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International Journal of Pharmaceutics 189 (1999) 7–17

international journal of pharmaceutics

www.elsevier.com/locate/ijpharm

Influence of the process parameters on the characteristics of starch based hot stage extrudates

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Received 4 March 1999; received in revised form 29 June 1999; accepted 4 July 1999

Abstract

The influence of the process parameters on the characteristics of matrix formulations produced by means of hot stage extrusion was investigated using three experimental designs. The first one was designed to evaluate the importance of the screw speed (150–450 rpm) and the feed rate (2–12 kg/h), while the second and the third were designed to study the importance of the temperature profile (60–120°C). The extrudates were produced with a laboratory twin screw extruder equipped with a 3-mm cylindrical die. The formulations consisted of 53% corn starch, 15% sorbitol, 2% glyceryl monostearate and 30% theophylline monohydrate as the model drug. The extrudates were characterized by Karl-Fischer titration, Hg-porosimetry, four-point bending and dissolution testing. From the first design it was concluded that the screw speed and feed rate hardly affected the water content of the extrudates, but that there was a clear influence on the extrudate radius, porosity, mechanical strength and dissolution behaviour. High screw speed-high feed rate processes in comparison with low screw speed-low feed rate processes caused an increase in extrudate radius and porosity and a decrease in mechanical strength and drug release rate from the matrix. It was clear that the contribution of the feed rate was higher than that of the screw speed. Expansion, promoted under certain extrusion conditions, could explain the obtained results. The second and third design revealed that only the maximum barrel temperature and not the whole temperature profile was responsible for the temperature effects on the extrudate characteristics. It was concluded that the maximum barrel temperature was the most critical parameter of the hot stage extrusion process.

Keywords: Hot stage extrusion; Starch; Process parameters; Matrix formulation; Drug release

1. Introduction

Hot stage extrusion finds its roots in the polymer and food industry (van Zuilichem, 1992). In the pharmaceutical industry, where this technique has been studied for the last 15 years (Mank et al., 1989, 1990; Follonier et al., 1994, 1995; Gruenhagen, 1996; Sprockel et al., 1997), it is applied to produce matrix formulations into which a drug is homogeneously embedded. The advantage over the more conventional matrix production methods is the continuity of the pro-

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0378-5173/99/$ - see front matter
PII: S0378-5173(99)00229-X

duction process (mixing, melting, homogenizing and shaping are carried out in a single machine) which can result in a decrease in investment costs and increased automation of the production. Furthermore this technique is characterized by a high throughput and low material loss, a good homogeneity of the products, the absence of organic solvents in the production process, the ability to make solid solutions in order to improve the bioavailability of poorly soluble drugs and the possibility of minimizing the use of excipients (Mueller et al., 1992; Breitenbach et al., 1995).

The objectives of this and previous work were to examine the possibilities of starch based hot stage extrusion formulations as matrices for controlled drug delivery. Starch, a widely used pharmaceutic aid due to its low cost, high availability and non-toxicity, had not been studied yet in this respect although its excellent feasibility for hot stage extrusion had been established by a variety of applications in the polymer, food and agriculture technology (Launay and Lisch, 1983; Doane, 1992; Fritz and Widmann, 1993; Shogren et al., 1993; Carr et al., 1994; Krishnan et al., 1994; Schreiber et al., 1994). In a previous paper (Henrist et al., 1999) the in vivo behaviour of such a matrix (consisting of 53% corn starch, 30% theophylline monohydrate, 15% sorbitol and 2% glyceryl monostearate) produced with a standard set of extrusion parameters (a total feed rate of 3 kg/h, a screw speed of 200 rpm and a temperature profile of 60-90-100-100-80°C from the powder feeder to the die) was evaluated and it was concluded that the drug release from the extrudates was retarded but was still faster than that observed for the commercially available controlled release system Xanthium®. In another paper (Henrist and Remon, 1999) it was investigated if the drug release and other extrudate characteristics could be affected by changes in formulation composition in order to be able to improve the in vivo behaviour of these extruded starch based matrices. In that regard the influence of the starch, the plasticizer and the lubricant type and concentration were investigated in matrices with 30% theophylline monohydrate as a model drug. It was concluded from this study that only minor effects on the extrudate characteristics could be reached by changing the formulation composition.

