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COMMUNICATION

Comparative Tablet and Rheological Properties of New Microcrystalline Cellulose: Direct Compression and Wet Granulation Methods

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ABSTRACT

The overall objective of this study was to compare the rheological properties and tablet characteristics of two new varieties of celluloses (Vivacel 101 and 102), recently produced and commercialized, with the classical varieties of celluloses (Avicel and Elcema). The results showed no significant differences in the rheological properties of Vivacel and Avicel, while significant differences were found between the two celluloses and Elcema. Furthermore, there were no statistically significant differences in the disintegration times and T_d *values of Vivacel and Avicel. In conclusion, it was found that these new celluloses offer all the known advantages of Avicel.*

INTRODUCTION

Cellulose is a widely used natural material. It is principally obtained from fibrous plants (cotton and wood fiber), which are mechanically transformed in wood pulp and chemically in paper pulp, followed by spray-drying, to cellulose with the chemical formula $(C_6H_{10}O_5)_n$ (1). In this formula, *n* has a value of 500 or more. Microcrystalline and powder cellulose are available on the market. Both powder or microcrystalline cellulose contain the alpha cellulose in their chemical compositions. The differences between them result only from the manufacturing process. The powdered cellulose is obtained by mechanical treatment of alpha cellulose, while microcrystalline cellulose is obtained by chemical treatment of alpha cellulose (2). According to the manufacturer, cellulose grades differ from each other by particle size and moisture content.

Natural cellulose is considered as an excellent excipient and may be used in several different industrial appli-

cations. In pharmaceutical formulations, it is used principally as a binder, a filler, a disintegrating agent, and even as a lubricant (3,4). A considerable number of celluloses have been marketed by various industries. Recently, two new varieties of cellulose (Vivacel 101 and Vivacel 102) were produced by the JRS Company (Germany). The aim of this study was to compare the properties of tablets containing this new cellulose and those containing classical cellulose.

MATERIALS AND METHODS

The following materials were used as received: theophylline monohydrate (Cooper); classical cellulose Avicel PH 101 and PH 102 (Seppic), Elcema P050 and G250 (Degussa); new cellulose Vivacel 101 and 102 (JRS); lactose HMS, cornstarch, and magnesium stearate (Cooper). Table 1 shows the formulas of the 500 mg tablets obtained containing 20% theophylline monohydrate.

These formulations were either prepared by direct compression or by wet granulation. In either case, the methodologies used for compressed tablets was described in an earlier study (5).

For differential thermal analysis (DTA), approximately 25 mg of each cellulose were weighed and put in flat-bottomed open platinum pans. The samples were heated in dynamic air (0.5 l/hr), and curves were obtained on a Setaram TG-DTA 92 apparatus. Thermograms were obtained by heating at a constant rate of 2°C/min over the 20°C to 650°C temperature range.

Pure powder particle size distribution was carried out using a laser light-scattering analyzer (Malvern MasterSizer X), while the dried granules were sieved using a vibrating sieve (Retsch 3D) according to Afnor norms (NF ISO 2591).

The weight uniformity and thickness of the tablets were determined by an analytical balance (Mettler LP 12) and a micrometer (Roche), respectively. The hardness and friability were measured by a tablet hardness tester (Vanderkamp) and friability tester (Erweka TAR, 40 rpm for 15 min). The disintegration test was carried out on six tablets at 37°C in distilled water using the European Pharmacopoeia method II apparatus Erweka ZT3 without disks. The dissolution test was carried out using the USP XXIII method II. An automatic Pharma test PTW3C dissolution apparatus (Prolabo/France) was coupled to a CamSpec M330 ultraviolet/visible (UV/Vis) spectrophotometer with continuous flow to provide drug dissolution data. Six samples from each formulation were tested using 1000 ml of simulated gastric fluid (pH 1.2) at 37°C and with a stirring rate of 100 rpm. The drug release was determined at a wavelength of 253 nm.

