Application of low substituted hydroxypropylcellulose (L-HPC) in the production of pellets using extrusion/spheronization

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Summary

Low-substituted hydroxypropyl cellulose (L-HPC) was used as a binder and disintegrant in granulation and tabletting. The influences of L-HPC on the extrusion process and the characteristics of pellets prepared by extrusion/spheronization were studied. In one trial the type of L-HPC was varied, in a second the amount of L-HPC LH 20. In both trials pellets were manufactured using different quantities of granulation fluid. Depending on the formulation a working range for water contents leading to beads was defined. In the upper part of the working range the quality of the spheres was good in terms of aspect ratio and sphericity. However, the dissolution rate was found to decrease as the water content of the extrudate increased. All types of L-HPC accelerated the dissolution of acetaminophen. There was no strong correlation between porosity and dissolution time, but increasing porosity tended to lead to faster dissolution. Pellets without L-HPC combined low dissolution rate with low porosity while those with L-HPC LH 20 showed the highest dissolution rate and the greatest porosity.

Introduction

In low-substituted hydroxypropyl cellulose (L-HPC) only a small proportion of the three free hydroxyl groups per glucose subunit is converted to a hydroxypropyl ether. L-HPC is insoluble in both water and alcohols, but swells in water. There are several types of L-HPC available with different degrees of substitution and average particle sizes (Shin-Etsu, 1991; Table 1). L-HPC can be used in granulation and tabletting as a binder and/or disintegrant.

Ueda et al. (1988) reported on the use of L-HPC in pellet production. They used L-HPC as a swelling agent in pellets manufactured in a

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TABLE 1

L-HPC types

Particle size (μm)	Hydroxypropyl content (%)		
	8	11	13.5
50		LH 11	
40	LH 22	LH 21	LH 20
25	LH 32	LH 31	LH 30

120

centrifugal granulator using sucrose granules as starter.

The objective of this study was to assess the suitability of L-HPC in extrusion/spheronization to preparation of round, rapidly dissolving spheres. The effect on pellet properties of the type and quantity of L-HPC used was studied. The effect on the pellet properties of varying the water content of the extrudate was also assessed.

Materials and Methods

Materials

Four types of L-HPC (Shin-Etsu Chemical Co., Tokyo, Japan) were used in this study: LH 11 with 11.1% hydroxypropyl content (Certificate of Analysis), LH 20 with 13.3%, LH 21 with 11.3% and LH 32 with 7.6%. Acetaminophen USP (Mallinckrodt, Raleigh, U.S.A.), microcrystalline cellulose (Avicel PH 101, FMC Inc., Philadelphia, U.S.A.) and Aerosil 200 (Degussa, Frankfurt, Germany) were used as received.

The moisture content of the different powders was determined by weighing before and after drying the powders at 105°C for 18–24 h. Demineralized water was used as the granulation liquid. Other materials were of analytical grade.

Experimental design

Power consumption vs water content

In this trial composition 1 was used (Table 2). For L-HPC the four types LH 11, LH 20, LH 21 and LH 32 were inserted. Additional runs were performed using Avicel PH 101, PH 102 and PH 105 instead of L-HPC. The water content of the extrudate was varied in a broad range from 35% up to approx. 60–65% (w/w).

Extrusion was performed with a co-rotating twin-screw extruder using a single step granulation/ extrusion process (Kleinebudde and Lindner, 1993). Extrusion of the 1.5 kg blends started at a high level of water content for the respective formulation. Extrusion was performed continuously with 25 g min⁻¹ of dry powder blend reducing the liquid feed rate every 200 s. The readings

for power consumption during the second half of each interval were used for the construction of power consumption-water content curves. The extrudate was not spheronized in this trial. The exact water content was determined by drying samples taken during extrusion.

Trial type L-HPC

The trial was performed using four types of L-HPC (LH 11, LH 20, LH 21 and LH 32), including three degrees of substitution and three different average particle sizes (Table 1). 1500 g of each blend (Table 2, composition 1) was extruded in randomized order, using three different water content levels. The levels for the water contents designated as 'wet', medium' and 'dry' (Table 3) were dependent on the type of L-HPC. For each level the production started after a lag time of 200 s and continued until about 750 g extruded mass was collected.