Therefore the objective of this paper was to investigate the influence of the process parameters on the characteristics of starch based hot stage extrusion formulations in order to obtain high quality and high efficacy controlled release matrices with a slower in vitro drug release profile in comparison with the formulation that was tested in vivo in previous work (Henrist et al., 1999).

2. Materials and methods

2.1. Materials

Corn starch (C*PHARM 03302) and sorbitol (C*Sorbidex P 16616) were received from Eridania Béghin Say Cerestar (Vilvoorde, Belgium). Theophylline monohydrate was supplied by Ludeco (Brussels, Belgium) and glyceryl monostearate was obtained from Mosselman (Brussels, Belgium). The materials were used as received. The exact composition of the glyceryl monostearate (GMS) was $39.6 \pm 0.43\%$ of monoglycerides, $46.44 \pm 0.34\%$ of diglycerides and $13.95 \pm 0.29\%$ of triglycerides.

2.2. Production process

Prior to hot stage extrusion, the different components of the formulation were premixed in a Hobart A 200 planetary mixer (Kampenhout, Belgium). The mixture consisted of 53% corn starch, 15% sorbitol as a plasticizer, 30% theophylline monohydrate as the model drug and 2% glyceryl monostearate as the lubricant. The composition of this mixture was based on patent literature (De Bock et al., 1993, 1994) and on prior experience.

The extrusion was performed on a MP 19 TC 25 laboratory scale co-rotating twin screw extruder of APV Baker (Newcastle-under-Lyme, UK) with a L/D ratio of 25/1. The machine was equipped with a control panel (for the installation and/or control of the barrel and melt temperatures, the screw speed, the powder feed rate, the die pressure and the torque), a standard screw profile with two mixing sections, a 3-mm cylindri-

cal die, a twin screw powder feeder and a peristaltic pump connected to the first barrel zone of the extruder. The pump was used for the addition of water, acting as a plasticizer, during the extrusion.

The water supply during the process was kept constant at 20% (based on the wet mass). The screw speed, feed rate and temperature profile were installed on the control panel; the exact parameters depended on the experiment performed.

After extrusion, the extrudates were manually cut into pieces of approximately 10 cm and, prior to further analysis, were oven dried at 60°C during 48 h, until equilibrium moisture content was reached.

2.3. Characterization

The moisture content of the extrudates was determined using a Mettler DL35 Karl Fischer titrator (Mettler-Toledo, Beersel, Belgium) in combination with a Mettler DO337 oven operated at 200°C. The samples were cut into small pieces and placed in a Pyrex vessel inside the oven. During 15 min the water freed from the sample was carried to the titration vessel by a nitrogen stream of 300 ml/min, after which the titration was started. Hydranal® Composite 5 (Riedel-de Haën, Seelze, Germany) with a theoretical titer of 5 mg H_2O/ml was used as the titrant solution. The analysis was performed in triplicate.

The mechanical strength of ten samples of approximately 10-cm length was determined using a four-point bending test performed on a Lloyd 1000 R tensile testing machine (Lloyd Instruments, Fareham, UK) with a load cell of 20 N and a cross head speed of 1 mm/min. The test was automatically stopped when break was detected. The distance between the two points of support was 80 mm and between the two points of application 42 mm. The maximum load at break was used to calculate the maximum tensile strength (σ_{max}) for those samples which broke between the two points of application of the load. The following formula, derived from the theory of Timoshenko (1955), was therefore applied:

$$\sigma_{max} = (4Qx)/(\pi r^3)$$

where Q is load at one point of application, x is distance between point of support and point of application and r is radius of the extrudate at the point of break. The radius of each of the extrudates used for the four-point bending tests was measured in quadruplicate with an electronic digital caliper (Bodson, Liège, Belgium).

The porosity was measured in duplicate by means of an Autopore III 9140 mercury porosimeter (Micromeritics, Zaventem, Belgium). A calibrated solids penetrometer with a 5-ml sample vessel and a 0.38-ml stem was therefore used.