Statistically, release data were analyzed according to the equations of Weibull (6) and Kitazawa (7).

RESULTS AND DISCUSSION

The results from thermal analysis are shown in Table 2 and Fig. 1 (curves as an example). The first endothermic peak at 50°C–60°C is due to sample humidity. Elcema P050 and P250 showed a weight loss higher (5.76% and 6.17%, respectively) than the first four samples (4.38%, 4.53%, 4.55%, and 4.32%, respectively). The endothermic peak near 290°C was not always present. For the first exothermic peak, Elcema P050 and P250 presented a lower temperature (311°C and 312°C, respec-

Table 1

Formulation Ingredients Used and Their Percentage

Ingredients	F1	F2	F3	F4	F5	F6	F7
Theophylline	20	20	20	20	20	20	20
Lactose	68	34	34	34	34	34	34
Avicel PH 101		34					
Avicel PH 102			34				
Vivacel 101				34			
Vivacel 102					34		
Elcema P050						34	
Elcema G250							34
Cornstarch	11.7	11.7	11.7	11.7	11.7	11.7	11.7
Magnesium stearate	0.3	0.3	0.3	0.3	0.3	0.3	0.3

Table 2

TG-DTA Characterization of the Cellulose Samples

Batch	Endothermic Peaks °C	Endothermic Peaks Weight Loss (%), 130°C	Endothermic Peaks °C	1° Peak, Exothermic (°C)	1° Peak, DTG °C	1° Peak, DTG %/mn	Exo/MS (%)	DT (ATD-ATG)	2° Peak, Exothermic (°C)
Avicel 101	53	4.38	288	318	303	7.53	80.1	14.4	456
Avicel 102	55	4.53	—	319	307	8.38	78.5	12.1	448
Vivacel 101	58	4.55	288	318	302	7.07	80.4	15.5	454
Vivacel 102	56	4.32	291	317	306	6.88	80.4	15.0	455
Elcema P050	60	5.76	—	311	301	7.66	76.1	10.1	434
Elcema G250	58	6.17	—	312	301	6.19	76.4	11.4	437

tively) than the first four others (318°C, 319°C, 318°C, and 317°C, respectively). Similar data were observed for the differential thermal gravimetry (DTG) peak: 301°C and 301°C for Elcema P050 and P250, respectively, versus 303°C, 307°C, 302°C, and 302°C, respectively, for the first four others. There was no significant difference between the decomposition rate speeds (%/mn) of all samples except for Elcema P250 (6.19%). The loss of volatility near 300°C (Exo/MS) corresponds to 76.6% and 76.4% for Elcema P050 and P250, respectively, and 80.1%, 78.5%, 80.4%, and 80.4% for the first four others, respectively. The maximum peak temperature difference between DTA and DTG is 10.1°C and 11.4°C for Elcema P050 and P250, respectively, versus 14.4°C, 12.1°C, 15.5°C, and 15.0°C for the first four others, respectively. The second DTA exothermic peak of Elcema P050 and P250 presented lower temperatures (434°C and 436°C, respectively) than the 4 other samples (447°C to 456°C).