TABLE 2

Compositions

Composition 1	
Acetaminophen	30.0
L-HPC	20.0
Avicel PH 101	49.5
Aerosil 200	0.5
Composition 2	
Acetaminophen	30.0
L-HPC LH 20	0–20.0
Avicel PH 101	49.5–69.5
Aerosil 200	0.5

TABLE 3

Levels for water contents and working range for trial type L-HPC

Type	Water content (w/w)			Working range (w/w)
	Wet	Medium	Dry	
None	54.6	50.2	48.0	48–55
LH 11	61.6	57.4	53.3	52–62
LH 20	60.0	53.3	50.0	50–60
LH 21	62.2	57.6	54.3	54–62
LH 32	62.4	56.0	52.5	52–62

TABLE 4

Levels of water contents for trial fraction L-HPC LH 20

Fraction LH 20 (w/w)	Water content (w/w)		
	Wet	Medium	Dry
0.0	53.2	51.5	46.7
2.5	55.4	51.7	46.6
5.0	55.8	51.5	46.4
10.0	55.1	51.6	46.7
20.0	58.6	55.3	51.4

Trial fraction LH 20

The trial was performed with levels for L-HPC LH 20 of 0, 2.5, 5, 10 and 20% in composition 2 (Table 2, composition 2). 1000 g of each blend was extruded in randomized order at three different water content levels. The three different water content levels called wet, medium and dry were dependent on the amount of L-HPC LH 20 in the formulation (Table 4). For each level the production started after a lag time of 200 s and continued until about 350 g extruded mass was collected.

Production procedure

Blending and extrusion were performed as described previously (Kleinebudde and Lindner, 1993). The batch size was 1000 or 1500 g dry powder mass, corrected for the moisture content of the raw materials. For all trials the powder feed rate was 25 g min^{-1} and extrusion speed was fixed at 60 rpm. During extrusion several samples of the extrudate were drawn to determine the water content.

The extrudate was spheronized immediately after production. The spheronizer with a diameter of 320 mm (Type S-320, Nica, Mölndal, Sweden) was operated at 800 rpm (13.4 m s^{-1} radial velocity) with a residence time of 5 min. The wet spheres were dried in a fluid bed dryer (Glatt TR 2, Binzen, Germany) for 30 min with an inlet air temperature of 45°C and with the inlet air flow rate set at maximum.

Analytical methods

Sieve analysis

A pellet batch was divided into fractions using a Retsch spinning riffler (Type PT, Retsch KG, Haan, Germany). Sieve analysis was performed with a fraction sample of about 100 g pellets using a vibratory sieve (Type Vibro, Retsch KG, Haan, Germany) for 5 min at maximum amplitude. Mesh sizes of the sieves used were 1400, 1250, 1120, 1000, 900, 710 and 500 μm, respectively.

The results were evaluated with the help of the RRSB-graph (DIN 66145, 1976) leading to the parameters d' (RRSB diameter) and n (exponent) for the particle size distribution. d' is used to characterize a mean diameter of the pellets. n is a measure of particle size range: the greater the value of n the smaller the particle size distribution. The fraction of pellets in the particle size range of 900–1120 μm was also determined.

Image analysis

For image analysis (Leco 2001, Leco Instruments, St. Joseph, U.S.A.) a fraction of the unsieved pellets was distributed on an illuminated desk. A scan of 4×4 frames, containing about 2000–3000 particles, was performed and each individual pellet was inspected. All main parameters, i.e., area, length (= longest of 8 measured Ferets), width (= shortest Feret), aspect ratio (AR = length/width), roundness (= $4\pi \cdot$ area $\cdot$ perimeter^{-2}) and their respective standard deviations were evaluated. The sphericity (S) according to Lövgren and Lundberg (1989) was calculated from the aspect ratio distribution to provide additional data. For aspect ratio 25 classes were defined with 0.1 as class width. Sphericity allows a good differentiation between various shapes:

$$S = \frac{1}{\sum (b^2 \cdot \mathrm{rf})} \cdot 100 \qquad (1)$$

where S is the sphericity, b represents the lower class limit and rf is the relative fraction of the class.

