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Research paper

Dry coating: an innovative enteric coating method using a cellulose derivative

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Abstract

A novel enteric coating method was developed. This method involves direct feeding of coating polymer powder and simultaneous spraying of plasticizing agent, without either organic solvent or water, using a centrifugal granulator, fluidized bed, or tablet-coating machine. For film formation, a curing step was then necessary; this involved spraying a small amount (3–8% of core weight) of water or hydroxypropyl methylcellulose solution, followed by heating. Hydroxypropyl methylcellulose acetate succinate was used as the enteric coating polymer, and a combination of triethyl citrate and acetylated monoglyceride was used for plasticization. The coated beads and tablets were evaluated for gastric resistance, intestinal disintegration, and stability, in comparison with beads and tablets from a conventional aqueous coating with the same enteric polymer. The new method required a higher coating amount for gastric resistance compared with the conventional coating, but the processing time was dramatically reduced. The results show that this dry coating method is applicable to the preparation of enteric-coated beads and tablets using commercially available lab-scale apparatus.

Keywords: Enteric coating; Dry coating; Hydroxypropyl methycellulose acetate succinate

1. Introduction

During the last two decades, pharmaceutical coating technology has been shifting from organic solvent-based systems to aqueous systems, which are advantageous from the view points of environmental pollution, safety and cost [1–3]. Water-soluble materials, such as hydroxypropyl methylcellulose, are now widely used for aqueous film coating of pharmaceutical solid dosage forms [3]. Aqueous coating systems using water-insoluble materials, such as enteric coating polymers, have also been developed, and aqueous polymeric dispersions of acrylic resins, a vinyl polymer and cellulosic polymers are commercially available for this purpose [4–6]. However, aqueous coating systems are not always applicable, for example if the active ingredient is sensitive to water. From the view point of cost, usage of water in place of organic solvent is highly beneficial. However, reduction of processing time and coating level are also important. A simple way to shorten coating time is to use a coating solution or dispersion of higher concentration, but this approach is limited by the viscosity increase of the solution or blocking of the spray nozzle.

To overcome the limitations of aqueous coating and to reduce further the cost, we have developed a novel approach for enteric coating. Our basic concept was to achieve enteric coating without any solvent, either organic solvent or water by applying the polymer coating powder directly to the core to form a film. This concept was not fully realized, since a small amount of water is still required in our method for the final curing process to achieve film formation. This technique, which we call dry coating, even though this is not strictly the case, should be especially useful when the active ingredient is sensitive to water, and its cost is considerably reduced because the process time is much shorter and the preparation of coating fluid is not necessary. In a preliminary study, a commercial cellulosic enteric coating agent, hydroxypropyl methylcellulose acetate succinate (HPMCAS) was found suitable for dry coating. The objective of this study was to investigate the practicality of this techni-

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que for both bead and tablet coating, using HPMCAS. Coating experiments were performed using commercially available lab-scale apparatus, and the coating performance, including gastric resistance, coating efficiency, and stability was evaluated.

2. Experimental

2.1. Materials

A micronized grade of hydroxypropyl methylcellulose acetate succinate (HPMCAS; Shin-Etsu AQOAT®, type AS-MF; Shin-Etsu Chemical Co., Ltd., Niigata, Japan) was used as the enteric coating polymer. Talc (type SP-GA, Kihara Kasei, Tokyo, Japan), triethyl citrate (Citroflex®-2, Morflex, NC, USA), mineral oil (liquid paraffin, JP grade), acetylated monoglyceride (Myvacet®, type 9-45, Eastman, TN, USA), olive oil (Wako Chemicals, Tokyo, Japan), diethyl phthalate, triacetin, glyceryl caprylate, glycerin, propylene glycol, polyethylene glycol 400, and Polysorbate 80 were used as coating additives. Hydroxypropyl methylcellulose (HPMC; Pharmacoat®, type 645W, Shin-Etsu Chemical Co., Ltd., Tokyo, Japan) was used for subcoating of tablets. Pancreatin (JP grade, Amano Pharmaceutical, Nagoya, Japan) was used as the active ingredient.

2.2. Coating procedure

2.2.1. Preparation of core dosage forms

Both beads and tablets were used as the solid dosage forms in this study. By using a centrifugal granulator (CF-granulator®, model CF-360, Freund Industrial, Tokyo, Japan), the core beads were prepared by coating pancreatin on sugar seeds (Nonpareil®-101, Freund Industrial, Tokyo, Japan). Corn starch and hydroxypropyl cellulose (HPC-L; Nihon Soda, Tokyo, Japan) were used as the filler and binder, respectively. Pancreatin, sugar seeds, corn starch and binder were 39.4%, 39.4%, 20.7%, and 1.5%, respectively. The resulting spherical beads had a particle size range from 500 to 850 μm. Their disintegration time in water was 10 min.

