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RESEARCH PAPER

Investigation of Different Vegetable Cell Walls as Disintegrants in Direct Compression of Tablets

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ABSTRACT

The present work investigated the disintegrating action of vegetable cell wall textures of two different plants. We observed high swelling volumes and Enslin values for the powder in dependence on the particle size, high swelling displacements, and short disintegration times for tablets containing Emcompress® and magnesium stearate. The results were compared at the same concentrations with other common disintegrants: cross-linked polyvinylpyrrolidone, microcrystalline cellulose, and maize starch. It was established that the vegetable cell walls showed disintegration properties similar to those of Kollidon® CL. The disintegrating effect of the vegetable materials was based essentially on the volume increase of the dry, shrunken cells in contact with liquids. It was stated that the maximum swelling displacement is not the most important value in describing the disintegrating action, but rather the maximum swelling speed we obtained after fitting the Weibull function. The large maximum swelling displacements are prerequisite to a good disintegrating effect and so it could be postulated that the vegetable cell wall material is qualified for use as a disintegrating agent in solid drug forms.

***Key Words**: Cell walls; Direct compression; Disintegrants; Swelling displacement; Swelling speed.*

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INTRODUCTION

Many authors have dealt with the search for the mode of action of various disintegrants in tablets produced by direct compression. Many theories of the disintegrating action have been presented and many of them really concerned only particular materials. Disintegrating substances are responsible for a rapid disintegration of the tablet, and this is the first step in achieving rapid availability of the active ingredients of the compact. Fielder (1), Lowenthal (2), and other authors divided disintegrants into three types: first, those substances that effect a rapid disintegration by evolution of gases; second, surfactants that improve the moisture uptake; third and most important, macromolecular materials that increase their volume and the swelling pressure by water uptake.

The effect of volume increases on disintegration was investigated by Modrzejewski et al. (3). Hüttenrauch and Jacob (4) established that the capillary effect, and not the increase of volume, is the main reason for the disintegrating action. The porosity and the diameter of the pores were found to be important by Nogami et al. (5). The effect of the hydrophilicity on the mode of disintegration was researched by Kolarski and Krowczynski (6). Other authors (7,8) investigated the effect of swelling pressure, swelling volume, and tableting conditions on the efficiency of substances for the disintegration of compacts.

In this work we present the application of two kinds of vegetable cells, which consist only of pure cell walls (cellulose) as disintegrating agents, effecting the disintegration essentially by volume dilatation. The cell walls of *Chenopodium album* L. and *Beta vulgaris* L. were investigated and compared with common disintegrants based on the Enslin value and maximum swelling volume of the powders, axial swelling displacement, and disintegration time of tablets containing Emcompress® as filler-binder and magnesium stearate as lubricant.

MATERIALS

Production of the Vegetable Cell Material

A technique for production of vegetable cell wall material was described by Ehwald et al. (9,10). They used suspension cultures of whole plants or cell textures of some plants. At the end of the production process they obtained intact cell wall textures possessing no other cell materials such as nucleus or chloroplasts. The cell walls produced were dried with a suitable drying procedure. It was necessary to remove the water completely (i.e., with organic solvents) because, first, the cell wall textures could tear and so be destroyed, and second, they could shrink and glue up irreversibly. If the cell walls glue up they can never reach their real volume.

In our work we used two different plants with different cell diameters, *Chenopodium album* L. (diameter measured by light microscopy about 30 μm) and *Beta vulgaris* L. (d = 20 μm). At the end of the drying process we obtained white, dry powders.

Materials for Direct Compression

As filler-binder we used Emcompress® ($CaHPO_4 \cdot 2H_2O$; Fa. E. Mendell); as lubricant, magnesium stearate (Laborchemie Apolda); and as other disintegrants for comparison microcrystalline cellulose (Avicel® pH 101, Fa. FMC), cross-linked polyvinylpyrrolidone (Kollidon® CL, Fa. BASF), and maize starch (Fa. Caesar & Lorentz).

