DFE pharma

# Primellose® is an excellent choice as superdisintegrant in ODT applications


*The pursuit of excipient excellence*

## Summary

In orally disintegrating tablets, the excipients of choice in direct compression are mannitol as filler binder and crospovidone as the superdisintegrant. An alternative superdisintegrant, Primellose® , is produced from natural resources in contrast to some other superdisintegrants. Here we show that Primellose® (croscarmellose sodium) gives fast disintegration of tablets. Therefore, we conclude that Primellose® is very effective and an excellent choice as superdisintegrant in ODT applications.

## 1 Introduction

Orally disintegrating tablets are tablets that should do what is in their name: disintegrate in the oral cavity. To do so, the tablet should disintegrate quickly, with a limited supply of water, and mask the taste of the dispersing drug. Fast disintegration is described by FDA to be faster than thirty seconds,[1] but in practice it should be even faster. Several strategies exist in order to prepare ODT tablets. For practical and economic reasons, an interesting method for preparation of ODT tablets is by direct compression (DC).[2] A number of combination products have been developed such as Ludiflash and Parteck-ODT. The majority of DC tablets for ODT are formulated with mannitol as filler-binder and crospovidone as disintegrant.[3] These types of tablets have been reported to disintegrate between 10-60 seconds.[4]

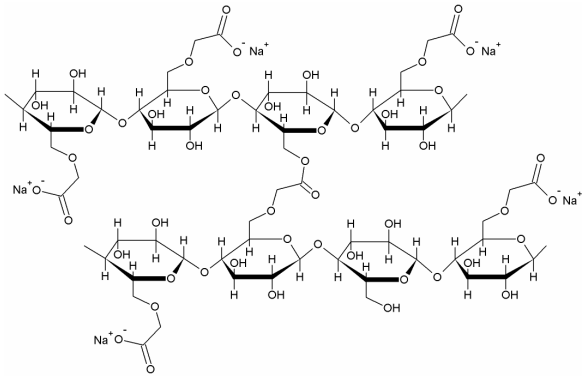

***Figure 1.*** *Chemical structure of Primellose*

Here we will show that (placebo) tablets formulated with Primellose® as the superdisintegrant gave tablet disintegration comparable to that of DC tablets designed for ODT applications. For economic reasons, croscarmellose sodium is the preferred superdisintegrant. And because it is based on cellulose, it is produced from natural and renewable resources, in contrast to for instance crospovidone which is completely synthetic in nature.

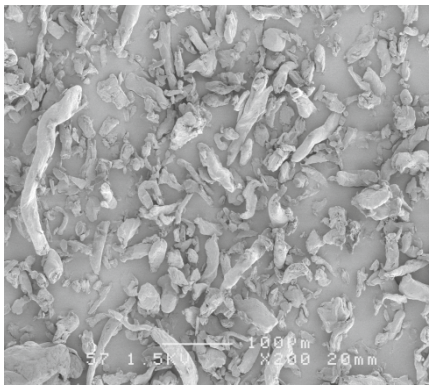

***Figure 2****. SEM picture of Primellose*

## 2 Methods and Materials

Placebo tablets were prepared with croscarmellose sodium (Primellose®, DFE Pharma), and with lactose (SuperTab® 30GR, DFE Pharma) or mannitol (Pearlitol SD, Roquette) according to Table 1. SuperTab® 30 GR is agglomerated α-lactose monohydrate. For each formulation (500 gr), SuperTab® 30 GR or

mannitol and Primellose® were blended in a Turbula blender for eight minutes at a rate of 90 rpm. Then magnesium stearate (Sigma) was added and blending was commenced for another two minutes. The blend was fed to a RoTab tableting press with a die filling of 250 mg and a tableting force of 4, 6, 8, and 10 kN.

***Table 1.*** *Placebo formulations, amounts in milligrams/tablet*

| | Supertab® 30GR | Mannitol | Primellose® | Mag. St. |
|---|---|---|---|---|
| **1** | 248.75 | | | 1.25 |
| **2** | 243.75 | | 5 (2%) | 1.25 |
| **3** | 238.75 | | 10 (4%) | 1.25 |
| **4** | 233.75 | | 15 (6%) | 1.25 |
| **5** | | 242.5 | 6.25 (2.5%) | 1.25 |
| **6** | | 236.25 | 12.5 (5%) | 1.25 |

Tablet disintegration was measured on the Erweka Disintegration tester model ZT122 in water at 37°C. Tablet friability and tablet hardness were tested according USP methods.

## 3 Results and Discussion

Tablet strength was determined, and as expected the strength increased with increasing tableting force and is dependent on the major excipient (Supertab® 30GR and mannitol). The tablet hardness was not or only slightly dependent on the amount of superdisintegrant.