The core tablets were prepared on a rotary tableting machine (model HT-P18, Hata Iron Works, Kyoto, Japan). The ingredients were spray-dried lactose (Pharmatose®, DCL-11, DMV, Veghel, The Netherlands), corn starch, low-substituted hydroxypropyl cellulose (L-HPC®; type LH-11, Shin-Etsu Chemical Co., Ltd., Tokyo, Japan), and Mg stearate. Their percentages were 75.5, 19.0, 5.0, and 0.5, respectively. No active ingredient was included. The tablet had a diameter of 8 mm, and a radius of curvature of 6.5 mm. Other properties were as follows; weight, 183 mg/T; hardness, 10 kg; and disintegration time in water, 2.1 min. Prior to enteric coating, the tablets were coated with HPMC at a coating amount of 2% (polymer basis) by a routine spray coating method [7].

2.2.2. Bead coating

The CF-granulator and a fluidized bed (Flowcoater®, model FLO-5, Freund Industrial, Tokyo, Japan) were employed for bead coating. Both of them were coupled with a powder feeding system and liquid spray system. Figs. 1 and 2 show schematic diagrams of the systems. In the case of the fluidized bed, a flexible tube was inserted to deliver the powder materials. This tube (polyethylene, 22 mm in inner diameter) was fixed so that the distance between the end of the tube and the bottom screen of the vessel was approximately 5 cm, while the nozzle for liquid spraying was installed at the upper section as in regular top-spray coating. An attachment was used at the tube outlet (Fig. 3). Five hundred grams of the core beads were charged per batch for the CF-granulator, and 10 kg was used for the fluidized bed. The coating process included quantitative feeding of the powder material and simultaneous spraying of the plasticizing fluid, under heated air. The beads were heated to 40°C prior to the powder feeding. The powder materials were mixed in a quantitative powder feeder (Spiral Feeder®, model NX-3000, Seishin Enterprise, Tokyo, Japan) and passed directly to the cores. The liquid plasticizer mixture was delivered with a peristaltic pump. The rates of powder feed and liquid spray were adjusted so that the two processes were started and ended simultaneously. After the powder feed, the beads were subjected to a curing process, during which film formation proceeded. This was performed using the same apparatus as follows; the connection of spray line was switched from the plasticizing mixture to water or a solution of HPMC, and it was sprayed into the beads in approximately 5 min. The beads were then dried with heated air until the outlet temperature reached 50°C.

2.2.3. Tablet coating

A lab-scale ventilated pan coater (Hicoater® model HCT-48N, Freund Industrial, Tokyo, Japan) was used with a minor modification as shown in Fig. 4. As in the fluidized bed, a tube (of the same type as that used for the fluidized bed) was inserted into the pan to deliver the powder materials (Fig. 5). The powder was quantitatively passed from the powder feeder and directly delivered to the cores through the tube by means of compressed air (approxi-

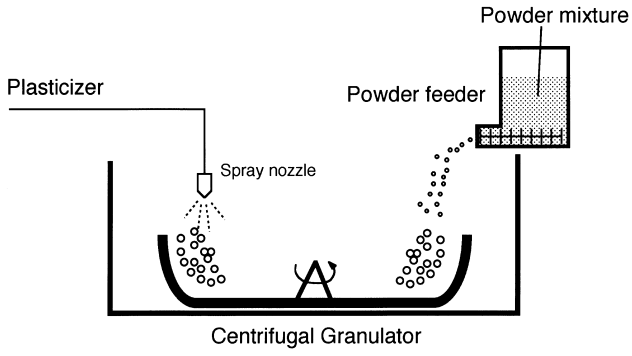

Fig. 1. Schematic illustration of dry coating with a centrifugal granulator.

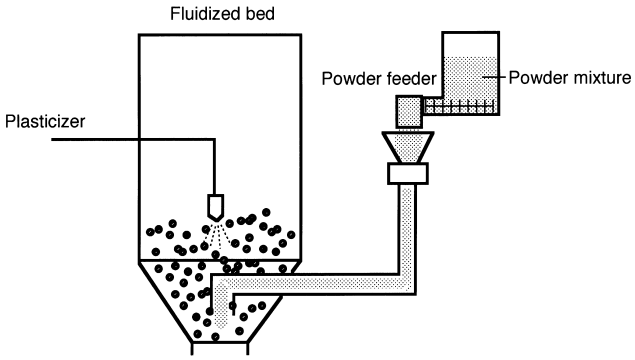

Fig. 2. Schematic illustration of dry coating with a fluidized bed.

mately 150 kPa). The outlet of the tube was approximately 20 cm from the surface of the tablet bed. The operation was similar to that for the bead coating, including the powder feeding and liquid spraying, followed by the curing process.