The dissolution was performed in sixfold on extrudates of approximately 3-cm length in a VK 7000 dissolution system with a VK 8000 automatic sampling station (VanKel Industries, NJ, USA). The system was operated at 37 ± 0.5°C and 100 rpm using the paddle method (Eur. Ph.). Water was used as the dissolution medium and samples were taken after 0.5, 1, 2, 4, 6, 8, 12, 16, 20 and 24 h. After dilution (1:11) the samples were measured at 272 nm with a Perkin Elmer Lambda 12 UV-VIS double beam spectrophotometer (Zaventem, Belgium). The theophylline monohydrate concentrations were calculated from a calibration curve between 0 and 0.025 g/l. To compare the dissolution profiles, area under the curve (AUC) values were calculated with the trapezoidal method. The AUCs were determined between 0 and 8 h as the drug release at this last time point was between 70 and 90% (Anderson et al., 1998).

2.4. Experimental set-up

The influence of the process parameters on the characteristics of extrudates produced by means of hot stage extrusion was evaluated by means of three experimental designs.

The first one was designed to study the importance of the screw speed and the feed rate. For all the experiments of this design a basic temperature profile of 60-90-100-100-80°C from the first to the fifth barrel zone was installed. In a first approach the following ranges of screw speeds and feed rates were examined: 150–250 rpm and 2–4 kg/h.

After evaluation of the results, however, it was clear that an expansion of the design was necessary to draw valid conclusions. No experiments were performed in the high feed rate-low screw speed domain because of practical limitations of the process: when high feed rates were used together with low screw speeds, a powder flood occurred at the feed funnel. Neither was the high screw speed-low feed rate domain included in the design. The parameter combinations in that region did not cause practical processing problems, but were of minor interest regarding future applications.

The aim of the second design was to investigate the influence of changes in feed temperature (temperature of the first barrel zone, T1) and in maximum process temperature (temperature of the third barrel zone, T3) on the extrudate characteristics. The temperature of the second zone (T2) was (T1 + T3)/2 and the temperature installed in the third zone (T3) was maintained in the fourth and the fifth barrel zones (T4 and T5). In this way there were only two variables under investigation: T1 and T3. The following range of temperatures was investigated: 60–80°C for T1 and 80–120°C for T3.

In a third part of the study five experiments were performed with the same maximum process temperature but a different temperature profile over the five barrel zones. The objective of this last design was to evaluate the influence of a temperature gradient.

For all the temperature experiments a basic extrusion process was used with a total feed rate of 3 kg/h (2.4 kg/h powder and 0.6 kg/h water (20%)) and a screw speed of 200 rpm.

3. Results and discussion

3.1. First experimental design

Table 1A shows, by means of an example, the variability on the different extrudate characteristics within a batch. The values presented in Table 1A are representative for all the experiments performed, unless otherwise stated. The coefficients of variation for the water content, the AUC, the percentage drug released at a certain time point and the radius of the extrudates were below 5%. For the porosity and the mechanical strength the coefficients of variation were below 10%. This means that it was possible to obtain homogeneous products with the above described hot stage extrusion process and that the extrudates were adequately characterized.

Although the intrabatch variability was good, the interbatch variability was generally higher (Table 1B and C). The coefficients of variation for most of the results were still lower than 10%, but their absolute values were generally higher between batches than within batches. The reason for the high interbatch variability could be of different origins. Environmental conditions certainly play a role in the characteristics (water content and flowability) of the powder mixture fed inside the extruder, during the drying process and for the final characteristics of the dried extrudates. Additionally the twin screw powder feeder and the peristaltic pump for the water addition could have an influence on the extrudate characteristics: minor differences in their performance could lead to formulations differing slightly in powder/water composition.

Despite these observations, it was possible to discover some major trends in the results of the first experimental design concerning the influence of the screw speed and the feed rate on the extrudate characteristics (Figs. 1 and 2; for the sake of clarity the AUC values were divided by 200 for presentation in Fig. 1). The observed trends were confirmed by repeating two experiments (3 kg/h-200 rpm and 12 kg/h-450 rpm) on the same day in order to eliminate the variability in environmental conditions. It is concluded from Table 2 and Figs. 1 and 2 that a clear trend exists for the radius and the porosity of the extrudates and for their dissolution behaviour and mechanical strength. Extrudates produced with a high screw speed and a high feed rate were thicker, weaker, more porous and showed a slower drug release than extrudates produced with a low screw speed and feed rate. The drug release from a non-soluble matrix is dependent on the length of the drug diffusional path and is as a consequence slower when the extrudate diameter increases. Al-

