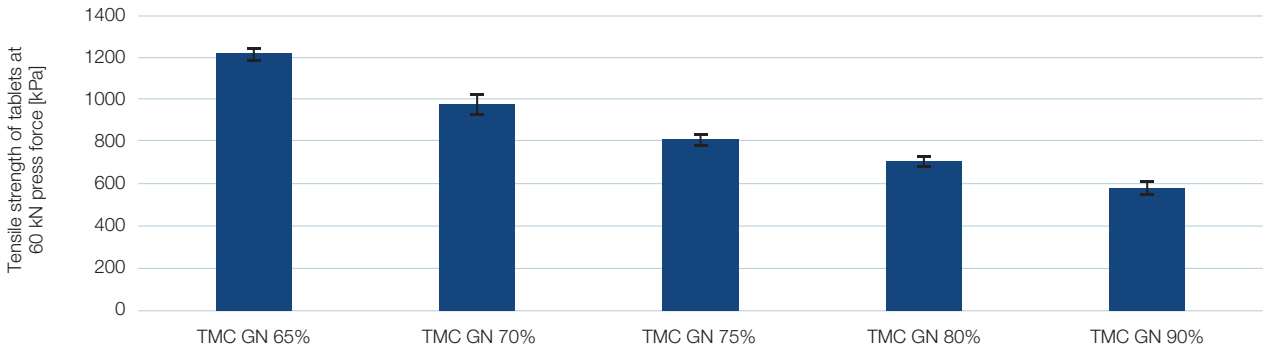


**Figure 2: Tensile strength of tablets with varying percentages of trimagnesium citrate anhydrous GN (TMC GN), analysed with tablet hardness tester PTB 511E, Pharma Test, according to Ph. Eur. 2.9.8.**

Comparing the tensile strength of tablets containing trimagnesium citrate anhydrous GN with tablets containing trimagnesium citrate anhydrous fine at 45 kN and 60 kN press force shows that there is a slight difference. The tablets with trimagnesium citrate anhydrous fine are slightly harder with the same press force (figure 3).

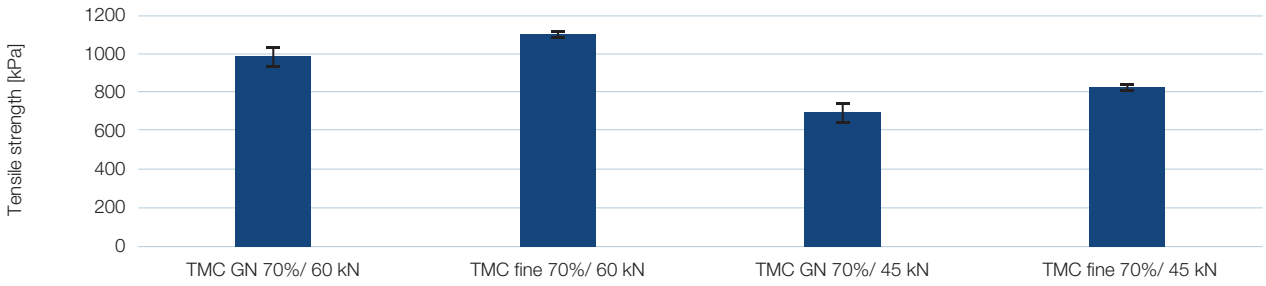


**Figure 3: Tensile strength of tablets with trimagnesium citrate anhydrous GN (TMC GN) or trimagnesium citrate anhydrous fine (TMC fine) with different press force, analysed with tablet hardness tester PTB 511E, Pharma Test, according to Ph. Eur. 2.9.8.**

### Tablet recipe

The final recipe was adjusted to a TMC GN content of 66% to achieve 200 mg magnesium per 2.0 g tablet (table 2). The diameter of the round, flat tablets was also 18 mm and the press force for the final recipe was adjusted to 57 kN to set the tensile strength to 1.0 MPa for further coating and testing.

