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COMMUNICATION

Rotary Tangential Spray Technique for Aqueous Film Coating of Indobufen Pellets

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ABSTRACT

Indobufen pellets, previously prepared by direct pelletization employing the rotary tangential spray fluidized bed (Rotoprocessor), were coated using the same equipment setup as for the film coating process. Different amounts of the aqueous-based ethylcellulose dispersion (Aquacoat) were easily applied on the active cores of different compositions with no spray blocking or pellet sticking. The coating process was not influenced by changing the ethylcellulose (Aquacoat® ECD-30) formulation with soft acrylic resin (Eudragit® NE 30D) or by adding water-soluble polymers (Pharmacoat® 606 and PEG 6000) to the coating dispersions. Simple setup, flexibility of operation, and short manufacturing times were the advantageous features of the tangential spray equipment. These benefits were verified during the pellet coating process.

The composition of the cores and membranes were confirmed as the determining parameters with respect to the performances in terms of the drug release rate. The morphological and functional results clearly demonstrated the tangential spray rotary system as a promising one-step technique for the preparation of indobufen prolonged-release multiple-unit dosage forms.

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INTRODUCTION

The most attractive feature of centrifugal equipment is the ability to carry out both pelletization and coating in one machine. Generally, pellets are prepared by a layering technique which is based on the application of powder or solution/suspension on inert seeds (1).

The coating operations with a centrifugal equipment system yielded film characteristics similar to those obtained with the Wurster system, which can exploit a different bed expansion (2). When the rotary system is used for the coating process, the solution is sprayed tangentially in the same direction as that followed by the pellets in the bed. The pellets are rotated in a homogeneous spiral motion by the combined action of the fluidizing air, centrifugal force, and gravity. Both the very rapid tumbling and high particle viscosity in the spray zone typically allow a higher liquid application rate than other techniques. A shorter processing time is a benefit when accomplished by no changes of the desired film characteristics. A drawback of the tangential spray process is that the product is subjected to a high level of mechanical stress, so it is not recommended for brittle products; in addition, the process is more susceptible to the adhesion of particles to the upper walls of the chamber. In a previous work spherical granules (pellets) containing indobufen were prepared by rotary technology starting from pulverized raw materials (3). The coating of such pellets in order to obtain a prolonged drug release was the consequent development of our studies regarding the rotary tangential spray equipment.

Therefore, the aims of this work were to verify the feasibility of coating pellets previously prepared in the same machine, and to obtain prolonged drug release from pellets coated with different film coating agents. Aqueous dispersions of cellulose derivatives and acrylic resins were chosen as coating formulations.

MATERIALS AND METHODS

The pellet preparation was reported in a previous work (3). Formula compositions were based on microcrystalline cellulose (Avicel® PH 101), 15, 30, and 45% w/w as the pelletization agent; in some formulations the microcrystalline cellulose was partially substituted with 10% w/w of different fillers (lactose, mannitol, calcium carbonate). Aqueous dispersions of ethylcellulose (Aquacoat® ECD-30, FMC Corp., Brussels, Belgium) and acrylic resins (Eudragit® NE 30D, Rohm Pharma, Germany) were used as coating systems. Acetylcitrate (Pfizer, NY, New York), talc (Talco e Grafite, Italy), hydroxypropylmethylcellulose (HPMC, Pharmacoat® 606, Shinetsu, Japan), and polyethylene glycol (PEG 6000, Hoechst, Germany), all USP grade, were used as adjuvant excipients in the coating formulations.

An MP1 multisystem fluidized bed (Niro-Aeromatic, Switerland) with Rotoprocessor insert was used as centrifugal equipment.

Coating Process

Active pellets (490 g) were coated by spraying the aqueous polymer dispersions at 10 g/min rate and 1.5 bar pressure until 3, 6, and 9% (w/w on dry bases) coating weight gains were realized.

The formulations of aqueous polymeric systems and the process conditions are reported in Tables 1 and 2.

During the coating process 40 g of pellets was withdrawn after the application of 3 and 6% coats, and dried in a tray oven at 50°C for 1 hr. The coating was then completed up to 9% coat and the pellets were dried as described above.

