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Research paper

A comparative study between conventional pan coater and quasi-continuous small batch coater on the stability of tablets containing acetylsalicylic acid

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ABSTRACT

The Supercell coater was developed as an in-line small batch tablet coater which uses air-fluidization for tablet coating. Coating time is very much reduced, with improved heat and mass transfer. It was hypothesized that the quasi-continuous Supercell coating process was more suitable for the aqueous coating of tablets containing moisture-sensitive drugs. Acetylsalicylic acid (ASA) was used as the model drug in this study. The extent of ASA degradation in Supercell coating was compared against that of tablets coated using the conventional pan coater. Less than 0.3% of ASA was degraded at the end of the coating process using either coater. The extent of ASA degradation was found to be more pronounced during storage. The Supercell coated tablets exhibited comparable or smaller percentage of ASA degradation than the pan coated tablets at the end of a storage period of 6 months under accelerated stability conditions (40 °C/75% RH) and 3 years under ambient conditions (25 °C/50% RH). The extent and rate of ASA degradation during storage were dependent on the processing conditions employed during Supercell coating. Increase in temperature generally led to a reduction in ASA degradation, while increase in spray rate and coating level caused more degradation. Greater extent of ASA degradation was observed on the surface of pan coated tablets compared with Supercell coated tablets due to greater moisture contact and the slower and wetter coating process. Changes to the processing conditions also influenced the residual moisture content (0.55–2.86%) of the tablets. However, no direct correlation between the residual moisture content of the tablets after coating and the extent of ASA degradation during storage was found.

1. Introduction

Film coating of solid oral dosage forms is carried out to improve the esthetics, packaging efficiency, patient compliance, swallowability and/or stability of the product. Aqueous film coating has largely replaced organic-solvent based coating due to safety, economic and environmental reasons. However, it has also introduced concerns due to the exposure of tablet cores to elevated temperatures and the aqueous environment [1]. During aqueous film coating, water may penetrate into the tablet causing core expansion, changes to the structure of the film-core interface and greater risk of degradation of moisture-sensitive drugs.

The low evaporative capacity of water requires high drying efficiency of the aqueous film coating equipment. The Supercell coater is developed as a quasi-continuous article coater with improved drying efficiency and utilizes air-fluidization technique for coating. Small batches of tablets are coated, each within a minute or so, in sequential batches by a quasi-continuous mode. The Supercell coater allows moisture to be removed three-dimensionally by a constantly renewing air stream. In contrast, the pan coater uses a unidirectional stream of drying air to extract moisture from a tumbling tablet bed. However, the pan coater is currently the most commonly used equipment for tablet coating and is also the industrial gold-standard for tablet coating.

It was hypothesized that the Supercell coater was more suitable for the coating of tablets containing moisture-sensitive drugs compared with the pan coater due to its superior water removal efficiency. The water removal efficiency will affect the residual moisture of the coated tablets, which may in turn increase the risk of undesirable degradation of a moisture-sensitive drug [2]. Acetylsalicylic acid (ASA), also commonly known as aspirin, was used as the model drug in this study. ASA is hydrolyzed into acetic acid and salicylic acid (SA) when exposed to high humidity and elevated

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temperatures [3]. In tablet coating, these conditions are realized by the introduction of the aqueous coating dispersion and by drying with hot air. Several process parameters were therefore varied in Supercell coating to evaluate the influence of the Supercell processing conditions on the stability of ASA in tablets. In this study, the effects of spray rate, inlet temperature and coating level were studied in the Supercell coater and the extent of ASA degradation during tablet coating and storage was compared with that of tablets coated using the pan coater.

2. Materials and methods

2.1. Production and characterization of tablet cores for coating

A directly compressible formula consisting of agglomerated lactose (Tablettose 80, Meggle, Germany), microcrystalline cellulose (Avicel PH102 JP, Asahi Chemical Industry, Japan), pregelatinized starch (STA1500, Colorcon, USA), acetylsalicylic acid (ASA) (BP grade, Sintor, Romania) and stearic acid (Tristar NF, Hemo Asia, Malaysia) was prepared according to the composition shown in Table 1. All materials used were pre-sieved through a 500 μm aperture size sieve. They were mixed, without stearic acid, using a double cone blender (AR 400E, Erweka, Germany) at 40 rpm for 50 min. Stearic acid was then added and mixing was continued for another 10 min. The resultant powder blend was used to prepare round, biconvex, bevelled tablets with a diameter of 7.5 mm using a rotary tablet machine (Rimek II, Karnavati Engineering, India). The tablets were then employed as cores for coating. Table 2 shows the physical and drug content properties of the tablet cores.

