Evaluation of a new disintegrant mixture from natural resources

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Introduction

Tablet disintegration is most often required to divide a tablet into suitably small sub-units that facilitate achievement of the desired drug dissolution rate, which is essential for the therapeutic effect. While semi-synthetic or synthetic super-disintegrants such as croscarmellose sodium, crospovidone, or sodium starch glycolate are commonly the materials of choice in the pharmaceutical world, there is a strong demand for options of more natural origin for nutraceutical applications [1]. Currently only few natural disintegrants are available and these sometimes do not achieve optimum disintegration due to lack of disintegrant action. To provide satisfactory disintegrant action one or more disintegration mechanisms can be facilitated. Swelling and wicking are usually considered the main drivers in tablet disintegration while strain recovery, dissolution mechanisms and the addition of surfactants are also reported to provide some disintegrative action [2]. Over twenty natural materials, mostly fibers, starches, gums and cellulose types, were tested regarding their swelling behavior and water uptake speed to determine good candidates. Enabling synergistic effects of materials assisting swelling and wicking effects a mixture of natural materials (containing gellan gum, potato fiber, cellulose powder and natural potato starch) was optimized regarding the disintegration of various tablet formulations. The work presented here shows the disintegrant effect of this natural disintegrant mixture (CompactCel® DIS) in comparison to the disintegrant effect of a selection of natural disintegrant materials on their own (two types of starch and two types of cellulose.

Materials

All materials were used as supplied by the manufacturers without further conditioning. Materials were obtained from: Porous tribasic calcium phosphate (TCP 500) and a DC grade anhydrous dibasic calcium phosphate (DCPA 150) / Chemische Fabrik Budenheim KG, DC grade microcrystalline cellulose (MCC 200) / Mingtai Chemical CO, LTD; Magnesiumstearate (Mg-St) from Peter Greven GmbH; caffeine (Caff) / Buxtrade GmbH; coarse crystalline saccharose (Sacc) / Südzucker AG; gellan gum / Jungbunzlauer Ladenburg GmbH; potato fibre as well as cellulose powder with a D50 of 70µm (CP_2) / CFF GmbH & Co KG; cellulose fine powder with a D50 of 30 µm (CP_1) / Jelu-Werk GmbH & CO KG; native potato starch / Agrana Zucker GmbH; pregelatinized corn starch / Roquette GmbH

Methods

Powder Characterization

The materials were characterized regarding their particle size distribution (not shown here) water uptake speed (WUS), water uptake (WU) and swelling capacity (SC) using the setup comprising a glass vessel with a glass-sinter bottom as shown in Figure 1.

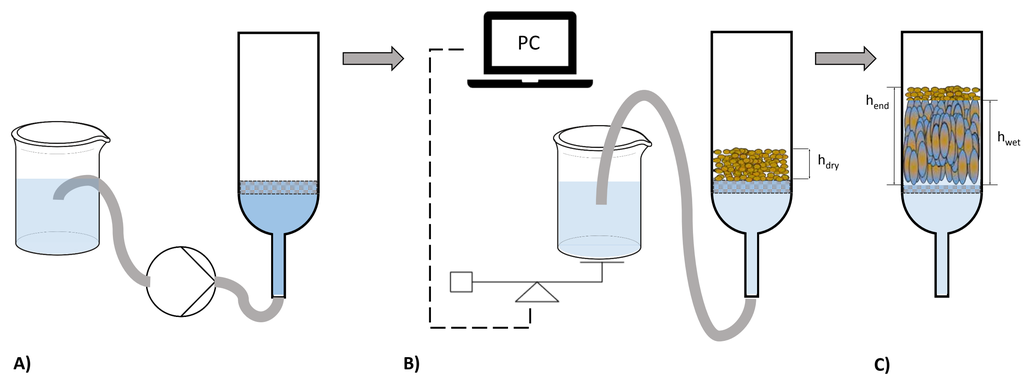

Figure 1: **Apparatus for measuring the swelling capacity, the water uptake water uptake speed A) filling stage B) water uptake measurement C) measurement of powder swelling**