2.3. Evaluation

2.3.1. Contact angle (preliminary experiment)

Tablets (10 mm in diameter, flat-faced) were prepared from a blend of HPMCAS and talc (10:3) using the tableting machine described before. The contact angle of plasticizing agents on the tablet was optically measured using a contact angle meter (FACE®, model CA-D, Kyowa Interface Science Co., Ltd., Tokyo, Japan).

2.3.2. Gastric resistance

The gastric resistance of the coated pancreatin beads was determined by using a dissolution tester (JP XIII) with rotating baskets. Nine hundred milligrams of the coated beads was put in the basket, and rotated in 900 ml of the simulated gastric fluid (the first fluid in the JP XIII disintegration test, pH 1.2) at 100 rpm for 2 h. Percent release of pancreatin after 2 h was determined by measuring the UV absorbance at 265 nm. The remaining beads after the test were then subjected to a disintegration test using simulated intestinal fluid (the second fluid in the JP XIII disintegration test, pH 6.8).

Gastric resistance of the coated tablets was measured using a disintegration tester (JP XIII) with the simulated gastric fluid. A hundred tablets were treated with the test fluid for 2 h, and the number of damaged tablets was counted. For intact tablets, uptake of gastric fluid (%) was determined from the weight increase of the tablet. After the test, the tablets remaining intact were subjected to the disintegration test in simulated intestinal fluid (pH 6.8) according to JP XIII to measure the disintegration time.

2.4. Coating efficiency

The coating efficiency (%) was calculated from actual weight gain of coated samples divided by the theoretical weight gain.

2.5. Stability test

Both coated tablets and beads were stored in closed vials at 40°C for 6 months. The appearance, gastric resistance and intestinal disintegration of the samples were measured and compared with the initial data. The gastric resistance of coated beads was also evaluated by measuring the amylase activity (starch digestive power) as follows. The coated beads were treated in the simulated gastric fluid at 37°C for 2 h using a disintegration tester. The beads were then picked up and subjected to the assay of starch digestive power according to JP XIII. The activity was compared with that before the gastric fluid treatment.

3. Results and discussion

The fine particle grade of HPMCAS was originally developed for aqueous enteric coating. Its particle size is not more than 10 μm [8]. The regular coating method with the polymer is to utilize an aqueous dispersion containing the polymer powder, talc, triethyl citrate, and a surfactant [9]. Modifications of the formulation have been made to improve productivity, but it is difficult to increase the polymer concentration due to nozzle blocking [10]. We therefore decided to remove the water and apply the polymer powder directly to the cores. A commercially available quantitative powder feeder was employed to carry out this novel dry coating operation.

3.1. Preliminary experiment using a CF-granulator

In a preliminary experiment, we examined bead coating using the CF-granulator, which was considered to be convenient for this new method because mechanical modification was not necessary. Talc has been found to enhance the surface smoothness of the coating layer and to prevent stickiness in aqueous-based HPMCAS coating. So we decided to use it for dry coating as well. A blend of HPMCAS and talc (10:3) was used as the powder mixture and triethyl citrate was used as the plasticizer. The operating parameters are shown in Table 1, except that the initial trial was done without any water in the curing process. However, the resulting beads did not have satisfactory gastric resistance. When a small amount of water (8% of core weight) was included in the curing process, the gastric resistance was significantly increased. In this experiment, approximately 50% triethyl citrate with respect to the polymer weight was necessary to obtain a sufficient gastric resistance. When the level of triethyl citrate was higher than 50%, the beads tended to be sticky and became severely agglomerated. Coating efficiency was less than 85% throughout the range of plasticizer levels investigated. From these results, it was concluded that the formulation should be modified to obtain higher coating efficiency and to avoid stickiness. It was considered that the problems

Fig. 3. Dry coating system with a fluidized bed (Flowcoater FLO-5).

might be overcome by the addition of some other agent, which is oily and compatible with the polymer. Other plasticizing additives, including oily materials, were screened to

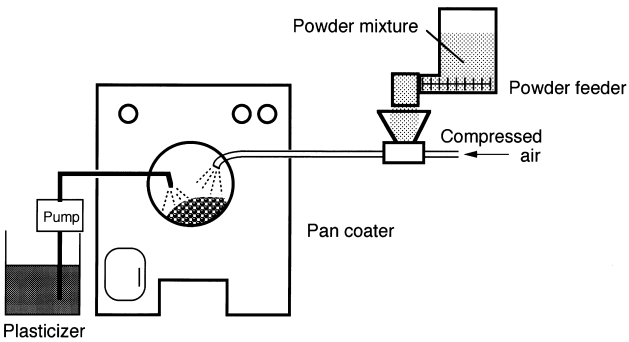

Fig. 4. Schematic illustration of dry coating with a tablet coating machine.