Dissolution testing

Dissolution testing was performed using the paddle method at a rotation speed of 100 rpm. The dissolution apparatus (Apparatus 2, USP XXII, Type Sotax AT6, Sotax AG, Basel, Switzer-

122

land) was interfaced to a spectrophotometer (Type DU 50, Beckmann Instruments, Fullerton, U.S.A.). The UV absorbances at 280 nm were measured automatically at each sampling time point and stored on a computer.

For the dissolution experiments pellet fractions in the particle size range 1000–1120 μm were used. Each dissolution test was performed on six 250 mg samples of pellets with 900 ml of phosphate buffer pH 7.5 (ionic strength 0.1) heated to 37°C.

The amount of acetaminophen released was calculated using a value for $A_{1\ cm}^{1\%}$ of 117. Six samples per pellet batch were tested, in a randomized order, to obtain the average release profile and determine the reproducibility of drug release. For a parametrization of the dissolution curve all data up to 80% release of acetaminophen were fitted to the Weibull function (RRSB plot) according to Langenbucher (1972). The data showed no lag time for dissolution, so only the estimation of dissolution time T_d, the time interval when 63.2% of drug is released, is necessary. The calculation of dissolution time is based on the whole release profile up to 80% release. T_d can be estimated precisely and is able to differentiate between various dissolution profiles.

Porosity

The porosity of the pellets was calculated from Eqn 2:

$$\epsilon = 100 \cdot \left(1 - \frac{\rho_a}{\rho_t}\right) \qquad (2)$$

True density (ρ_t) was determined with a Beckmann air comparison pycnometer (Model 930, Beckmann Instruments, Fullerton, U.S.A.). Apparent density (ρ_a) was determined using mercury intrusion porosimetry (Porosimeter 2000, Carlo Erba Instruments, Milano, Italy). All measurements were repeated once. Using the mean of true density measurements for a batch, porosities for each apparent density measurement were calculated separately.

Results

Power consumption vs water content

In Figs 1 and 2 the power consumption-water content profiles for the tested formulations are shown. It was not necessary to correct power consumption for the power consumption of the empty extruder, since all data were generated using the same screw speed. Here, there is no judgement placed on the ability of the extrudate to form spheres. All curves show a decrease of power consumption with increasing water content. The curves for the three Avicel types have very similar shapes. The profiles for the L-HPC containing formulations are flatter when compared to those containing Avicel.

The appearance of the extrudate was not satisfactory across the whole range of water contents. At high water contents, especially for the Avicel formulations, the extrudate existed as a suspension without any significant coherence. At slightly lower water contents the extrudate was a uniform wet mass sticking readily together. Over a specific range of water contents the extrudate appeared to be of satisfactory quality. Reducing the water content below the minimum level of this range, however, increased the brittleness of the extrudate and its plasticity was significantly reduced. Power consumption, pressure of the extrudate at the die plate and extrusion temperature were all found to increase as the water content of the extrudate decreased. The water content range for preparation of good quality extrudate was dependent on the formulation.
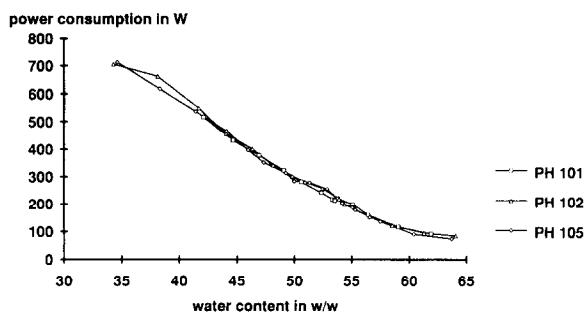

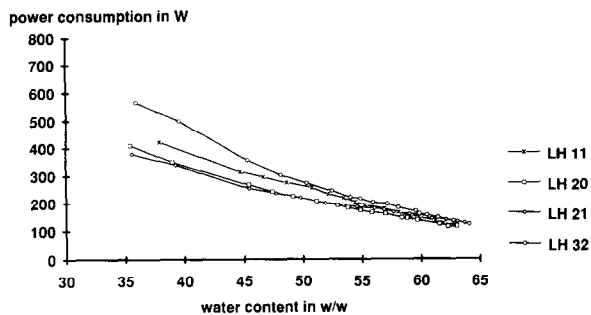Fig. 1. Power consumption-water content profile for different Avicel types.

