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Dry coating in a rotary fluid bed

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ABSTRACT

A highly efficient dry coating process was developed to obtain an enteric film avoiding completely the use of organic solvents and water. Using hydroxypropyl methylcellulose acetate succinate (HPMCAS) an enteric coat should be obtained without adding talc as anti-tacking agent because of problems arising from microbiological contamination. Further on, a method was developed preparing isolated films in order to determine the glass transition temperature (T_g) and the required process temperature.

The process was conducted in the rotary fluid bed with a gravimetric powder feeder achieving an exact dosage in contrast to volumetric powder feeder. A three way nozzle was aligned tangential to the pellet bed movement feeding simultaneously powder and plasticizer into the rotary fluid bed.

The determined coating efficiency of the talc-free formulation was high with 94% and storage stability regarding tacking could be achieved using colloidal silicium dioxide as top powder. The T_g of the enteric coat could be determined analyzing the T_g of isolated films obtained by coating celluloid spheres instead of pellets using the dry coating process in rotary fluid bed. The dry coating process has been demonstrated to be a serious alternative to conventional solvent or water based coating processes.

1. Introduction

1.1. State of the art

Coating with polymer powders is an innovative and promising alternative to the conventional coating technology with organic polymer solution or aqueous polymer dispersion. Conducting organic solvent based processes the solvent needs to be recovered due to environmental pollution. Coating processes with aqueous dispersions are very time and energy consuming (Wheatley and Steuernagel, 1997) caused by the low concentration of coating polymer and large amounts of water which need to be evaporated. Furthermore the spray nozzle has a tendency to be blocked caused by premature coalescence of the polymer in the dispersion. Compared to both the dry coating method is favorable regarding environmental friendliness, safety and cost. It is a coating process without any use of water or organic solvent. Because of their absence, water or organic solvent do not need to be evaporated which leads to shorter processing times and consequently to a lower energy demand. The process is simplified because important parameters of solvent- or aqueous dispersion-based processes have not to be considered e.g. evaporation parameters. Using the dry coating method a continuous enteric film formation can be achieved on the basis of simultaneously feeding/spraying the dry polymer powder and a plasticizer mixture on the pellets. It might be a very suitable coating method in order to coat drugs which are sensitive to organic solvents or water.

New coating processes have been developed layering polymer powder particles on the pellet or tablet surface by

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simultaneously feeding/spraying polymer powder and plasticizer followed by a curing phase at increased temperatures. Using a pan coater tablets were coated by adding polymer powder and plasticizer composition separately by a powder feeder and a spray nozzle. Afterwards film formation was induced by spraying a small amount of water on the coated beads and increasing the temperature facilitating coalescence (Obara et al., 1999). Pellets were coated with polymer powder and plasticizer mixed to an emulsion with HPMC solution using a Wurster insert with a powder feeder and separate spray nozzle (Pearnchob and Bodmeier, 2003a,b). However, this process does not meet exactly the conditions of the dry coating process using an emulsion containing water. Recently, tablets were coated with polymer powder which prior to the coating process had been preplasticized by mixing polymer powder with plasticizer and sieving afterwards (Cerea et al., 2004) or rather by a hot-melt extrusion process with plasticizer and thermal lubricant followed by cryogenically grinding of the extrudate (Zheng et al., 2004). The disadvantages of these processes are the small batch size of 50 g and the need of additional processing time and equipment for preparation of the coating material.

1.2. *Present study*

In contrast to the already published research work, in this study the dry coating process is carried out applying different formulations in rotary fluid bed equipment with a three way nozzle aligned to the direction of the fluid bed movement. The polymer is passed as dry powder via a powder feeder to the three way nozzle which is able to transport separately but closely together the plasticizer composition and the dry powder into the pellet bed. This method secures a homogeneous application of the coating material onto the pellets compared to separated addition which was performed by Obara et al. (1999). Due to the optimized process conditions using the rotary fluid bed the pellet bed has a higher density avoiding an excessive loss of polymer powder and preventing pellet agglomeration in comparison to conventional fluid beds. Furthermore, the process described by Obara et al. (1999) included talc as anti-tacking agent and water as curing enhancer which is not necessary according to the dry coating process of this study. In addition, important parameters for the film formation during the process for obtaining a functional film coating were analyzed and isolated films were produced by coating celluloid spheres with the dry coating method in the rotary fluid bed and afterwards peeling off the film. Thus, the achieved isolated films correspond exactly to the films of the dry coated pellets.