Table 1

Composition of Polymeric Dispersions (%)

	Ethylcellulose		Acrylic Resins	
Formulations	E1	E2	A1	A2
Aquacoat	80.5	80.5	—	—
Triethylcitrate	6.0	6.0	-	-
Eudragit NE 30D	—	—	43.5	43.5
Talc	-	-	6.5	6.5
Simethicone emulsion	—	—	0.2	0.2
Water	13.5	10.2	49.8	48.0
Pharmacoat 606	—	2.4	—	1.3
PEG 6000	—	0.9	—	0.5

Table 2

Film Coating Process Conditions

	Ethylcellulose		Acrylic Resins	
Formulations	E1	E2	A1	A2
Inlet temperature, °C	47	49	36	37
Outlet temperature, °C	33	35	33	33
Air volume, m^3/hr	320	240	220	250
Disk rotation, rpm	100	100	100	100
Process time, min	52	53	54	55

Physical Testing

The moisture content was determined on the basis of the weight loss at 100°C for 20 min (thermobalance Mettler PC 440 with IR ray oven).

The bulk density was determined by pouring, through a glass funnel, weighted amounts of pellets into a steel cylinder (volume 97.36 ml).

The release tests were carried out using the USP paddle apparatus (pH 7.5 phosphate buffer, 1 liter 37°C); indobufen concentrations were assayed spectrophotometrically at 280 nm (Perkin-Elmer, Lambda 15).

Photomicrographs of pellets, splutter-coated with gold to improve the conductivity, were taken with a scanning electron microscope (SEM, Cambridge Stereoscan Mark IIA, UK).

RESULTS AND DISCUSSION

The coating operations carried out with different aqueous-based polymeric dispersions proved the rotary tangential spray equipment to be a complete one-step machine for preparing coated multiple-unit dosage forms. Pellets obtained by direct pelletization showed adequate characteristics for the subsequent coating process carried out on the same equipment.

The coating liquid flow was continuous with no spray system blocking, and the pellets showed no tendency to aggregate forming double or triple units. The well-known features of the tangential spray technique (i.e., the droplets application to the substrate which occurs before much evaporation), because the nozzle was closely surrounded by the product, allowed films to be formed with good technological properties. The morphological aspect of the films was similar to that shown by films obtained when the Wurster equipment was used (4).

SEM photomicrographs of coated pellets in cross-sectional view are shown in Fig. 1; the applied film appears to be smooth, continuous, and uniform in thickness. In general, these characteristics of the films were obtained irrespective of the starting core composition, thus indicating an adequate balance between spray-drying and fluidizing operating conditions.

The coating of the active pellets with aqueous-based ethylcellulose dispersion determined the prolongation of indobufen release. The drug release curves of pellets of different compositions and coated with increasing amounts of polymeric film are reported in Figs. 2 and 3. In all cases a modulation of drug release was obtained, thus indicating the ability of the tangential spray coating process to differentiate the release on the basis of the amount of polymer applied. The results seem to

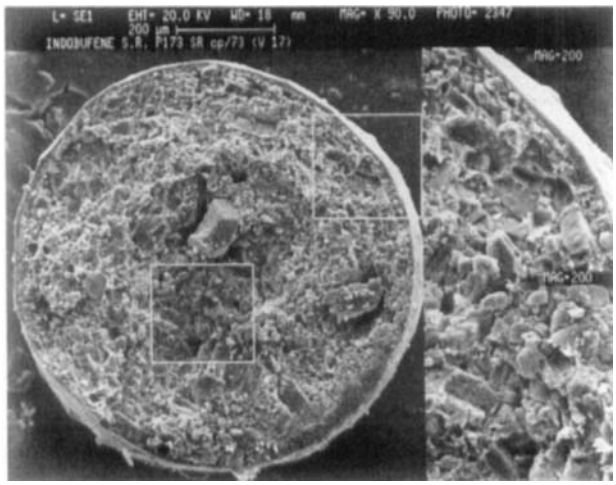

Figure 1. Cross-section of coated pellets obtained with ethylcellyulose dispersions (Aquacoat). Core composition: indobufen/Avicel PH 101 70/30; 6% coat.