power consumption in W

Fig. 2. Power consumption-water content profile for different L-HPC types.

length in mm

Fig. 3. Dependency of pellet length on particle size of incorporated L-HPC for different water contents of extrudate.

area in mm^2
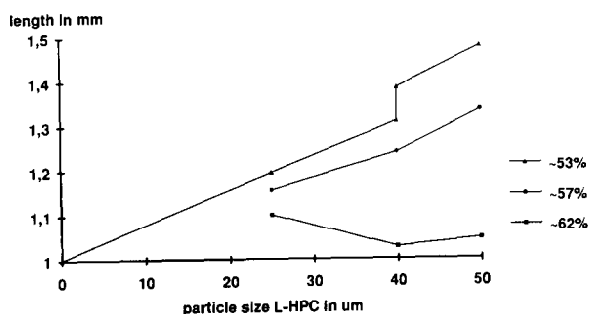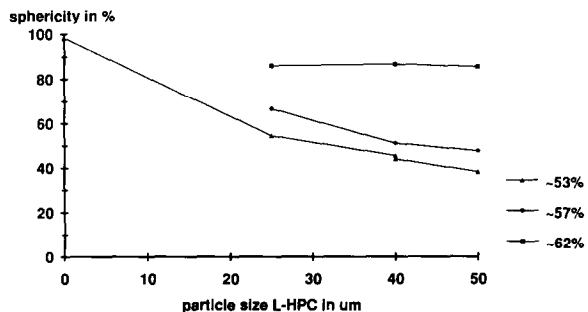
Fig. 4. Graphical representation of pellet area as function of water content of extrudate for different L-HPC types.

sphericity in %

Fig. 5. Graphical representation of pellet sphericity as function of water content of extrudate for different L-HPC types.

sphericity in %

Fig. 6. Dependency of pellet sphericity on particle size of incorporated L-HPC for different water contents of extrudate.
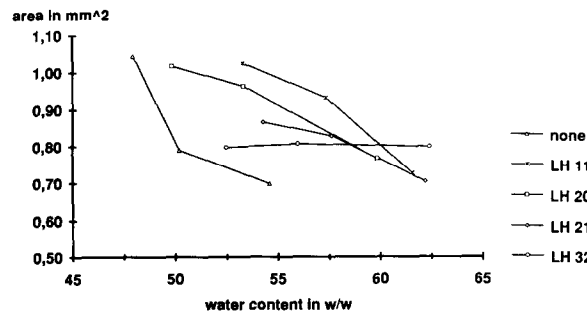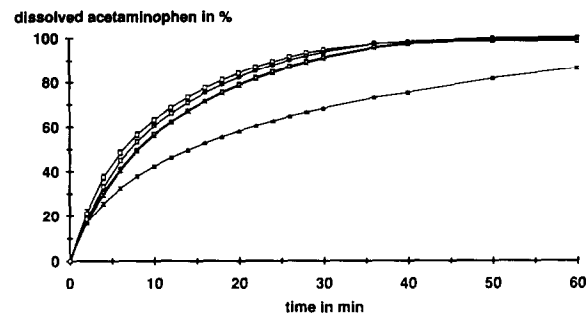
dissolved acetaminophen in %

Fig. 7. Dissolution profiles for pellets containing different L-HPC types prepared from extrudates with 52% water content (SD, $n = 6$): ($\triangle$) none, ($*$) LH 11, ($\square$) LH 20, ($\diamond$) LH 21, ($\circ$) LH 32.

TABLE 5

Results of sieve analysis for trial type L-HPC

Type	d' (μm)			n			Fraction 900–1 120 μm (%)		
	Wet	Medium	Dry	Wet	Medium	Dry	Wet	Medium	Dry
None	1 001	961	975	15.1	8.6	10.3	74.9	62.8	71.4
LH 11	1 007	969	922	15.1	13.8	12.8	76.7	63.4	44.7
LH 20	1 079	979	979	10.0	12.7	10.0	61.3	63.9	58.4
LH 21	978	920	911	14.2	14.9	12.9	67.7	47.4	38.7
LH 32	990	915	934	21.8	11.0	13.6	87.6	52.3	62.8

Trial type L-HPC

Sieve analysis

The results for d', n and fraction between 900 and 1120 μm are shown in Table 5. There are no obvious trends in the data for the three parameters.