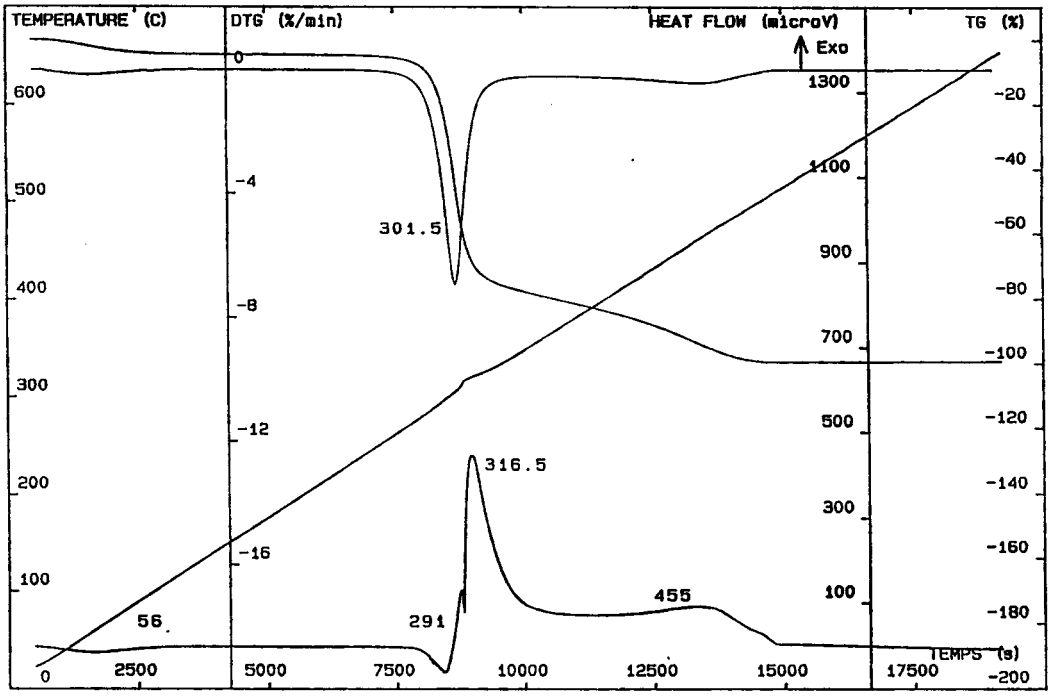

Figure 1. TG-DTA profile of Vivacel 102.

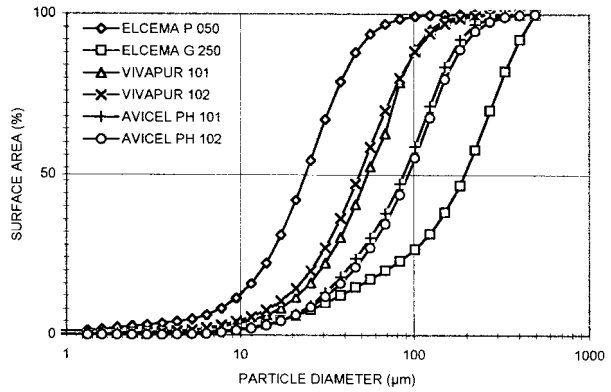

Figure 2. Particle size distributions determined by laser light scattering.

Also, it is higher and sharper (surely due to a sudden combustion).

From this preliminary evaluation, it seems that two groups can be distinguished: the first group contains Avicel 101 and 102 and Vivacel 101 and 102, while the second group contains Elcema P050 and P250.

A comparison of the profiles of particulate diameter of cellulose powders (Fig. 2) showed no significant difference between Avicel grades and corresponding grades of Vivacel. Similar results were obtained for D_{50} of cellulose powders, D_{50} of granules, flowability, and compaction of mixed powders and nonlubricated granules. However, compared with Elcema grades, the results for these two celluloses (Avicel/Vivacel) were significantly different and confirmed the DTA conclusion.

During wet granulation, the amount of water necessary to granulate a formulation without cellulose (100 ml) was less important than the amount required to granulate a formulation containing cellulose (170 ml). The high presence of lactose with high affinity for water in the reference formulas could explain this difference. In all cases, the formulations produced tablets with good mechanical properties: uniformity of weight and thickness and hardness with good friability ($\%F < 1$). There was very rapid disintegration for all direct compression formulations. The difference in the values observed between formulations were slight enough for them to be considered comparable. These observations led us to use wet granulation only. The results obtained by this method (Table 3) showed that the disintegration times of tablets made with cellulose were much faster than for tablets without cellulose. This might be due to the disintegration effect of cellulose, as shown by different researchers (8).