Fig. 5. Dry coating system with a Hicoater (HCT-48N).

select those with good wettability for the polymer. This was carried out by measuring the contact angle on the polymer. Acetylated monoglyceride, mineral oil, and olive oil exhibited relatively low contact angle (Fig. 6). Each of these candidates was added to the formulation and the coating experiments were carried out again. The results are shown in Fig. 7, which presents the relationship between the coating efficiency and the contact angle. Higher coating efficiency was seen from the materials with lower contact angles. Using these oily materials with low contact angles, the problem of agglomeration was also solved, probably because the materials made the coated surface slippery. The final formulation chosen was that shown in Table 2, with a combination of triethyl citrate and acetylated monoglyceride as the plasticizing agent. Gastric resistance was not obtained when acetylated monoglyceride was used

Table 1

Processing conditions for dry coating in a CF-granulator

Charge	0.5 kg
Slit air flow	0.1 m^3/min
Inlet air temperature	80°C
Exhaust air temperature	42°C
Spray nozzle	PSA-3 × 1
Nozzle diameter	0.7 mm
Atomizing pressure	100 kPa
Disk speed	150 min^{-1}
Spray rate (liquid)	5.2 g/min
Powder feed rate	13 g/min
Curing	
Slit air flow	0.1 m^3/min
Inlet air temperature	80°C
Exhaust air temperature	42 → 36 → 50°C
Disk speed	150 min^{-1}
Water spray rate	7.5 g/min
Water amount	40 g

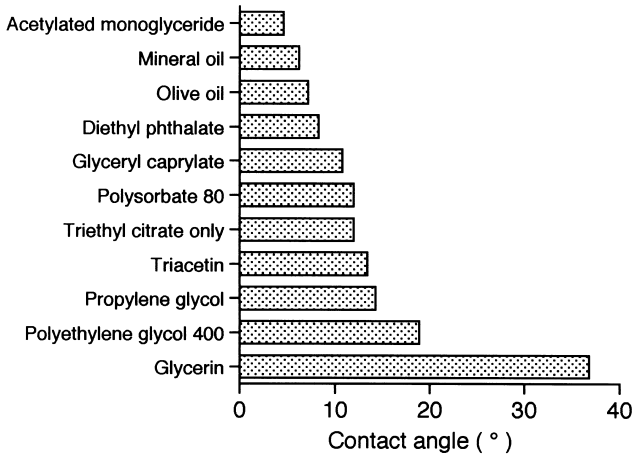

Fig. 6. Contact angle of plasticizing agents. Each material was used in combination with triethyl citrate (2:5), except 'triethyl citrate only'.

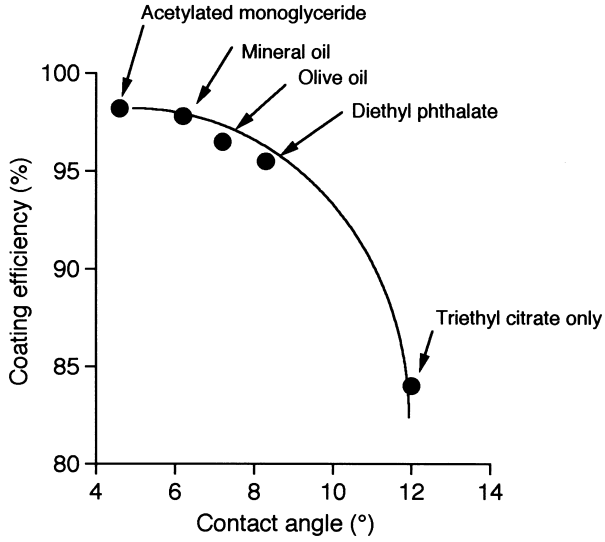

Fig. 7. Relationship between coating efficiency and contact angle. Each material was used in combination with triethyl citrate (2:5), except 'triethyl citrate only'.

alone, due to lack of film formation by incompatibility to the polymer. The coated beads obtained by the dry coating technique had sufficient gastric resistance when the coating amount (polymer basis) was 30%.

3.2. Bead coating with fluidized bed

Fluidized beds are currently the most widely used equipment for bead coating. We therefore examined dry coating utilizing a fluidized bed. The powder was supplied through a tube inserted into the vessel. Negative pressure inside the vessel during fluidization automatically pulled the powder inside. The fluidizing level (air flow) was set lower than the regular level because excessive fluidizing caused a severe loss of powder. The charge amount of core beads was greater than the regular level, since this was also effective to decrease the powder loss. Table 3 shows the processing conditions in the fluidized bed. The outlet temperature was maintained at 42°C. Blocking in the powder feed line did not occur during the process.