METHODS

Water Uptake

The water uptake capacity of the disintegrants was measured as the Enslin value. This is the volume of water uptake per gram of substance during 15 min.

Swelling Volume

The swelling volumes of the disintegrants were established by a simple method of Hüttenrauch and Jacob (11). We suspended a defined volume of our disintegrant in water, and after filtration 1 hr later we measured the final volume.

Direct Compression

We produced, per charge, 20 flat-faced tablets with a diameter of 11 mm and a weight of 300 mg, using a rotary tablet machine (Pharmapress 100, Fa. Korsch) with low speed of 10 rpm. Produced tablets consisted of 0.5 disintegrant, 1% magnesium stearate as lubricant, and Emcompress as filler-binder. Compaction pressure was selected so that the tablets received a radical crushing strength of nearly 65 ± 2 N (Erweka strength tester).

Disintegration Time

For measuring the disintegration time of the tablets we used the DAB10 disintegration apparatus with disks in water at 20°C. The tablet was disintegrated if all fragments of the tablet passed the net used.

Maximum Swelling Displacement and Swelling Speed

The axial expansion of the tablet during water uptake and swelling was measured with a method described by List and Muazzam (12), modified to an isobar method by Lorenz (13). Lorenz applied a constant force (we used 980 mN) on the tablet and registered the axial volume dilatation measured by a strain gauge and recorded by a computer. Using the Weibull function, the maximum swelling displacement and the maximum swelling speed could be calculated.

RESULTS AND DISCUSSION

First we investigated the effect of the particle size of the connected cell walls on water uptake and volume dilatation. Therefore we separated the powder by sieving into four particle sizes: <180 μm, <250 μm, <355 μm, and <500 μm. We observed an increase in Enslin values and swelling volumes (up to 4000%) for the cell wall powder with increasing particle size (Fig. 1). The reason could be the extraordinary development of the shrunken cells in aqueous liquids. Moreover, both values of the cell wall material of *Chenopodium album* L. were higher than these of the *Beta vulgaris* L. cells, which is attributed to the larger cell diameter of the first. Contrary to the substances mentioned, the common disintegrants showed only a small volume increase during swelling: for Kollidon® CL 50%, for Avicel® pH 101 55%, and for maize starch only 13%.

In the powder investigations that followed we produced tablets containing Emcompress®, 1% magnesium