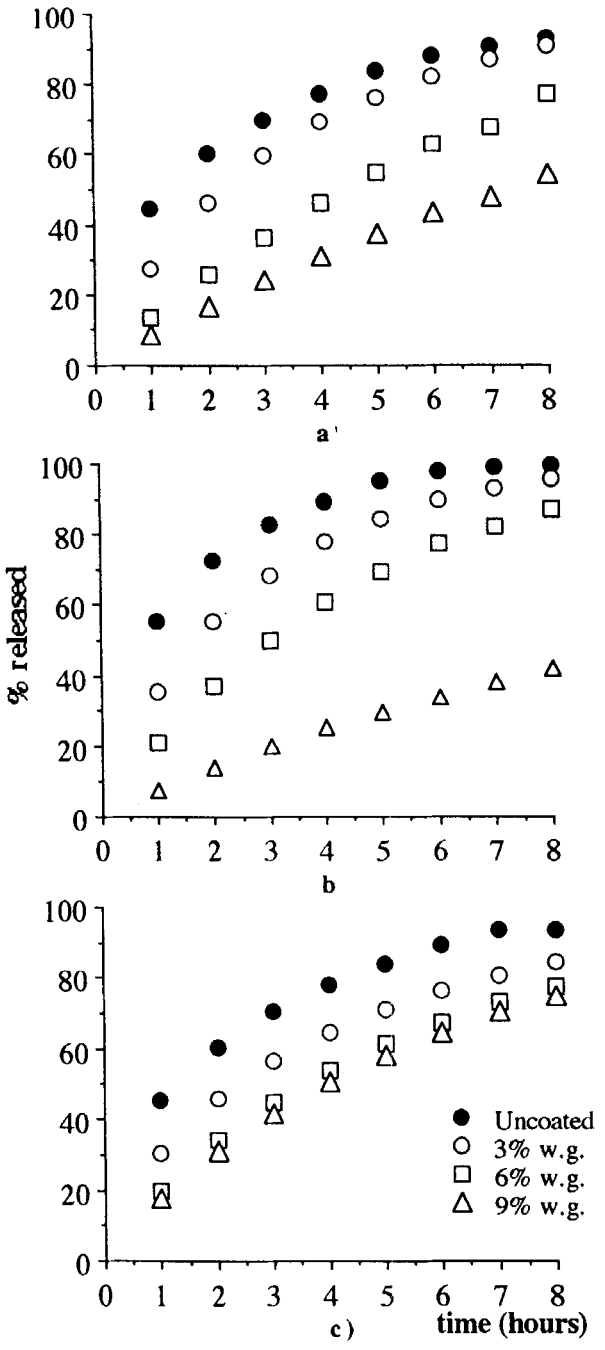

Figure 2. Release profiles of uncoated and ethylcellulose-coated pellets with increasing amounts of coating applied (w.g.: weight gain): (a) core composition: indobufen/Avicel PH 101 85/15; (b) core composition: indobufen/Avicel PH 101 70/30; (c) core composition: indobufen/Avicel PH 101 55/45.