**Table 2: Final tablet recipe with 200 mg magnesium for coating process**

| Ingredient [%] | Final recipe |
|---|---|
| Trimagnesium Citrate Anhydrous GN | 66.0 |
| Microcrystalline Cellulose 102 | 28.9 |
| Croscarmellose Sodium | 4.0 |
| Magnesium Stearate | 1.1 |

### Coating

A coating is mandatory for all tablets with trimagnesium citrate anhydrous, as trimagnesium citrate anhydrous is hygroscopic and the tablets would otherwise not be stable. The coating must form an efficient barrier against moisture absorption from the environment.

The project tested the polymers hydroxypropylmethylcellulose (HPMC), hydroxypropylcellulose (HPC) and polyvinyl alcohol (PVA) for their efficiency as moisture barriers. The coating recipes were provided by an external partner, who carried out the coating process.

### Stability

A stability test was performed in a climate chamber with conditions of 30°C (86 °F) and 50% relative humidity for 90 days. Coatings with different polymers (5% HPMC, 5% HPMC/HPC and 4% PVA based coating) were tested together with two different commercially available benchmark products containing trimagnesium citrate anhydrous (coating type unknown). Both the coating containing PVA as polymer and the coating of benchmark 2 withstood the storage without any visible damage or alteration of the coating shell.

In comparison the coatings with HPMC, HPMC/HPC (not shown in the table) as polymer and the coating of benchmark 1 showed cracks and irregularities on the surface (table 3).

**Table 3: Storage stability of two benchmark magnesium tablets compared to Jungbunzlauer tablets with PVA coating. Storage in climate chamber at 30°C (86 °F) and 50% relative humidity for 90 days**

| | Benchmark 1 | Benchmark 2 | PVA coating |
|---|---|---|---|
| Tablets before storage |  |  |  |
| Tablets after storage |  |  |  |

**Disintegration time**

The disintegration time of magnesium citrate tablets is challenging. It is a balance between stability, hardness and low friability of the tablets on the one hand and an acceptable disintegration time on the other. Commercially available products show a disintegration time of up to a few hours in water.

Disintegration tests of coated tablets were performed by the external coating partner according to Ph. Eur. 2.9.1.. Figure 4 shows the disintegration time of two commercially available benchmark tablets containing trimagnesium citrate anhydrous compared to the Jungbunzlauer tablets with PVA coating. The disintegration time of the Jungbunzlauer tablets was half that of benchmark 2. The tablets of benchmark 1 had hardly disintegrated at all even after 2 hours. The test was stopped after 2 hours. The tablet recipe with trimagnesium citrate GN had a disintegration time of 15 minutes, which was substantially shorter than that of the commercially available benchmark product.