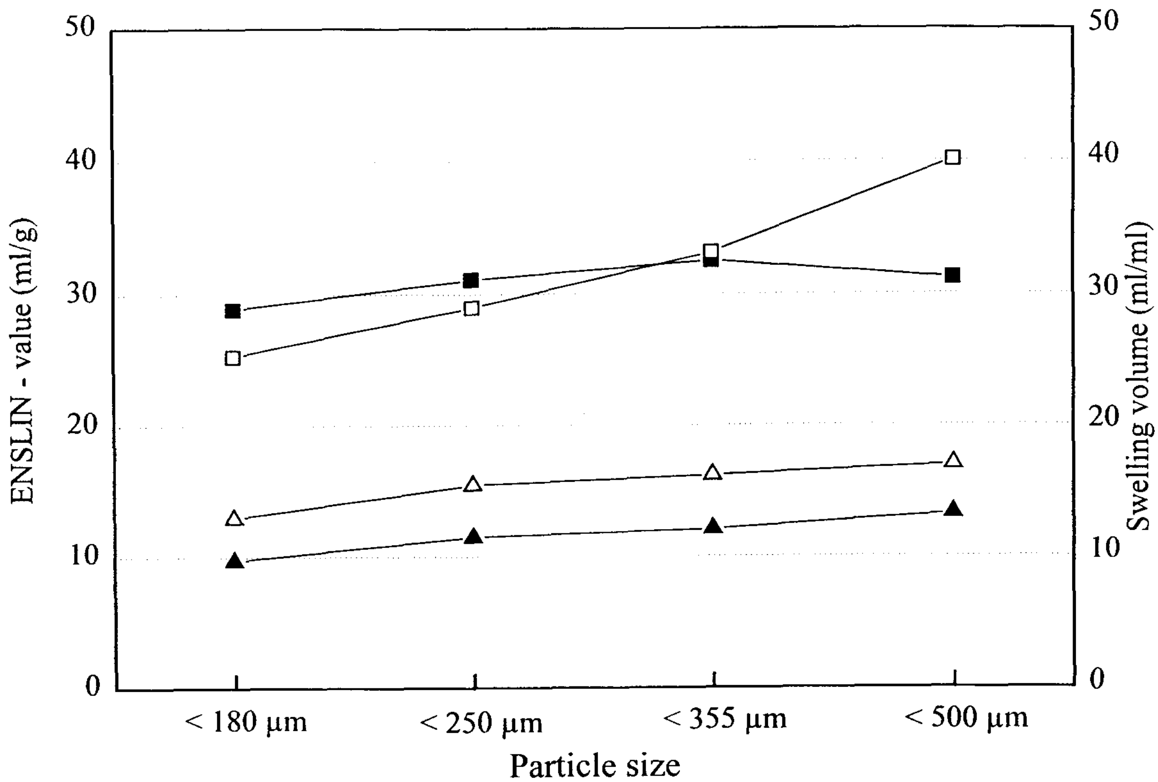

Figure 1. Dependence of Enslin value (▲, ■) and swelling volume (Δ, □) on the size of the cell powder of *Chenopodium album* L. (□, ■) and *Beta vulgaris* L. (Δ, ▲) at a concentration of 0.5%.

stearate, and as disintegrating agent 0.5% of the different cell wall sizes of both plants. Although during the powder investigation, we found lower Enslin values and swelling volumes for the smaller particles of the vegetable material, we observed larger maximum swelling displacements and shorter disintegration times for the tablets containing these disintegrants than for the tablets containing the larger cell wall particles (Fig. 2). So this confirmed the results of List et al. (14), who established that not only the swelling volume but also the swelling force determines the disintegrating effect. The smaller cell wall particles produced higher maximum swelling displacements because they consisted of more particles better distributed in the compact in such low concentrations than is the case for larger particles. So it was necessary to use small cell wall particles for the following investigations.

The next step was to compare tablets containing the cell powder of *Beta vulgaris* L. powder (average particle size of 100 μm) with tablets containing the other common disintegrants. We observed excellent disintegration properties for the vegetable cell wall material at a concentration of 0.5%, comparable to Kollidon® CL (Fig. 3). But for the other disintegrants we measured significantly lower maximum swelling displacements and therefore longer disintegration times than for the cell material of *Beta vulgaris* L.

Although the maximum swelling displacement for Kollidon® CL was lower than for *Beta vulgaris* L., we noticed shorter disintegration times. After analysis of the swelling diagrams (Fig. 4) we established that not only the maximum swelling displacement was important for the rapid disintegration of the tablets but also the maximum swelling speed. So we obtained higher values for the maximum swelling speed of Kollidon® CL than for the vegetable disintegrant (Table 1), probably due to the different disintegrating mechanisms of these substances—the vegetable cell walls needed more time to