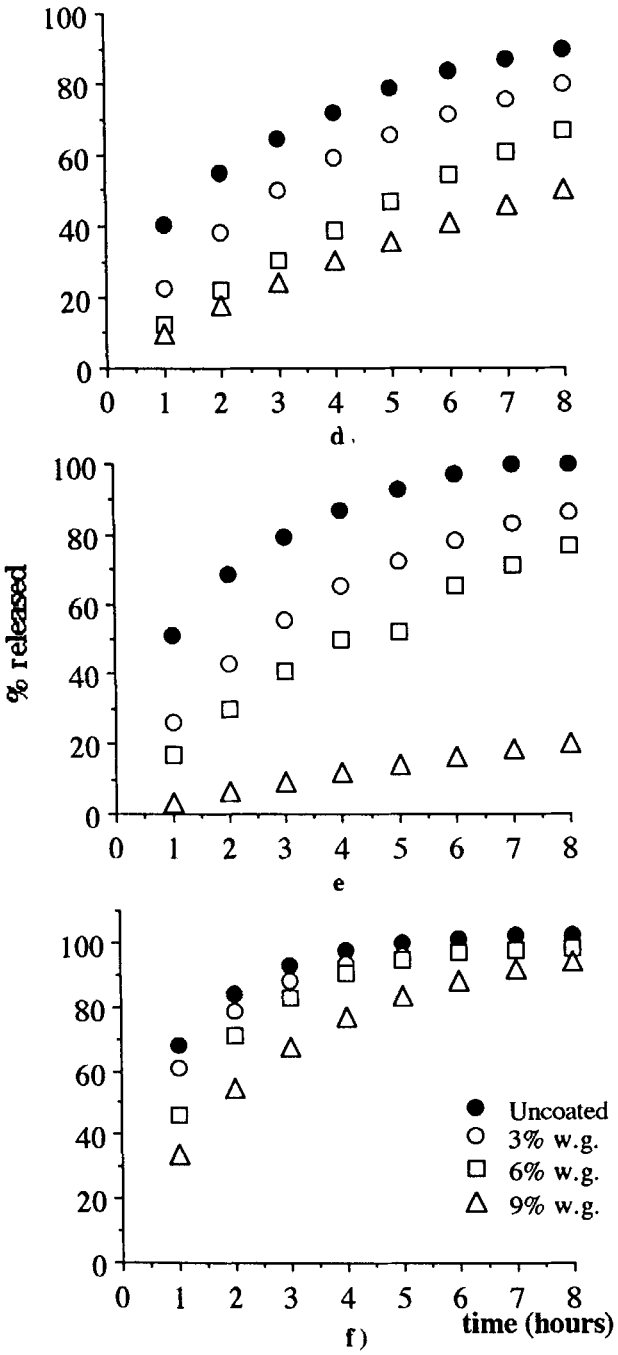

Figure 3. Release profiles of uncoated and ethylcellulose-coated pellets with increasing amounts of coating applied (w.g.: weight gain); (d) core composition: indobufen/Avicel PH 101/lactose 70/20/10; (e) core composition: indobufen/Avicel PH 101/mannitol 70/20/10; (f) core composition: indobufen/Avicel PH 101/calcium carbonate 70/20/10.

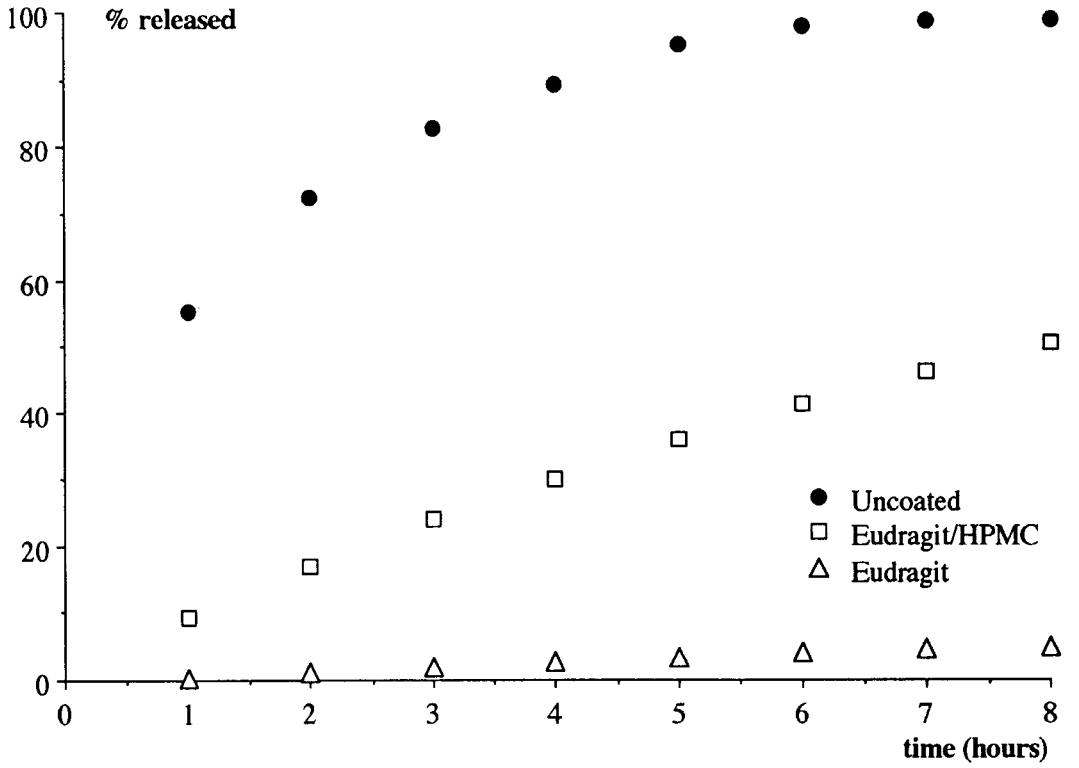

Figure 4. Release profiles of uncoated and acrylic resin-coated pellets with or without soluble ingredients, PEG 6000 and Pharmacoat 606. Core composition: indobufen/Avicel PH101 70/30; 3% coat.