As a model coating material hydroxypropyl methylcellulose acetate succinate (HPMCAS) is used which has characteristically good gastric resistance and dissolves quickly over a wide range of pH once the acid stage is overstepped and shows a good compatibility with plasticizers (Nagai et al., 1989). The coating process was performed with triethyl citrate as plasticizer and Myvacet® as wetting agent playing both besides the reduction of the T_g a critical role in the performance of the film due to the inhibition of cracking or splitting (Felton and McGinity, 1997). As anti-tacking additives talc and colloidal silicium dioxide were compared. The effects of the formulation additives on drug release, agglomeration tendency and coating efficiency were evaluated and the film properties were analyzed by determining the T_g, the film thickness and the morphology.

2. Material and methods

2.1. *Materials*

Materials used were theophylline pellets (Klinge Pharma, München, Germany), hydroxypropyl methylcellulose acetate succinate (HPMCAS, AQOAT®, Shin-Etsu Chemical Co., Niigata, Japan) as enteric film former, talc (Erbslöh KG, Krefeld, Germany) as glidant and anti-tacking agent and colloidal silicium dioxide (Aerosil® 200, Degussa AG, Duesseldorf, Germany) as well as anti-tacking agent. As liquid plasticizers triethyl citrate (TEC, Jungbunzlauer Ladenburg GmbH, Ladenburg, Germany) and glycerol triacetate (Triacetin, Riedel de Haën, Seelze, Germany) as well as acetylated monoglyceride (AMG, Myvacet®, 9-45K, Quest International, Zwijndrecht, Netherlands) as wetting agent were used.

2.2. *Methods*

2.2.1. *Particle size measurements*

Laser light diffraction (Helos/KF-Magic, Sympatec GmbH, Clausthal-Zellerfeld, Germany) including a dry dispersing system (Rodos, Sympatec GmbH, Clausthal-Zellerfeld, Germany) was used to determine the particle size distribution of the coating powder. The value of the median is the average of three measurements.

2.2.2. *Contact angle measurements*

The contact angles of a composition of HPMCAS and talc (10:6) and pure HPMCAS were determined by the sessile drop method. Tablets of the micronized powders (diameter: 13 mm, weight: 0.1 g) were compressed using an IR press (64 kp/cm^2, hydraulic IR press, Perkin-Elmer, Germany). The achieved flat faced compacts were placed on an adjustable platform and the plasticizer compositions were dropped on the tablet with a micrometer syringe (5 μl). The determination of the contact angle was carried out by measuring the tangent to the curve of the droplet on the surface of the compact after 1 min ($n = 6$).

2.2.3. *Preparation of coated pellets and coating level*

The process was conducted in a rotary fluid bed (Glatt Rotor-GPCG-1.1, Glatt GmbH Binzen, Germany) with a three way nozzle aligned to the direction of the fluid bed movement. Different powder compositions were quantitatively passed with a powder feeder (K-Tron Soder K-CL-24-KT20, K-Tron, Gelnhausen, Germany) to the three way nozzle and were applied together with the plasticizer compositions through the nozzle (Fig. 1). The powders and plasticizer formulations are shown in Table 1. Additionally to the formulation of Table 1, for which the coating level (weight of the polymer powder divided by the weight of uncoated pellets) was 25%, formulations with a coating level of 20% were conducted. The anti-tacking agent talc was mixed with HPMCAS before the coating process whereas colloidal silicium dioxide was added as a top powder to the coated pellets after curing.