Image analysis

The results of image analysis are listed in Table 6. Length, width and area describe the particle size distribution. The width was defined by the die diameter and showed only minor variations. Variations in particle size were a result of differing pellet lengths. Fig. 3 shows the dependence of the length on the mean particle size of the L-HPC type at different water contents of the extrudate. At low water content the length increased with L-HPC particle size. However, at high water content all pellets had the same small length. Another important parameter for pellet size was the area. In Fig. 4 area vs water content plots are shown for the different formulations. For the formulation with LH 32 the area was small and nearly independent of the water content. The other formulations show a decrease in area with increasing water content of the extrudate. The final values for the respective wet masses are of comparable magnitude independent of the absolute water content.

Aspect ratio, roundness and sphericity all define the shape of the beads. The three parameters showed the same trends, but aspect ratio and sphericity are considered to be the most appropriate for accurately assessing bead shape. Aspect ratio can be detected more precisely than roundness by image analysis, especially for small parti-
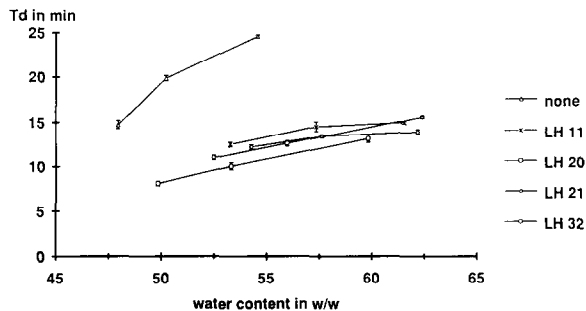

Fig. 8. Interrelation between dissolution time (T_d) and water content of extrudate for different types of L-HPC (SD, $n = 6$).

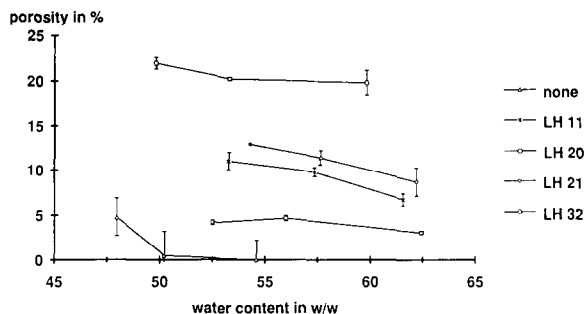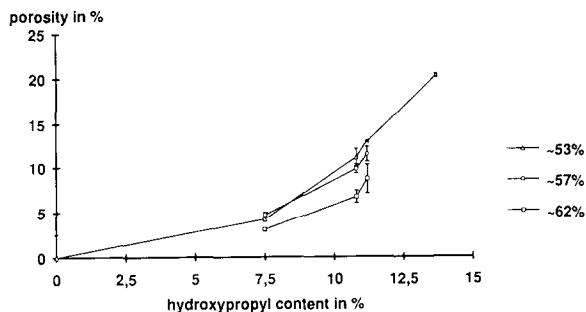Fig. 9. Pellet porosity as a function of water content of extrudate for different types of L-HPC (SD, $n = 2$).

Fig. 10. Dependency of pellet porosity on hydroxypropyl content of incorporated L-HPC for different water contents of extrudate (SD, $n = 2$).

TABLE 6

Results of image analysis for trial type L-HPC (standard deviations in parentheses)