Table 1
Intra- and interbatch variability for the extrusion of the reference formulation consisting of 53% corn starch, 15% sorbitol, 30% theophylline monohydrate and 2% glyceryl monostearate at different process parameters

	Water content (%), $n = 3$[b]	Porosity (%), $n = 2$[b]	Max. tensile strength (N/mm^2), n = max. 10[b]	Dissolution (% after 4 h), $n = 6$[b]	Dissolution (% after 8 h), $n = 6$[b]	Dissolution (% after 12 h), $n = 6$[b]	AUC (% h), $n = 6$[b]	Radius (mm), $n = 10$[b]
A. Intrabatch variability (3 kg/h, 200 rpm; 60-90-100-100-80°C)[a]								
Mean	4.90	7.8	24.1	50.9	73.7	85.6	375	1.55
CV	3.9	6.4	5.5	1.9	1.9	1.5	1.8	1.8
B. Interbatch variability (3 kg/h, 200 rpm; 60-90-100-100-80°C; n = 5)								
Mean	4.92	7.6	23.5	54	77	90	398	1.51
CV	2.9	7.7	9.3	5.7	6.2	5.6	5.7	3.2
C. Interbatch variability (7 kg/h, 400 rpm; 60-90-100-100-80°C; n = 3)								
Mean	4.4	17.2	19.5	50	71	83	372	1.82
CV	8.2	16.6	10.1	7.2	3.2	1.4	6.1	1.1
D. Interbatch variability (3 kg/h, 200 rpm; 70–85–100–100–100°C; n = 3)								
Mean	4.99	7.1	24.0	56.9	81.4	93.2	419	1.51
CV	3.5	2.2	11.7	1.8	0.9	0.8	1.5	1.8

[a] The values of the intrabatch variability presented are representative for all the extrusion experiments, unless otherwise stated.
[b] The n-value represents the number of measurements per batch.

Table 2
Influence of the screw speed and the feed rate on the in vitro extrudate characteristics, presented as mean values[a]

Feed rate (kg/h)	Screw speed (rpm)	Water content (%)	Porosity (%)	Max. tensile strength (N/mm^2)	Dissolution (% after 4 h)	Dissolution (% after 8 h)	Dissolution (% after 12 h)	AUC (% h)	Radius (mm)
A. Experiments of the design									
2	150	5.27	7.1	24.4 ($n=7$)	63.4	83.5	92.8	454	1.47
	250	5.17	7.5	22.1 ($n=6$)	60.7	84.2	95.8	445	1.44
3	150	4.32	7.6	23.1 ($n=10$)	53.2	77.3	89.6	403	1.54
	200	4.92[b]	7.6[b]	23.5[b]	54.0[b]	77.3[b]	90.0[b]	398[b]	1.51[b]
4	150	4.81	9.6	21.4 ($n=9$)	54.8	77.4	88.5	399	1.61
	200	5.52	9.9	19.5 ($n=10$)	50.6	72.1	84.2	375	1.61
	250	5.11	8.7	22.2 ($n=4$)	50.0	74.2	87.5	375	1.72
	350	5.07	8.0	22.9 ($n=9$)	55.5	78.4	90.5	408	1.60
5	300	4.67	11.3	18.6 ($n=10$)	46.7	69.8	81.5	351	1.82
6	250	4.01	19.6	20.6 ($n=6$)	55.8	75.8	89.2	408	1.65
	350	4.78	13.6	20.6 ($n=7$)	52.6	74.3	86.9	388	1.73
	450	4.61	17.3	22.0 ($n=9$)	51.2	73.1	83.1	380	1.71
7	400	4.39[c]	17.2[c]	19.5[c]	50.4[c]	71.2[c]	83.0[c]	372[c]	1.82[c]
8	350	4.71	16.6	20.5 ($n=8$)	50.9	72.4	83.4	373	1.88
	450	4.37	18.0	16.0 ($n=9$)	48.2	68.6	80.2	357	1.95
12	450	3.95	20.1	17.3 ($n=10$)	41.4	62.1	75.0	310	2.09
B. Replication of two different experiments on the same day (in two-fold)									
3	200	4.39	7.9	24.4 ($n=7$)	60.3	87.3	96.4	450	1.50
12	450	4.22	23.0	21.4 ($n=8$)	47.9	70.2	81.2	362	1.90
3	200	4.79	7.1	23.4 ($n=7$)	58.0	83.9	95.9	427	1.47
12	450	4.15	21.6	20.9 ($n=7$)	47.8	71.5	84.7	364	1.86