The apparatus was prepared by pumping water until the glass sinter was wetted evenly. A powder sample of an average mass of 5.0 g was inserted into the vessel on top of the glass sinter followed by slight manual levelling and compression to obtain an even powder bed. The connection to the water supply was opened and data recording started simultaneously. The height of the wetted and swollen powder bed was determined as well as the height of the unwetted powder bed after a run time of 30 min. The swell capacity was calculated from the volume of the actually wetted dry powder and the volume of the swollen wet powder.

$$SC = \frac{V_{swollen}}{V_{wetted}} * 100 \qquad \text{Equation 1}$$

$$D = \frac{L^2}{t} \qquad \text{Equation 2}$$

The Diffusion Coefficient was determined by measuring the water penetration over time into a powder bed filled into 6 mm glass tubes and calculation with the simplified Washburn Equation (Figure 2 and Equation 2).

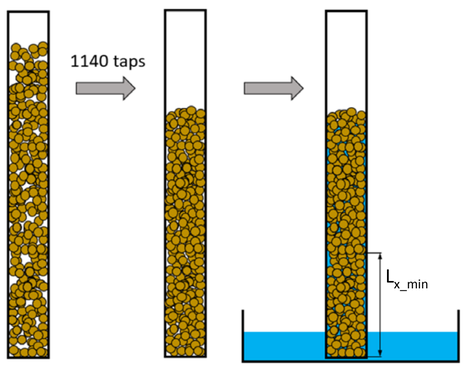

Figure 2: **Method for determination of diffusion coefficient**

Material	F1	F2
TCP 500	24.5	–
DCPA 150	62.2	41.2
MCC 200	9.8	4.9
Mg-St	1.5	1.5
Caff	–	32.6
Sacc	–	17.8
Disintegrant	2	2

Table 1: **Tablet Formulation Composition in %**

Tablet Formulations and Tablet Testing

Tableting mixtures were prepared by mixing the components as shown in Table 1 in a Turbula blender (Willy A. Bachofen AG) for five minutes (without Mg-St) and a further three minutes after addition of Mg-St. Mixtures were compressed on a RoTab T (Luxner Spezialmaschinen GmbH) rotary press using flat-faced 11.28-mm punches. For F1 the main compression force (MCF) was 18.5 kN. Tablets were tested regarding their breaking force, dimensions and mass on a P5 tablet testing system (Charles Ischi AG). Disintegration was measured using an apparatus with integrated end-point determination DISI-EVO (Charles Ischi AG).

Results

Figures 3 and 4 show the results of the water uptake and swelling tests. The water uptake capacity and the swelling capacity of the new disintegrant mixture is significantly higher than that of the cellulose and starch materials. In contrast to that the rate of water uptake is much faster for cellulose powders than for starches or the new CompactCel® DIS mixture. It can be observed that smaller cellulose particles effect a faster uptake. Comparing native potato starch with pregelatinized corn starch, it can be observed that the processed starch shows only very slow water uptake. Disintegration times for F1 (Figure 5) seem to be generally faster than those for F2 (Figure 6) while cellulose powders seem to show little disintegration action for F1. Starches show a good disintegration effect for F1 but not for F2. CompactCel® DIS shows a good disintegration effect in both formulations.