Fig. 8 shows the gastric resistance of the coated beads from both the CF-granulator and the fluidized bed, in comparison with that of beads given a conventional aqueous coating with the same polymer. The target level of the active ingredient released at pH 1.2 in 2 h was less than 5%. This was achieved when the coating level (polymer basis) was more than 25% for dry coating, and 18% for the conventional coating. These results indicate that the dry coating method requires a greater coating amount than conventional aqueous coating. However, this level is regarded as acceptable, and rather than the coating amount, the processing time is more important in the comparison (discussed later). A dry-coating sample of 30% coating level and an aqueous-coating sample of 20% coating level were used for further evaluations. The percent release of the active ingredient from the dry-coating sample was 1.2% at pH 1.2 in 2 h, and that of the aqueous-coating sample was 0.5%. The disintegration time of the dry-coated beads at pH 6.8 was 6 min, whereas that of the samples with aqueous coating was 3 min, probably due to the difference in coating level. Although the two methods do not produce identical results, it is clear that the dry coating technique can be successfully applied using commercially available coating machines.

3.3. Tablet coating

We next examined dry coating for tablets using a commercially available coating machine. In order to deliver the powder uniformly onto the tablets in the pan, compressed air was used to force the powder out of the tube, like a liquid spray. The processing conditions are shown in Table 4. The outlet temperature was controlled at approximately 42°C during the coating process, as in the other experiments. During the process, no blocking was observed in the powder feed line. Before the curing process, the coated surface was rough, and film formation was not observed, but after it, the surface layer formed a continuous film. Surprisingly, the film formed within a very short time, approximately 10 min, after the addition of a small amount of water (3% of dry core). Fig. 9 shows the gastric resistance of the coated tablets. The required coating level (polymer basis) for suffi-

Table 2
Formulation for dry coating

	Ingredient	Parts[a]
Powder mixture	HPMCAS	100
	Talc	30
Liquid mixture	Triethyl citrate	30
(Plasticizer)	Acetylated monoglyceride	20

[a]The amount of each ingredient is based on the weight of HPMCAS = 100.

Table 3
Processing conditions for dry coating in a fluidized bed (Flowcoater)

Charge	10 kg
Inlet air flow	2.0 m^3/min
Inlet air temperature	55°C
Exhaust air temperature	42°C
Spray nozzle	FO × 1
Nozzle diameter	1.2 mm
Atomizing pressure	200 kPa
Spray rate (liquid)	26 g/min
Powder feed rate	65 g/min
Curing	
Inlet air flow	2.0 m^3/min
Inlet air temperature	60°C
Exhaust air temperature	42 → 34 → 50°C
Water spray rate	45 g/min
Water amount[a]	500 g

[a]Water containing HPMC (4%).

cient gastric resistance was 8% with respect to the core weight. Uptake of the gastric fluid was 2.1%, which was almost the same level as that of tablets with aqueous coating. The disintegration time at pH 6.8 was 10 min, again similar to that of tablets with the conventional coating. The appearance of the tablet surface is important for pharmaceutical products, and the surface of the tablets obtained by dry coating was slightly rougher than that of the samples with conventional coating, but was regarded as being in the acceptable range. The surface appearance depended on the oily additive used, and was smoothest when acetylated monoglyceride was used.

In this study, the core tablets were coated with HPMC prior to dry coating. Without the sub-coating, the gastric resistance after dry coating was not satisfactory. This may be because the sub-coating layer prevents from the penetration of plasticizer into the core, or because the uncoated surface was damaged and became rougher during the curing process. The beads did not require sub-coating.

Table 4
Processing conditions for dry coating of tablets (Hicoater)

Parameter	
Charge	5 kg
Inlet air flow	1.5 m^3/min
Inlet air temperature	60°C
Exhaust air temperature	42°C
Spray nozzle	ATF × 1
Nozzle diameter	1.2 mm
Atomizing pressure	80 l/min
Spray rate (liquid)	5.2 g/min
Powder feed rate	13 g/min
Curing	
Inlet air flow	1.5 m^3/min
Inlet air temperature	80°C
Exhaust air temperature	43 → 38 → 50°C
Water spray rate	100 g/min
Water amount[a]	150 g

[a]Water containing HPMC (4%).