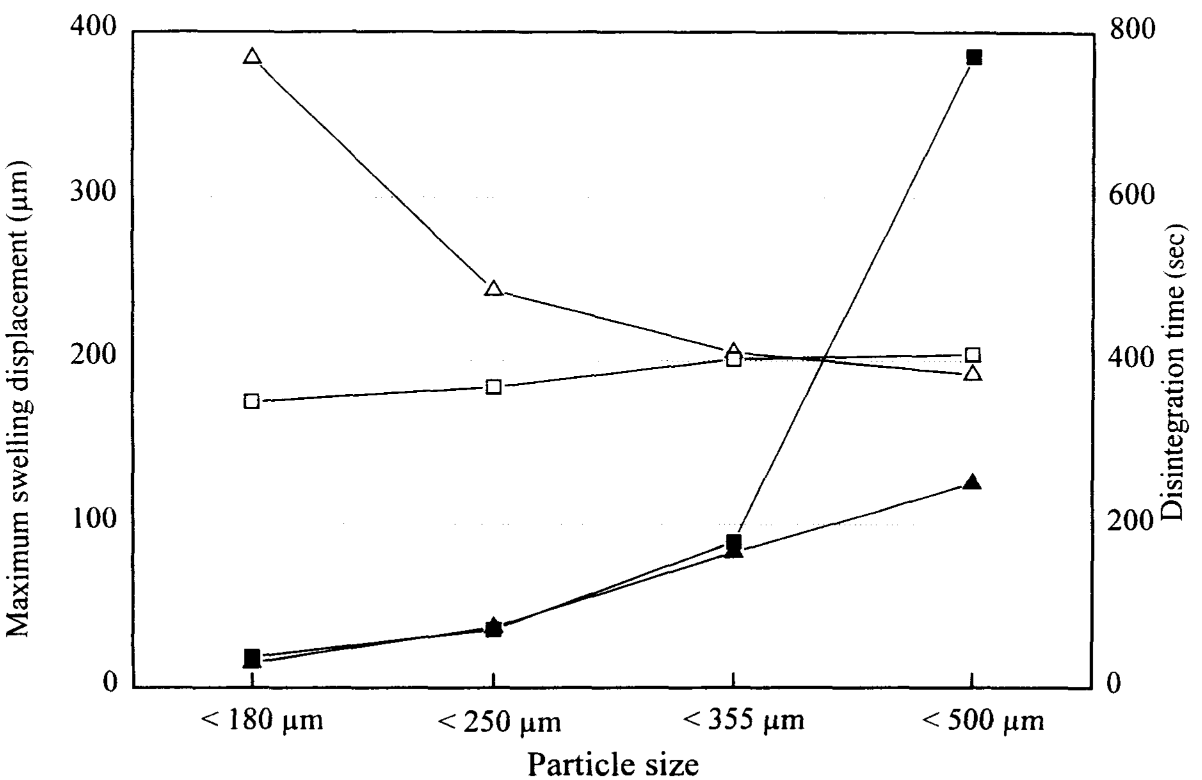

Figure 2. Dependence of maximum swelling displacement (Δ, □) and disintegration time (▲, ■) on the size of the cell powder of *Chenopodium album* L. (□, ■) and *Beta vulgaris* L. (Δ, ▲) at a concentration of 0.5%.

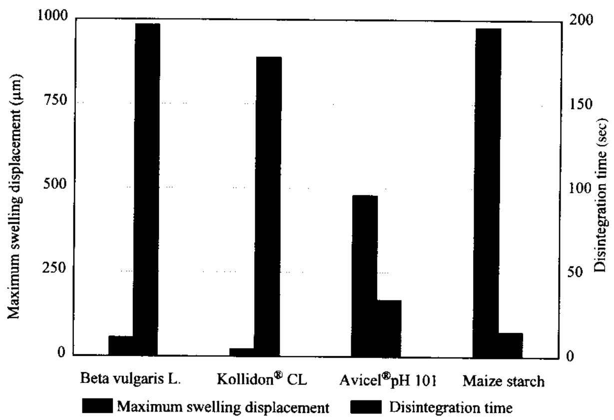

Figure 3. Comparison of maximum swelling displacement and disintegration time of the cell powder of *Beta vulgaris* L. with different disintegrants at a concentration of 0.5%.

swell. Nevertheless we noticed that the vegetable cell wall material was suitable for use as a disintegrating agent for direct-compressed tablets.