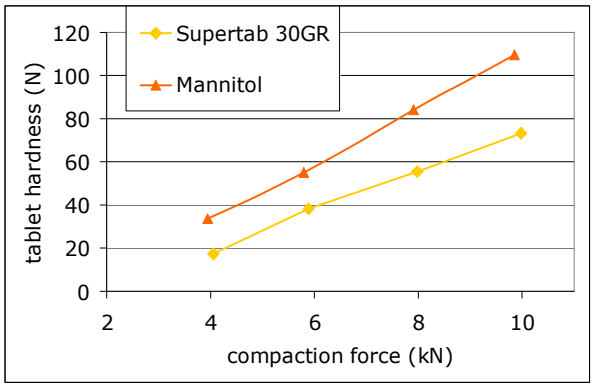


***Figure 3****. Relation of tablet hardness vs. compaction force*

Friability of the tablets was determined and found to be dependent on the compaction force. Tablets pressed at 4 kN where the most friable with weight losses in the order of 1%. At higher compaction forces, the weight losses were in general in the order of <0.2%.
The disintegration time of the placebo tablets with 30 GR and Primellose are depicted in Table 3.

***Table 2.*** *Disintegration time of Supertab 30GR tablets with Primellose as disintegrant (friability and tablet hardness in brackets)*

| Compaction force (kN) | Primellose® concentration | | | |
|---|---|---|---|---|
| | **0%** | **2%** | **4%** | **6%** |
| **4** | 332 s (1.1%; 16.5N) | 42 s (1.1%; 16.8N) | 44 s (1.4%; 14.9N) | 42 s (2.5%; 12.2N) |
| **6** | 410 s (0.5%; 39.4N) | 56 s (0.4%; 38.4N) | 47 s (0.4%; 36.5N) | 49 s (0.4%; 32.5N) |
| **8** | 385 s (0.3%; 55.5N) | 38 s (0.3%; 54.3N) | 45 s (0.2%; 53.1N) | 46 s (0.2%; 51.3N) |
| **10** | 427 s (0.2%; 73.4N) | 28 s (0.1%; 75.3N) | 47 s (0.1%; 73.0N) | 47 s (0.1%; 70.6N) |

It can be concluded that addition of superdisintegrant has a profound effect on the disintegration time. Secondly, it can be concluded that the disintegration time is hardly dependent on the tablets hardness. Disintegration times of direct compression based tablets have been reported to be in the order of 20-60 seconds, in accordance with these lactose based tablets.
The most widely used excipient for ODT applications is mannitol. Therefore, tablets based on mannitol were prepared as well. Disintegration of those tablets is depicted in Figure 4 and it can be observed the disintegration time varies from 10-20 s and that there is a small dependence with the compaction force. Furthermore, decreasing the amount of Primellose® did not have a very large effect on the disintegration time, which was observed for the lactose based tablets as well.

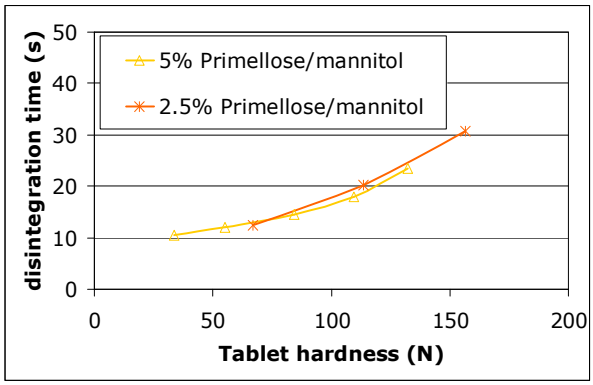


***Figure 4**. Tablet disintegration time of mannitol based tablets with 5% and 2.5% primellose*

The measured disintegration time is well in line or even better than reported tablet disintegration times of ODT formulation.

## 4 Conclusion

We conclude that Primellose® is an excellent superdisintegrant which gives tablets that disintegrate with a similar rate as is reported for DC based ODT tablets. Primellose® is already very effective at relative low concentrations.

## References

1. Guidance for Industry Orally Disintegrating Tablets (FDA, Rockville, MD), www.fda.gov/cder/guidance/index.htm, December 2008
2. WR Pfister, TK Ghosk, Pharm. Tech. 2005, 29(10), 136-150.
3. Y Zhang, A Wrzesinski, M Moses, H Betrand, Pharm. Tech., 2010, 34(7), 54-61.
4. JJ Hirani, DA Rathod, KR Vadalia, Tropical J. Pharm. Res., 2009, 8(2), 161-172.

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