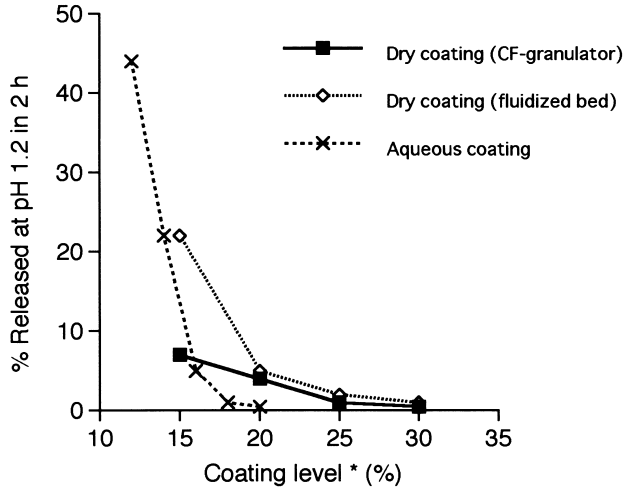

Fig. 8. Gastric resistance of enteric-coated beads. *Polymer basis.

3.4. Coating time and efficiency

Table 5 summarizes the coating time and efficiency of dry coating in comparison with a conventional aqueous coating with the same polymer. The required coating level for sufficient gastric resistance was higher for dry coating for every system. This was probably because the distribution of the coating materials on the core surface is less uniform than in the conventional aqueous coating. It was observed that the gastric resistance was decreased as the powder feed rate was increased, and this suggests that it takes a certain time for the powder material to spread over the core surface, and a longer mixing time leads to a more uniform powder distribution. Mechanical improvement, such as the use of an output attachment of appropriate dimensions, should improve the powder distribution and decrease the minimum coating level required. The coating efficiency was also slightly less than that of conventional coating, but was more than 90% for all equipment used in

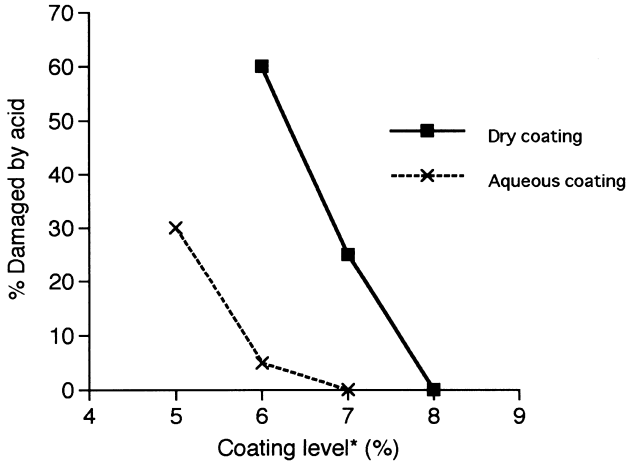

Fig. 9. Gastric resistance of enteric-coated tablets. *Polymer basis.

Table 5
Processing time and coating efficiency of dry coating in comparison with conventional aqueous coating

Dosage form	Method	Batch size (kg)	Coating level[a] (%)	Processing time (min)			Coating efficiency (%)
				Powder feed (spray)	Curing (drying)	Total	
Beads (CF-granulator)	Dry coating	0.5	30	15	10	25	95
Beads (fluidized bed)	Dry coating	10	30	60	30	90	91
	Aqueous coating[b]	10	20	260	30	290	97
Tablets	Dry coating	5	8	40	10	50	92
	Aqueous coating[b]	5	7	111	30	141	96

[a]Coating level for sufficient gastric resistance.
[b]The coating was performed using an aqueous dispersion of HPMCAS according to a usual method [1].

this study. Other experiments have indicated that the efficiency is increased to more than 95% on pilot-scale equipment (data not shown), so the above coating efficiency in lab-scale apparatus can be regarded as acceptable. The most significant improvement was the reduction of processing time. The total processing time was approximately one-third of that with the conventional system for both bead coating and tablet coating. A unique feature of dry coating is that the coating time can be varied over in a wide range. For example, the processing time for powder feed was 40 min for 8% tablet coating, but this could be shortened to 30 min or elongated to 60 min simply by changing the powder feed rate. In the case of solution or dispersion coating, the choice of coating time would be limited by the polymer concentration and drying efficiency of the coating machine. In the dry coating process, it is hardly necessary to consider such limitations because no solvent is used, except for the small amount in the curing process. Nevertheless, excessively fast powder feeding resulted in a decrease in coating uniformity, so the optimum processing time in dry coating should be considered as the shortest time that gives a satisfactory coating performance.