Table 1

Maximum Swelling Displacement (s_{max}), Maximum Swelling Speed (v_{max}), and Time of the Maximum Swelling Speed of Tablets (t) with Different Disintegrants at a Concentration of 0.5%

	s_{max} (µm)	v_{max} (µm/sec)	*t* (sec)
Beta vulgaris L.	197	1.45	80
Kollidon CL	178	6.18	8
Avicel pH 101	38	0.08	111
Maize starch	15	0.01	618

CONCLUSIONS

To characterize the vegetable cell wall material, we established that the powders showed large values of water uptake and swelling volume, which increased with particle size. Good disintegration properties were observed for tablets containing the vegetable cell walls, similar to cross-linked polyvinylpyrrolidone in low concentration. The reasons for this were a good capillary

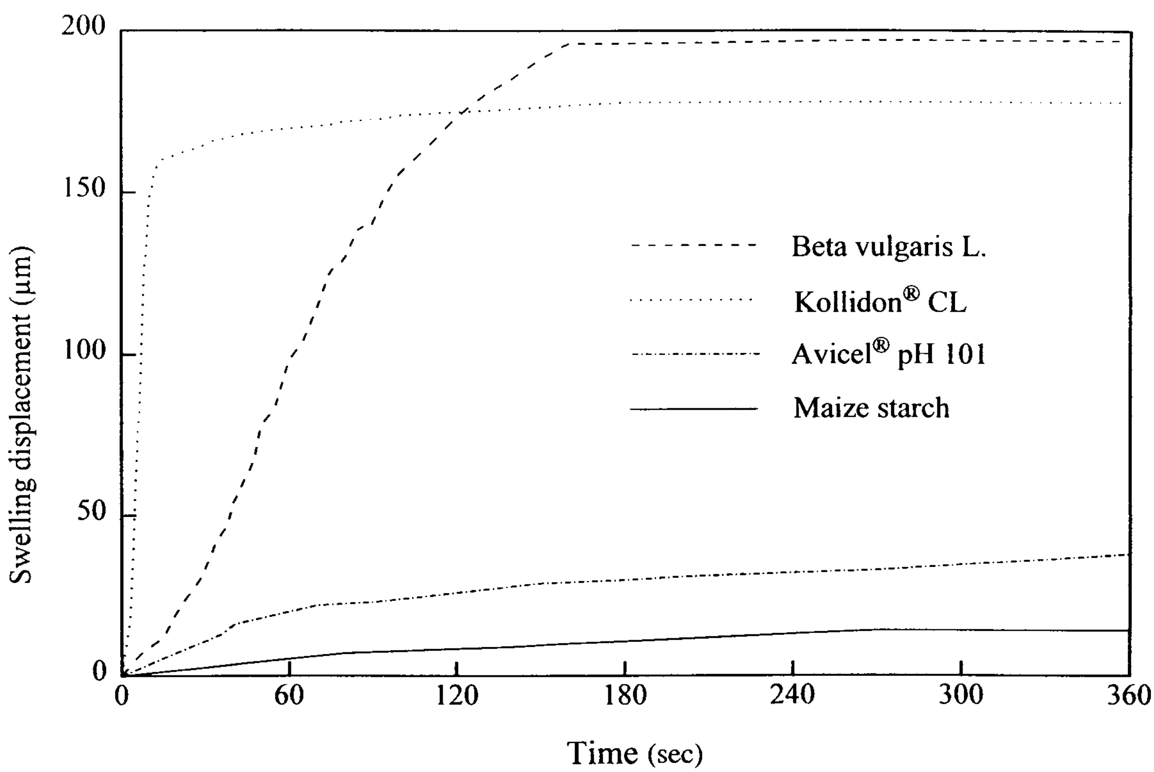

Figure 4. Development of the swelling displacement as a function of time (concentration of disintegrants 0.5%).

effect and high swelling forces of these substances, measured by the axial volume dilatation against a steady force. So they could be used in low concentrations. The disadvantage was the expensive production procedure.

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