[a] Blank cell represents same as previous.
[b] Mean value of five replicated experiments (Table 1B).
[c] Mean value of three replicated experiments (Table 1C).

though the drug release from the extrudates was slowed down under certain extrusion conditions, the differences in dissolution behaviour between the slowest formulation and the reference at 3 kg/h and 200 rpm were probably too small to obtain a significant improvement of the reference in vivo behaviour as reported previously by Henrist et al. (1999). The increase in extrudate radius and porosity can be explained by the same phenomenon namely 'expansion'. Expansion of starch containing extrudates at the extruder die is a phenomenon intensively investigated in the domain of food technology (Launay and Lisch, 1983; Chinnaswamy and Hanna, 1988a,b,c, 1990; Sokhey et al., 1994). Among the variables that govern expansion (extruder barrel temperature, screw speed, die design, screw design, moisture content of the feed material, starch composition, lipid and protein content, presence of sugars), only those concerning the extrusion process can contribute to the expansion seen in these experiments, since each extrusion was performed with the same formulation. In general, expansion of starch depends mainly on its degree of gelatinization, which in turn is determined by temperature, shear rate and water content of the feed material (Chinnaswamy and Hanna, 1988a). However, expansion not only depends on starch conversion. Lipids can inhibit expansion through amylose-lipid complex formation (Chinnaswamy and Hanna, 1988b). This complex formation occurs in the presence of amylose and lipids such as fatty acids and monoglycerides (in casu: glyceryl monostearate) and has already been observed during the hot stage extrusion process (Colonna and Mercier, 1983; Galloway et al., 1989; Bhatnagar and Hanna, 1994a,b). It can be stated that during hot stage extrusion of starch containing mixtures, expansion results from the competition between starch conversion and amylose-lipid complex formation. Both phenomena are partly dependent on the residence time of the materials in the extruder and this residence time is dependent on the screw speed and the feed rate. A high screw speed and feed rate decrease the residence time (De Ruyck, 1997) and so the reaction time between amylose and glyceryl monostearate, with less expansion inhibition as a result. A high screw

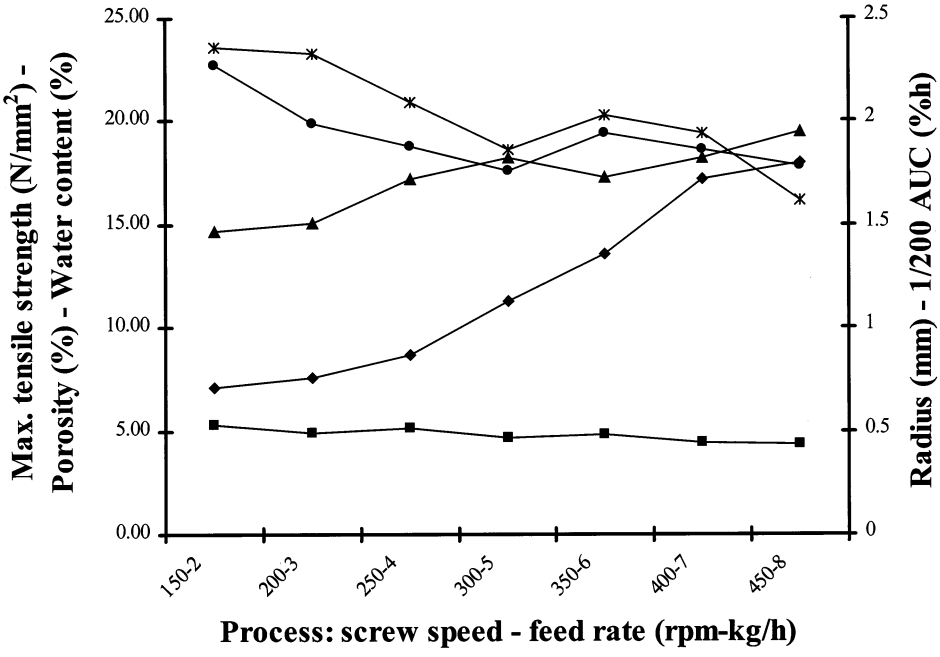

Fig. 1. Major trends in the results of the screw speed-feed rate experiments: water content (■), porosity (◆), mechanical strength (*), radius (▲) and 1/200 AUC (●).