| Type	Width (mm)			Length (mm)			Area (mm^2)		
	Wet	Medium	Dry	Wet	Medium	Dry	Wet	Medium	Dry
None	0.89 (0.11)	0.85 (0.11)	0.98 (0.12)	1.00 (0.12)	1.19 (0.21)	1.39 (0.26)	0.70 (0.15)	0.79 (0.19)	1.04 (0.26)
LH 11	0.89 (0.10)	0.88 (0.09)	0.88 (0.09)	1.05 (0.11)	1.33 (0.28)	1.48 (0.35)	0.70 (0.14)	0.83 (0.25)	0.87 (0.29)
LH 20	0.90 (0.13)	0.88 (0.10)	0.90 (0.10)	1.08 (0.16)	1.39 (0.36)	1.43 (0.39)	0.77 (0.20)	0.96 (0.31)	1.02 (0.35)
LH 21	0.88 (0.11)	0.85 (0.11)	0.85 (0.10)	1.03 (0.12)	1.24 (0.27)	1.31 (0.32)	0.73 (0.13)	0.93 (0.23)	1.02 (0.26)
LH 32	0.94 (0.08)	0.89 (0.10)	0.84 (0.08)	1.10 (0.09)	1.16 (0.18)	1.20 (0.21)	0.80 (0.13)	0.81 (0.19)	0.80 (0.18)
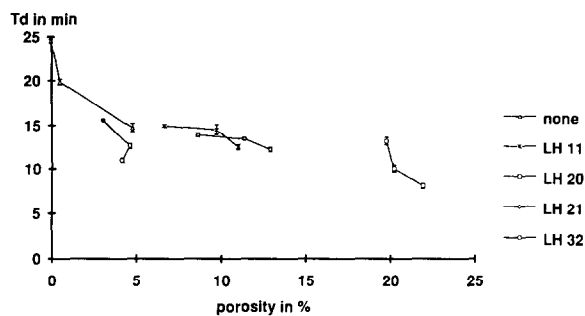
Fig. 11. Interrelation between dissolution time (T_d) and pellet porosity for different types of L-HPC containing pellets (SD, $n = 6$).

Fig. 12. Dissolution profiles for pellets containing different fractions of L-HPC LH 20 prepared from extrudates with 52% water content (SD, $n = 6$): (○) 0%, (∗) 2.5%, (□) 5%, (△) 10%, (◇) 20%.

cles. Sphericity is a parameter for the whole sample and allows good differentiation between batches. The sphericity for the different L-HPC types as a function of water content of the extrudate is shown in Fig. 5. The sphericity values are always greater for the wet masses than for the dry and medium masses. The best result was obtained for the wet formulation without L-HPC. The sphericity for the wet L-HPC containing pellets was of the same order, but lower than that for the L-HPC free pellets. For a constant water content the sphericity decreased with increasing particle size of the incorporated L-HPC type (Fig. 6). This effect was more pronounced for lower water contents. However, for wet masses this effect levels out.

Dissolution

The dissolution profiles for the five tested formulations at about 52% water content are shown in Fig. 7. The release from L-HPC free pellets was clearly slower than for the other pellets. Fig. 8 depicts the change in T_d for the five formula-
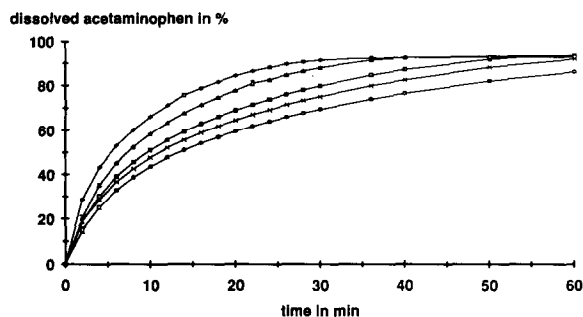
tions with respect to the water contents of the extrudate. The curve for L-HPC-free pellets is clearly different from those obtained for pellets containing the different types and quantities of L-HPC. The level of the curve is higher and the slope is steeper. The values for T_d of L-HPC-containing pellets were also found to increase as the water content of the extrudate increased. The results level out for pellets made from extrudate with high water contents. The fastest release was obtained with LH 20.

Porosity

The porosity results for the formulations as a function of water content are shown in Fig. 9. The lowest porosity was found for L-HPC-free pellets. True and apparent densities were very similar for these pellets. On the other hand, the highest porosities of more than 20% were found for pellets containing LH 20. There appears to be a slight tendency for the porosity to decrease with increasing water contents.