3.5. Scanning electron microscopy

The surfaces of beads and tablets sampled during the dry coating process were observed using a scanning electron microscope. Before the curing process, film formation progressed only slightly, and the coating layer consisted mainly of a deposit of solid particles (Fig. 10). After the curing process, the particles were fused and the layer was continuous. Conditions for film formation of HPMCAS in an aqueous system have been studied using a free-film preparation apparatus [11,12]. The minimum film formation temperature of HPMCAS plasticized by triethyl citrate was less than 23°C [12], so the outlet temperature during the dry coating process (more than 40°C) was regarded as sufficient. In the free-film study, the film strength of HPMCAS decreased at low moisture levels in the film formation process, indicating that the coalescence could not progress without water. Therefore, it seems that at least a small amount of water is an essential factor for the film formation of this polymer. Our initial goal was to remove all water from the system, but this proved unrealistic; a little was required at the curing process after all. However, the amount required is quite a small level (5% of core weight for a fluidized bed, 3% for tablet coating) and we think it is still reasonable to use the term dry coating for this technique. The mechanism of action of water in this film formation process has not been elucidated, but we speculate that the evaporation of water provides a driving force to fuse the polymeric particles

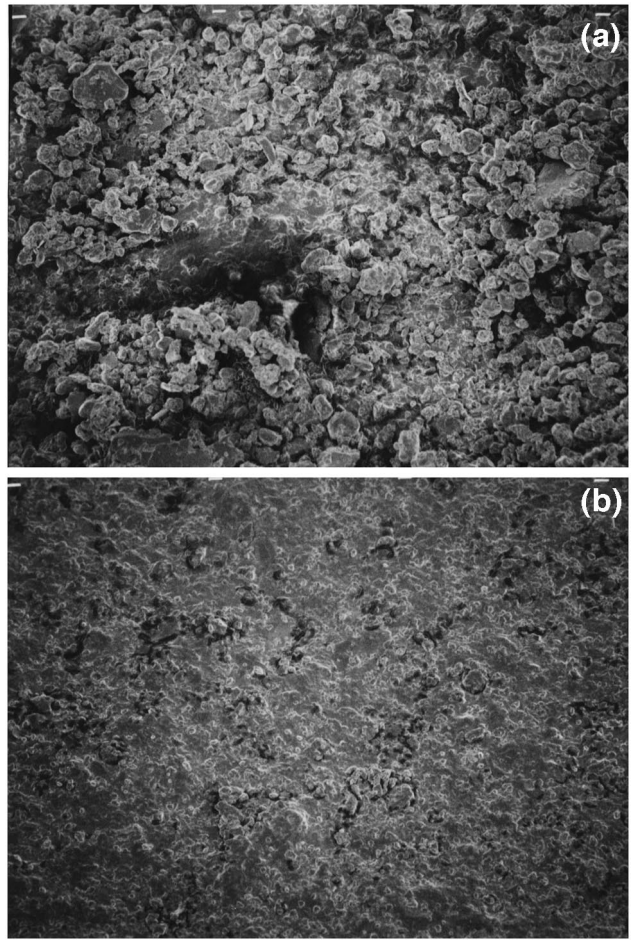

Fig. 10. Scanning electron microscope view of the surface coating layer on a dry-coated tablet. (a) Before curing; (b) after curing.

together, as in the film formation mechanism proposed for aqueous latex systems [13,14]. Water might act as a trigger or inducer of film formation.

A similar technique has been studied by Nakagawa et al. [15], using wax and HPMC to coat beads in a high-speed mixer. Wax generally has a low melting point, and may be easily fused by heating. In contrast, heating alone was insufficient for film formation of HPMCAS. We have tried to use the other coating polymers, such as HPMC and acrylic resins in the dry coating technique with aqueous curing, but without success. The usefulness of HPMCAS is probably because this polymer is easily softened by heating, and can be well plasticized to form a film in the presence of only a small amount of water.

3.6. Stability

Fig. 11 shows the change of amylase activity of the beads during the storage. The appearance of the samples was unchanged after 6 months, except that slight sticking was observed in cases where HPMC had not been used in the curing process. The amount of release of pancreatin at pH 1.2 and disintegration time pH 6.8 were not significantly changed in the stability tests. The amylase activity of uncoated beads was decreased approximately 40%, while coating by any method, strongly suppressed the enzymatic deactivation. The gastric resistance was not less than 95% in terms of enzymatic activity during the storage, and there was no difference between dry coating and aqueous coating.

Table 6 shows the results of stability tests of the tablets. No damaged tablets were observed in the gastric treatment