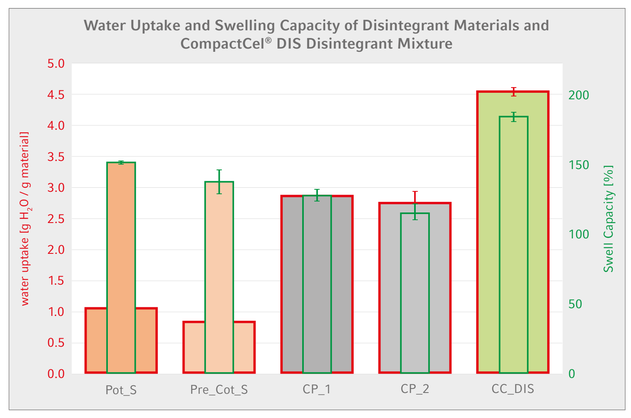

Figure 3: **Results for water uptake and swelling capacity**

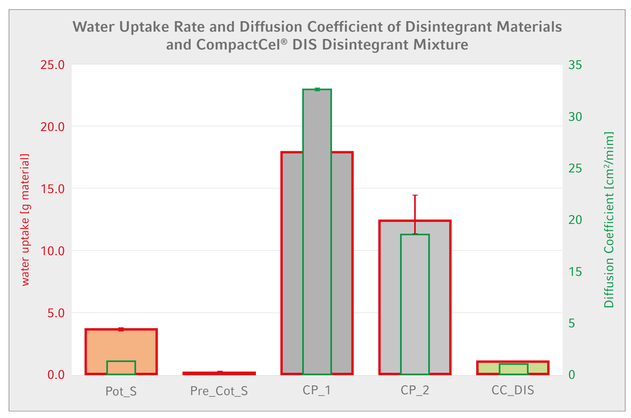

Figure 4: **Results for water uptake rate and diffusion coefficient**

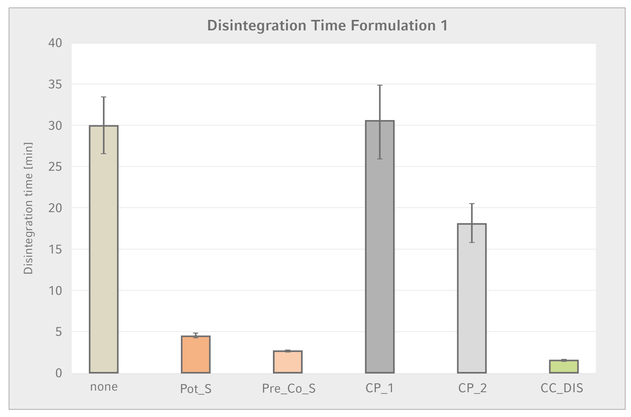

Figure 5: **Disintegration times for Formulation F1**

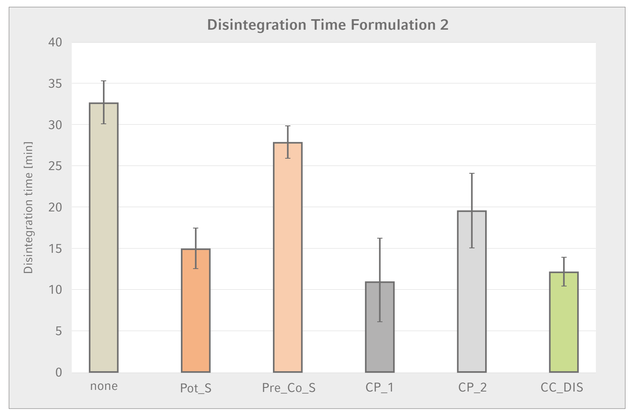

Figure 6: **Disintegration times for Formulation F2**

Conclusion

Tablet disintegration depends heavily on the tablet ingredients and the porosity of the compacts. The two examples above show that a fast uptake of water is not of paramount importance to achieve fast tablet disintegration. A high water uptake and swelling capacity is shown to be leading to faster disintegration in the given examples. The new CompactCel® DIS is an alternative disintegrant comprising only natural materials.

References:

[1] S. Panda, G. Sethi und P. Madhusrota, “Superdisintegrants from Natural Origin: An Update Review,” International Journal of Pharmacognosy and Phytochemichal Research, Bd. 12, Nr. 1, pp. 1-15, Januar 2020.

[2] D. Markl und A. Zeitler, “A Review of Disintegration Mechanisms and Measurement Techniques,” Pharm Res, pp. 890 - 917, 2017

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