TABLE 6 (continued)

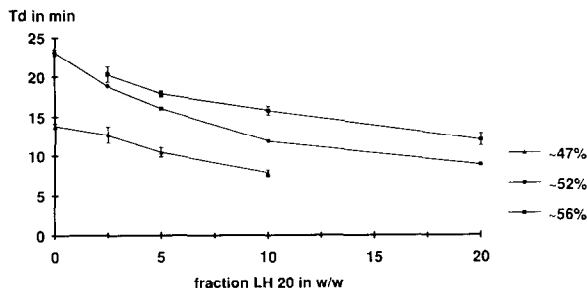| Aspect ratio			Roundness			Sphericity		
Wet	Medium	Dry	Wet	Medium	Dry	Wet	Medium	Dry
1.07 (0.05)	1.37 (0.23)	1.36 (0.24)	94.4 (2.2)	87.1 (5.9)	83.0 (6.9)	98.3	55.6	56.1
1.12 (0.09)	1.47 (0.25)	1.63 (0.34)	93.0 (2.8)	83.4 (7.6)	79.4 (8.5)	85.5	47.6	38.2
1.16 (0.11)	1.52 (0.32)	1.53 (0.36)	92.2 (3.3)	81.9 (9.0)	81.6 (8.9)	79.0	43.9	45.1
1.12 (0.09)	1.42 (0.24)	1.50 (0.31)	92.9 (2.7)	84.5 (7.2)	82.2 (8.4)	86.6	51.1	45.5
1.12 (0.09)	1.26 (0.15)	1.38 (0.22)	91.9 (3.3)	88.9 (4.9)	87.3 (5.6)	85.9	66.6	54.4

Td in min

Fig. 13. Interrelation between dissolution time (T_d) and water content of extrudate for different fractions of L-HPC LH 20 (SD, $n = 6$).

Plotting the porosities against the hydroxypropyl content of the L-HPC types for different water contents results in an increase of porosity with increasing hydroxypropyl content (Fig. 10).

The plot for T_d against porosity for the 15 pellet batches indicates a very rough relation between the two variables, but no strong correlation (Fig. 11). The higher the porosity the lower was the T_d.

Trial fraction LH 20

Dissolution of pellets containing different fractions of LH 20 was assessed. The dissolution profiles at 52% water content are shown in Fig. 12. As expected, the dissolution rate is accelerated as the level of LH 20 increases. Fig. 13 summarizes dissolution testing giving the T_d curves of different water contents vs the fraction of LH 20. Once again, the T_d is seen to increase with increasing water content.

Discussion

Power consumption vs water content

A number of papers have been published which show that during extrusion the power consumption, or comparable parameters, decreases as the quantity of granulation liquid increases (Harrison et al., 1985; Bains et al., 1991; Eerikainen, 1991; Elbers et al., 1992; Kleinebudde and Lindner, 1993). The particle size of the Avicel used in the product formulation had no influence on the power consumption/water content profile (Fig. 1; Baert et al., 1991). The power consumption/water content curves of formulations containing L-HPC were flatter than those for formulations without L-HPC. This is a first indication of a lower sensitivity of the formulation to water content of the extrudate in terms of the extrusion process. The reason may be due to the L-HPC exhibiting a lubricating effect in the extruder barrel and at the die wall.

The effective formation of particles is only possible within a certain range of water contents. The upper limit for water contents is well defined for given experimental conditions. If water levels above that upper limit are used, large agglomerates are formed during spheronization as a result of coalescence of the wet and sticky particles. This phenomenon is designated as 'snow-balling'. The lower limit for lower water content is not so well defined. Lowering the water content gradually leads to an extrudate with reduced plasticity. The lower the water of the extrudate the greater the difficulty in forming uniform round spheres. At the same time the dry 'fines' obtained during spheronization are unable to coalesce as effectively with the particles as wet 'fines'. Temperature, pressure and power consumption all rise as the water content is reduced.

It is necessary to define a working water content range for each formulation. Based on this working range it is then possible to define wet, medium and dry extrudates. Depending on the composition the working ranges for different formulations may not overlap. It may sometimes be more appropriate to compare extrudates with similar (relative) locations in the working range rather than extrudates with the same (absolute) moisture content. Breadth of working range and its location on water content scale are important parameters for a formulation. Breadth is an indicator for the sensitivity of a formulation to moisture concentration (Bains et al., 1991).

Trial type L-HPC and fraction LH 20

The working ranges for water content for the different formulations studied are given in Table 3. The substitution of 20% Avicel PH 101 for

L-HPC shifted the working range from 48–54 to 50–62%. L-HPC absorbs water more effectively than Avicel, so more water is needed to form a wet extrudate. At the same time the working range was broadened, indicating a lower sensitivity to moisture content.