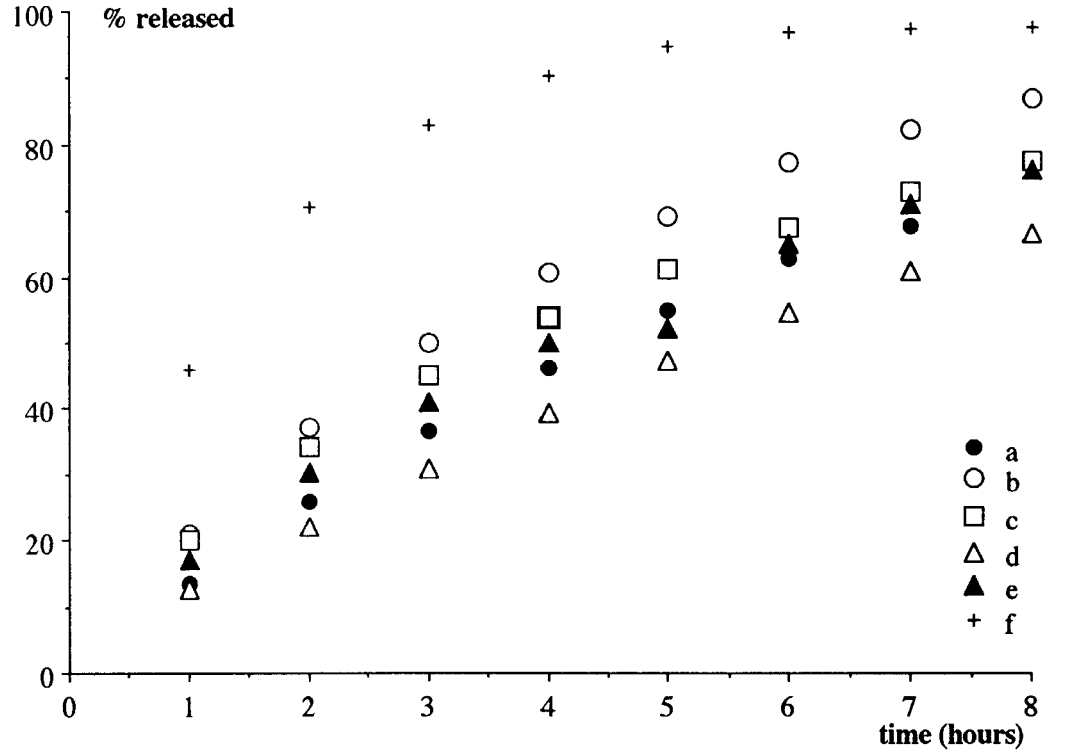

Figure 5. Release profiles of coated ethylcellulose pellets (6% coat) starting from core of different compositions (a) indobufen/Avicel PH 101 85/15; (b) indobufen/Avicel PH 101 70/30; (c) indobufen/Avicel PH 101 55/45; (d) indobufen/Avicel PH 101/lactose 70/20/10; (e) indobufen/Avicel PH 101/mannitol 70/20/10; (f) indobufen/Avicel PH 101/calcium carbonate 70/20/10.

demonstrate a correct and reproducible application of the ethylcellulose dispersions.

Analogous performances in terms of processing feasibility and technological characteristics of the coated pellets were obtained using acrylic resins dispersions. However, the drug release rates were dramatically lower than those shown by ethylcellulose-coated pellets at the same coating levels. A partial modulation of release was then achieved by modifying the acrylic film composition by introducing water-soluble ingredients (Pharmacoat 606 and PEG 6000). This demonstrated the flexibility of the tangential spray equipment while dealing with different coating formulations (Fig. 4). The ethylcellulose dispersion E2 containing the soluble ingredients led to a very permeable film which was unable to control the release of the drug.

In Fig. 5, a comprehensive picture of the release profiles of pellets coated with 6% ethylcellulose film is reported. The results showed, as previously reported (5), the major role played by pellet core compositions in determining the release characteristics.

CONCLUSIONS

Rotary tangential spray equipment is an alternative processing technique for the preparation and the coating of pellets to be used for prolonged drug release. Film coatings applied from aqueous polymeric dispersions show good technological characteristics in terms of the morphological aspects, smoothness, and thickness uniformity. The core composition was proven to be an essential parameter in determining the overall release performances of the coated pellets.

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