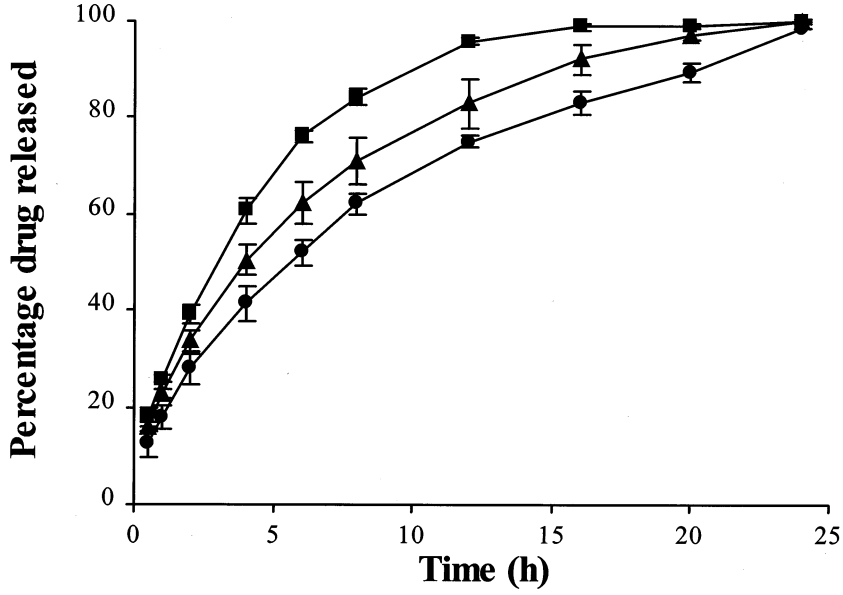

Fig. 2. Mean dissolution profiles (with standard deviations) of the following formulations of the first experimental design: 2 kg/h-250 rpm (■) ($n = 1$), 7 kg/h-400 rpm (▲) ($n = 3$) and 12 kg/h-450 rpm (●) ($n = 1$).

speed increases the shear and so the degree of starch conversion which results in a higher expansion (Barrès et al., 1990). As a result the expansion should increase with increasing screw speed-feed rate combinations, which was confirmed in the conducted experiments. Logical consequences of the expansion were a further increase of the extrudate porosity and a decrease of its mechanical strength. For the water content it was not clear whether the results followed a certain trend. It is possible that the water content decreased with increasing screw speed-feed rate combinations. This would be in agreement with the increasing trend seen for the porosity as water can be removed more easily from more porous matrices, but more experiments should be performed to confirm this assumption.

Another conclusion from the data of Table 2 is the fact that the same trend as described above was observed when the feed rate was increased at a constant screw speed, but not when the screw speed was increased at a constant feed rate. Therefore it was assumed that the contribution of the feed rate in the observed effects was higher than that of the screw speed.

3.2. Second experimental design

The variability of the different extrudate characteristics within a batch was comparable to the values presented in Table 1A. The coefficients of variation were below 5% for every test except for the porosity and the tensile strength measurements, where they were below 10%. This was true for all the experiments performed except for the experiments with the following temperature profiles: 60-70-80-80-80°C, 60-90-120-120-120°C and 80-100-120-120-120°C. These productions showed a higher variability for the maximum tensile strength and the last production also for the dissolution results due to one extrudate with a deviating release profile.

The interbatch variability was checked by means of a reference which was repeated three times during the experimental period (Table 1D). It was concluded that the interbatch variability for these experiments was better than the interbatch variability of the references of the first design. The interbatch variability of this design equaled the intrabatch variability for all the extrudate characteristics except for the mechanical

Table 3
Influence of the temperature on the in vitro extrudate characteristics, presented as mean values[a]