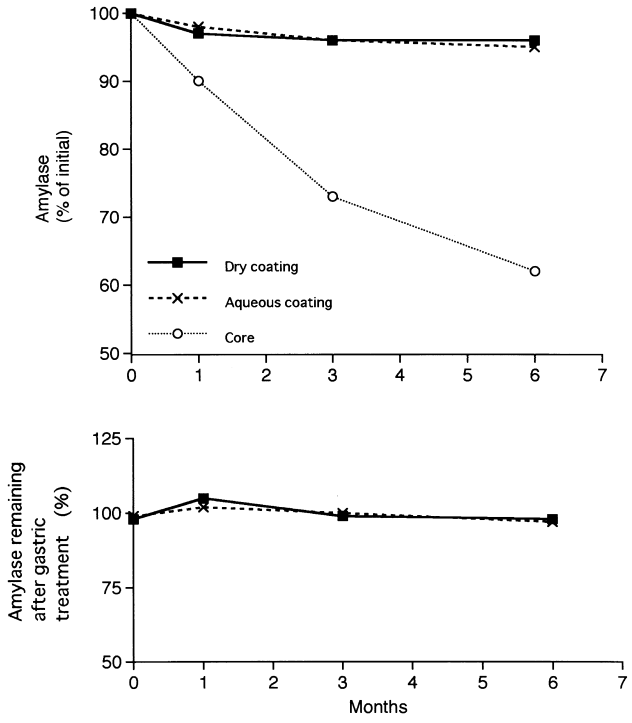

Fig. 11. Stability of enteric-coated beads based on amylase activity.

Table 6

Stability of tablets obtained by dry coating

	Initial	After storage for 1 month	3 months	6 months
Uptake of gastric fluid (%)				
Dry coating	2.1	1.8	2.1	2.0
Aqueous coating	2.3	1.8	1.9	2.0
Disintegration time (min) at pH 6.8				
Dry coating	10	11	12	14
Aqueous coating	10	12	13	14

throughout the period. Uptake of gastric fluid was not increased during storage, though a slight increase in the disintegration time in the simulated intestinal fluid was observed in both cases. This suggests that further gradual coalescence of the film may have occurred and the film density may have gradually increased during storage. In summary, there were no significant differences in the stability of samples obtained by dry coating (30%) and aqueous coating (20%), and the dry coating method did not show any disadvantages in terms of enteric performance.

4. Conclusions

The dry coating technique was proved to provide both bead and tablet products having sufficient gastric resistance, with a substantial reduction of processing time, in commercially available coating machines with minor modifications. Further experiments on pilot-scale and commercial-scale machines are in progress.

References

[1] H. Nakagami, T. Keshikawa, M. Matsumura, H. Tsukamoto, Application of aqueous suspensions and latex dispersions of water-insoluble polymers for tablet and granule coatings, Chem. Pharm. Bull. 39 (1991) 1837–1842.
[2] G.C. Ebey, A thermodynamic model for aqueous film-coating, Pharm. Technol. 11 (4) (1987) 41–46.
[3] S.C. Porter, Aqueous film coating - an overview, Pharm. Technol. 3 (9) (1979) 55–59.
[4] R.K. Chang, C.H. Hsiao, J.R. Robinson, A review of aqueous coating techniques and preliminary data on release from a theophylline product, Pharm. Technol. 11 (3) (1987) 56–68.
[5] G.S. Banker, G.E. Peck, The new, water-based colloidal dispersions, Pharm. Technol. 5 (4) (1981) 55–61.
[6] J.W. McGinity, Applications and physical-chemical properties of aqueous polymeric coatings for drug delivery systems. Proceedings of Pre-World Congress Particle Technology, Gifu, Japan, September 17–18, 1990.
[7] General brochure 'Pharmacoat', Shin-Etsu Chemical Co., Ltd., September, 1995.
[8] General brochure 'Shin-Etsu AQOAT', Shin-Etsu Chemical Co., Ltd., May, 1995.
[9] Technical information, 'An improved aqueous coating using Shin-Etsu AQOAT', Shin-Etsu Chemical Co., Ltd., February, 1994.

[10] T. Nagai, S. Obara, H. Kokubo, N. Hoshi, Application of HPMC and HPMCAS to aqueous film coating of pharmaceutical dosage Forms, in: J.W. McGinity (Ed.), Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms, Marcel Dekker, New York, 1997, pp. 177–225.
[11] S. Obara, J.W. McGinity, Properties of free films prepared from aqueous polymers by a spraying technique, Pharm. Res. 11 (1994) 1562–1567.
[12] S. Obara, J.W. McGinity, Influence of processing variables on the properties of free films prepared from aqueous polymeric dispersions by a spray technique, Int. J. Pharm. 126 (1995) 1–10.
[13] Y. Chevalier, C. Pichot, C. Graillat, M. Joanicot, K. Wong, J. Maquet, P. Lindner, B. Cabane, Film formation with latex particles, Colloid Polym. Sci. 270 (1992) 806–821.
[14] S.T. Eckersley, A. Rudin, Mechanism of film formation from polymer latexes, J. Coating Tech. 62 (1990) 89–100.
[15] A. Nakagawa, T. Ishizaka, K. Yano, M. Koishi, Granule surface modification by dry mixing and applications to sustained release preparations, Zairyo Gijyutsu 2 (1984) 595–606.