2.2. Coating dispersion

Red Opadry II (Colorcon, USA), consisting of polyvinyl alcohol (PVA) as film forming polymer, was used as the coating material. It was prepared according to the manufacturer's recommendation as a 20%, w/w dispersion. The coating dispersion was stirred for at least 45 min prior to use and agitation was maintained throughout the coating run.

Table 1
Composition of tablet cores.

Ingredient	Function	%	Weight per tablet (mg)
Agglomerated lactose	Filler	54	108
Microcrystalline cellulose	Filler	20	40
Acetylsalicylic acid (ASA)	Active	20	40
Pregelatinized starch	Disintegrant	5	10
Stearic acid	Lubricant	1	2
Total		100	200

Table 2
Properties of tablet cores used for coating.

Parameter	Measuring instrument	Values
Diameter and thickness (mm)	Micrometer (293-761-30, Mitutoyo, Japan)	7.546 ± 0.004 4.208 ± 0.100
Weight (mg)	Weighing balance (B-220, Fisher Scientific, Switzerland)	206.4 ± 8.3
Moisture content (% w/w)	Weighing balance (AG-135, Mettler-Toledo, Germany)	2.00 ± 0.08
Friability (%)	Friabilator USP (F2, Sotax, Switzerland)	0.048 ± 0.003
ASA content/tablet (mg)	HPLC (LC2010A, Shimadzu, Japan)	41.00 ± 1.58

2.3. Coating conditions

Coating was carried out using the Supercell coater (GEA Pharma Systems, UK) and the pan coater (Lab Coat I, O'Hara Technologies, Canada) respectively. Table 3 shows the processing conditions employed during both Supercell and pan coating.

Supercell coating was carried out under different conditions in accordance with a 3^3 full factorial design (Table 4), with triplicates for each coating condition. Three process parameters, namely, spray rate, inlet temperature and coating level were each studied at three levels. These factors were likely to affect the wetting and drying conditions within the Supercell coater. As the pan coater had been relatively well studied, only one set of coating conditions was employed for the different coating levels. The coating conditions selected for pan coating corresponded to the typical process parameters commonly employed for the pan coater and yielded good results. Pan coating runs were also triplicated.

It should be noted that each coating level selected for the Supercell coating requires a dedicated coating run while the various coating levels studied for pan coating could be collected from the same coating run. In addition, fewer coating levels were studied for Supercell coating as a full factorial design was performed to map the entire design space.

2.4. Percentage loss on drying (% LOD)

At every sampling point, 10 tablets were removed from the pan coating process run and weighed. The tablets were then transferred to an oven (600, Memmert, Germany) maintained at 60 °C and dried for 7 days then weighed again. The weight loss of the tablets was attributed to the moisture present in the tablets. The % LOD was calculated from the formula below, and is a reflection of the amount of residual moisture present in the tablets at each stage of the tablet coating process.

$$\text{Loss on drying } (\%) = \frac{\text{Loss in weight}}{\text{Initial sample weight}} \text{x} 100\%$$

2.5. Storage stability of ASA

The coated ASA tablets were placed in air-tight glass bottles immediately after coating. In order to evaluate the influence of % LOD on ASA degradation, the tablets were not allowed to equilibrate to atmospheric conditions after coating. The tablets were stored under accelerated stability conditions of 40 °C and 75% relative humidity (RH) [4] for 6 months. An incubator oven (WTC Binder, Germany) was used to maintain the accelerated stability conditions. At suitable time intervals, the tablets were analyzed for SA content. In addition, the extent of ASA degradation of tablets coated to 3% coating level was also evaluated at the end of a period of 3 years storage at ambient conditions (25 °C/50% RH). The difference in the extent of ASA degradation between the surface and the

Table 3
Coating conditions of the Supercell and pan coaters.

Operating variables	Supercell coater	Pan coater
Inlet temperature (°C)	60, 90, 120	40–45 (Bed)
Spray rate (mL/min)	2, 5, 8	3.7
Coating level (% w/w)	1, 2, 3	0.4, 0.8, 1.2, 1.6, 2, 3
Atomizing pressure (bar)	3	2
Pattern air pressure	–	2
Batch size (kg)	0.075	1
Pan speed (rpm)	–	10
Plenum pressure (mmWC)	1600	–