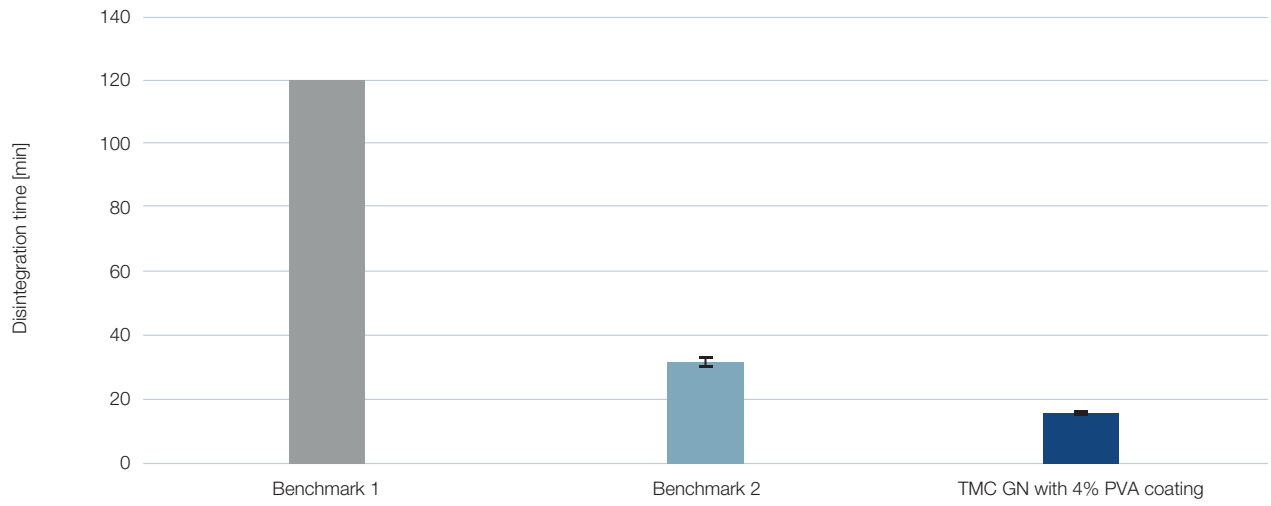


**Figure 4: Disintegration time of two benchmark magnesium tablets compared to Jungbunzlauer tablets with PVA coating. Disintegration tests of coated tablets were performed according to Ph. Eur. 2.9.1.**

**Upscale tablet formulation on a rotary tablet press**

The formulation in table 2 was successfully scaled up with smaller tablets (500 mg, 10 mm diameter) on a Fette Compacting F10i rotary tablet press with a throughput of 120,000 tablets per hour without any problems and with an excellent standard deviation press force of lower than 4%.

**Summary**

Trimagnesium citrate anhydrous is the ideal choice for the production of magnesium tablets with good properties (mechanical stability, storage stability and disintegration behaviour). As a granulated product trimagnesium citrate anhydrous GN combines excellent tablet properties with the advantages of a very low dust content. This makes trimagnesium citrate anhydrous GN the ideal choice for the production of magnesium tablets.

## Acknowledgements

We thank the external coating partner for their expertise and for performing the coating and disintegration tests. We also thank Fette Compacting GmbH (Schwarzenbek, Germany) for the opportunity to test the developed tablet formulation on a rotary tablet press.

## References

[1] EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). Scientific Opinion on the substantiation of health claims related to magnesium and electrolyte balance (ID 238), energy-yielding metabolism (ID 240, 247, 248), neurotransmission and muscle contraction including heart muscle (ID 241, 242), cell division (ID 365), maintenance of bone (ID 239), maintenance of teeth (ID 239), blood coagulation (ID 357) and protein synthesis (ID 364) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2009;7(9):1216.

[2] EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). Scientific Opinion on the substantiation of health claims related to magnesium and "hormonal health" (ID 243), reduction of tiredness and fatigue (ID 244), contribution to normal psychological functions (ID 245, 246), maintenance of normal blood glucose concentrations (ID 342), maintenance of normal blood pressure (ID 344, 366, 379), protection of DNA, proteins and lipids from oxidative damage (ID 351), maintenance of the normal function of the immune system (ID 352), maintenance of normal blood pressure during pregnancy (ID 367), resistance to mental stress (ID 375, 381), reduction of gastric acid levels (ID 376), maintenance of normal fat metabolism (ID 378) and maintenance of normal muscle contraction (ID 380, ID 3083) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1807.

[3] Health Claims According to Art. 13.1 or 14, Regulation (EC) No 1924/2006.

[4] Innova Market Insights, Innova Database, New Launched Supplements 2018–2022.

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## About Jungbunzlauer

Jungbunzlauer is one of the world's leading producers of biodegradable ingredients of natural origin. We enable our customers to manufacture healthier, safer, tastier and more sustainable products. Thanks to continuous investment, state-of-the-art manufacturing processes and comprehensive quality management, we are able to provide outstanding product quality.

Our mission "From nature to ingredients®" commits us to protecting people and their environment. Jungbunzlauer ingredients that can be used for tablet compression are produced by fermentation of natural, renewable resources and are therefore a good alternative to other fillers and excipients used in tablet applications.

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