Sieve analysis did not give clear information regarding the influences of L-HPC type or water content. It was found to be unsuitable for characterization of anisometric beads. In sieve analysis it was impossible to identify whether width or length of a particle was being measured. Increasing aspect ratio values led to increasing errors in sieve analysis. Therefore, it was difficult to compare the results for round and rod-like particles. As a consequence sieving was only used to prepare a 1000–1120 μm fraction for dissolution testing.

Image analysis led to much clearer results. It was evident that with decreasing water content the anisometry of the product was increased in all cases. The roundest particles were obtained at the highest water contents within the given working range, i.e., from wet extrudate. Aspect ratio and sphericity values for pellets formed from wet masses containing L-HPC are worse when compared to those produced from wet masses without L-HPC. The polymer increased the elasticity of the wet extrudate which led to less effective spheronization. The polymer with the highest hydroxypropyl content (LH 20) showed the worst sphericity. High aspect ratio values corresponded with a high length while the width remained almost constant. This is the reason for the correlation between aspect ratio on the one hand and length as well as area on the other. Larger particles were more anisometric; this explains why the sphericity of larger particles decreases.

Generally, the formation of good pellets, in terms of aspect ratio and sphericity, requires the extrudate to be adequately wetted. The area of round spheres as well as width were lower than expected. This is due to the swelling properties of L-HPC. Wet extrudate was found to shrink during drying. Detailed investigations into the swelling and shrinking properties of pellets were beyond the scope of this study and will form the basis of future research.

The inclusion of L-HPC in formulations led to accelerated dissolution. This was expected as L-HPC is used as both filler and disintegrant. The accelerated dissolution did not result in a disintegration of the pellets. As with pellets prepared using Avicel, pellets prepared using L-HPC swelled and softened during dissolution, but there was no disintegration. The dissolution profiles for pellets manufactured using the different types of L-HPC were only marginally different from those of pellets containing Avicel. Increasing water content led to an increase in T_d, i.e., to a slower dissolution rate. For a given formulation the best spheres in terms of sphericity showed the slowest dissolution. Both properties were influenced by the water content during extrusion. The sensitivity of T_d to changes in water content was much weaker for formulations containing L-HPC. The variation of the LH 20 fraction produced the expected result. With up to 20% LH 20 in the formulation the dissolution rate is continuously accelerated. However, at higher levels of LH 20 the efficiency at reducing T_d was less (Fig. 13).

A possible reason for the changes in dissolution rate lay with the different porosities of the pellet types. The Avicel pellets had nearly no porosity. Only the Avicel pellets from dry extrudate had a porosity of 5%. However, the pellets containing L-HPC had porosities of between 5 and 20%. The porosity of the pellet is strongly influenced by the type of L-HPC used. Increasing water contents resulted only in slightly lower porosities, which was in accordance with the slightly slower dissolution. The differences in porosity are more pronounced than those in T_d. The main reduction of T_d was seen between porosities of 0 and 5%. Increasing the porosity from 5 to 20% maintained the T_d almost constant.

Conclusions

The working range for water contents to obtain pellets from extrusion/spheronization is dependent on the formulation.

Addion of L-HPC to a formulation with acetaminophen, Avicel PH 101 and Aerosil 200 led

to a broader working range at higher water contents due to its superior absorption properties. The extrusion process is less sensitive to changes in water content.

Round spheres were most readily obtained using extrudates in the upper part of the working range. The use of L-HPC reduced the best possible results for sphericity and aspect ratio. In all cases, a reduction in the water content led to more anisometric particles. Low particle size L-HPC improved the sphericity of particles obtained from dry extrudate. L-HPC-containing spheres were found to shrink during drying.

The use of L-HPC resulted in faster dissolution of acetaminophen. T_d was reduced from 24.5 to 13.1 min for pellets made from wet extrudate.

Porosity is strongly influenced by the type of L-HPC used and less markedly affected by water content of the extrudate. Porosity increased with increasing hydroxypropyl content of the L-HPC. Increasing porosities corresponded with faster dissolution, but there was no strong linear relationship.

L-HPC with low particle size and high hydroxypropyl content is of interest for the production of round spheres with rapid dissolution by extrusion/spheronization.

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