Temperature profile (°C)	Water content (%)	Porosity (%)	Max. tensile strength (N/mm^2)	Dissolution (% after 4 h)	Dissolution (% after 8 h)	Dissolution (% after 12 h)	AUC (%h)	Radius (mm)
A. Influence of the feed and maximum temperature (second design)								
60-70-80-80-80	2.16	–	14.2 ($n = 8$)	98.2	98.7	99.0	684	1.49
80-80-80-80-80	3.65	–	20.1 ($n = 6$)	66.1	91.2	99.7	489	1.46
60-80-100-100-100	4.91	7.4	23.5 ($n = 6$)	60.1	83.4	95.8	438	1.50
70-85-100-100-100	4.99[b]	7.1[b]	24.0[b]	56.9[b]	81.4[b]	93.2[b]	419[b]	1.51[b]
80-90-100-100-100	4.93	7.4	25.4 ($n = 8$)	57.4	80.7	92.4	423	1.52
60-90-120-120-120	1.32	–	2.8 ($n = 9$)	96.5	98.7	97.7	722	2.02
80-100-120-120-120	2.00	–	2.4 ($n = 10$)	94.2	98.4	99.4	676	2.36
B. Influence of a temperature gradient (third design)								
60-70-80-90-100	3.37	–	20.3 ($n = 8$)	60.9	83.3	93.6	442	1.48
70-80-90-100-100	5.32	7.8	22.0 ($n = 9$)	60.9	85.7	96.9	451	1.53
80-90-100-100-100	4.73	6.3	24.8 ($n = 6$)	56.9	80.6	95.0	419	1.52
90-100-100-100-100	4.02	7.3	20.9 ($n = 8$)	60.6	84.9	94.5	442	1.44
100-100-100-100-100	5.15	6.7	22.2 ($n = 4$)	62.8	87.6	97.1	459	1.45

[a] –, No value available
[b] Mean value of three replicated experiments (Table 1D).

strength. The experiments of this design were all conducted in a period of 1 month, while the screw speed-feed rate experiments were performed discontinuously over a period of 6 months. This could explain the difference in the observed variability for both investigations.

The maximum barrel temperature T3 seemed to be the most critical process parameter for the hot stage extrusion of starch based formulations (Table 3A). The optimum temperature was 100°C for the formulation selected. At 120°C irregular foams were formed at the die as expansion increased with increasing temperature (Chinnaswamy and Hanna, 1988a) while at 80°C extrudates with a rough surface were produced probably due to a lower degree of starch gelatinization. The latter extrudates also showed a crack along the cylinder axis after drying with low strength as a consequence. The influence of extrusion at 80 and 120°C was an increased drug release rate, a lower water content and a lower mechanical strength of the extrudates due to a poor quality of the matrices.

The feed temperature seemed to be of minor importance (Table 3A), although a clear improvement of the product characteristics was seen in the experiment with the following temperature profile: 80-80-80-80-80°C. This was probably due to a longer exposure time at a temperature of 80°C in comparison to the other experiment with 80°C as the maximum temperature, where this temperature was only installed in the third barrel zone.

3.3. Third experimental design

From the data presented in Table 3B it is clear that a temperature gradient had no influence on the extrudate characteristics. The results of Table 3B were in good agreement with the results of the experiments of the second design with 100°C as the maximum barrel temperature (Table 3A). Therefore the results of the third design confirmed the conclusion of the second design that the maximum barrel temperature was mainly responsible for the effects on the extrudate characteristics.

4. Conclusions

The objective of this work was to evaluate the influence of the process parameters on the characteristics of starch based hot stage extrusion formulations in order to obtain high quality and high efficacy controlled release matrices with a slower in vitro drug release profile in comparison to the reference formulation which was tested in vivo in earlier work. Although it was possible to make high quality products with different process conditions, it was not possible to obtain high efficacy controlled release matrices by only modifying the process. Therefore the effects of the process parameters on the extrudate characteristics were too small.

Concerning the influence of the process parameters it can be concluded that the screw speed and feed rate barely affected the water content of the extrudates. However, they did have an influence on the extrudate radius, porosity, mechanical strength and dissolution behaviour. In that respect a simultaneous increase in screw speed and feed rate caused an increase in extrudate radius and porosity and a decrease in extrudate mechanical strength and in drug release rate from the matrix. The contribution of the feed rate to the effects was higher than that of the screw speed. The maximum barrel temperature was the most critical parameter of the hot stage extrusion process while the temperature profile over the five barrel zones was of minor importance. For the formulation selected 100°C was the optimum operating temperature.

Acknowledgements

D. Henrist is research assistant of the Fund for Scientific Research – Flanders (Belgium) (F.W.O.). The study was financially supported by the F.W.O. (grant number G0017.97).

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