The characteristic parameters of the RRSBW distribution are presented in Table 3. The high correlation coefficient R^2 values showed that the dissolution data obtained can be described by a Weibull equation. In all cases, the β values were higher than 1, which suggests fast drug release. On the other hand, all T_d values of formulations with cellulose were lower than those of formulations without cellulose. These differences showed that the incorporation of cellulose in the reference formula increased the dissolution rate, which confirmed the disintegration effect of these celluloses. By comparing the corresponding grade of Avicel and Vivacel, it is clear that the T_d values of Avicel 101 and Vivacel 101 or Avicel 102 and Vivacel 102 were similar. However, the T_d values of Elcema grades were different compared with other celluloses. This difference was observed also during DTA, for the rheological properties of powders and granules, and in thickness and disintegration studies and confirmed the existence of two cellulose groups.

Table 4 shows Kitazawa's parameters. All formulations exhibit two straight regression lines (k_1 and k_2) with changing slope and good correlation coefficients $R^2 > .99$. In all cases, the values of k_1 were inferior at those of k_2. We noted also that the times t_k at which the slope changes were almost identical for corresponding grades of Avicel and Vivacel. Good correlation was observed between these times and those obtained during the disintegration test (Fig. 3). In the case of the reference

Table 3

Disintegration Time and Parameters of Weibull (β *and* T_d)

Formulations	F1	F2	F3	F4	F5	F6	F7
Disintegration time (min)	24.4	6.5	11.2	6.5	10.3	9.1	9.1
β	2.12	2.22	2.38	2.20	2.60	2.93	3.16
T_d	14.0	7.8	9.15	7.54	9.16	9.0	6.78
R^2	0.998	0.996	0.999	0.993	0.996	0.997	0.999

Table 4

K_1, K_2, *and* t_k *Values Obtained form Kitazawa Equation*

Formulations	F1	F2	F3	F4	F5	F6	F7
K_1	0.05	0.10	0.18	0.11	0.16	0.05	0.26
K_2	0.28	0.38	0.43	0.37	0.60	1.00	1.14
t_k (min)	14.2	6.9	10.5	6	11	9.3	7.2

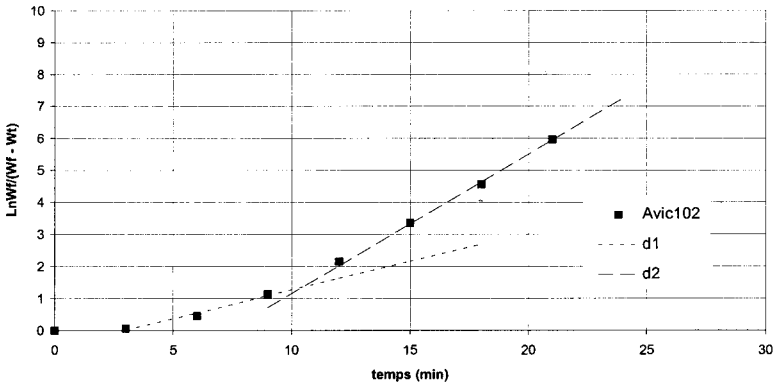

Figure 3. Plot of Vivacel 102 versus time following the model of Kitazawa.

formulation, it was not possible to find this correlation. This may be due to the fact that the reference formula did not contain any disintegrant. In conclusion, the Kitazawa model allowed estimation of the disintegration effect with the celluloses studied. It also permitted, as for the Weibull model, distinguishing two groups according to their disintegration.

CONCLUSION

This study showed that, in spite of differences in the manufacturing process, the rheological properties of Vivacel and Avicel showed no significant differences between their corresponding grades. In addition, there were no statistically significant differences in the disintegration times and T_d values of these two celluloses. The results were also tested using the Kitazawa model. Good correlation was obtained between the disintegration times and the time t_k at which changes of the slope was observed. In conclusion, Vivacel 101 and 102, two new microcelluloses recently produced and commercialized, can be used as alternatives for Avicel 101 and 102 in pharmaceutical formulations.

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