Study of Coat Quality of Tablets Coated by an On-line Supercell Coater

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ABSTRACT

The aim of this study was to investigate the nature of Supercell coating, an on-line tablet coater that employed a unique pattern of airflow. Tablets coated at different spray rates (4, 6, 8, 10, and 12 mL/min) were analyzed to investigate the influence of different wetting conditions on the quality of coats formed. Scanning electron micrographs showed that tablet coats formed at a spray rate of 4 mL/min consisted of spray-dried droplets that did not coalesce. At a spray rate of 6 mL/min, surface roughness was found to be lower than at the other spray rates, and the coat appeared smoothest, whereby droplets seemed fused together. At higher spray rates, the droplets appeared as branching arms and scale-like structures. This was attributed to the spread of spray droplets by the processing air and mass transfer of wet coating materials between tablets. Further tests showed that coats formed at higher spray rates had higher drug yield, drug uniformity, color uniformity, and density. However, the variability in coat thickness was increased due to the mass transfer of coats and dissolution of tablet core surfaces by the coating material. Since coats of different characteristics can be formed in Supercell coating, the choice of wetting conditions would depend on the type of coat required and the coating materials used.

KEYWORDS: Tablet, coating, coat quality, on-line coating.

INTRODUCTION

Film coating of tablets is a common pharmaceutical batch operation used to improve the aesthetic qualities of the product,[1] mask unpleasant odor,[2] mask unpleasant taste,[3] protect drugs from moisture,[3] and improve product stability,[4] and is also used for targeted drug release.[5]

The pharmaceutical coating field started out with the use of organic solvents. Later, safety concerns, such as explosion risks and health hazards, caused organic solvents to be slowly replaced by water.[6] The major difficulty using water as a solvent lies with its high heat of vaporization, making coats difficult to dry and less stable.[7] Hence, coating equipment such as coating pans, perforated pans, and fluid bed processors caused tablet coat defects such as cratering, picking, twinning of tablets, and inaccurate deposition of coating material that necessitated slower spray rates and long processing times.[8]

Several advances in tablet coating, including hot-melt coating[9] and dry-coating techniques,[10,11] have been attempted to shorten coating time. Although these processes were innovative and effective, the specialized coating materials required made adoption for general use unlikely. Moreover, hot-melt coating was limited by the requirement of high temperatures and uncertain in vivo fate of lipidic coating material.[9] Since aqueous coating materials are still widely used in the pharmaceutical industry, improvements in the tablet-coating process is best targeted using the same coating media. The idea of on-line tablet coating at the end of the compaction process is also a highly attractive option especially for a decorative coat. Hence, Supercell coating,[12] an on-line tablet coater for aqueous coating was adopted in this study.

The Supercell coater consists of a coating chamber with a two-fluid nozzle located centrally at the bottom of the chamber. Tablets are suspended by low-pressure swirling airflow generated by directional ducts in the perforated base plate (rotonozzle) around the nozzle (Figure 1). The ducts around the spray nozzle direct air to converge at an imaginary center column where the spray is released from the nozzle, muffling the atomizing air from the 2-fluid nozzle shortly above the nozzle, creating a composite 3-fluid nozzle (Figure 2). Previous studies have shown that Supercell coating could rapidly form coated tablets of high drug uniformity,[13] high inter- and intratablet color uniformity,[14] and fully functional enteric coat.[15]

Because of the intense turbulence created at the spray zone by the converging airflow, it was imperative to study the coating process and nature of coats formed. Hence, the aim of this study was to investigate the effect of the Supercell coating on tablet coat characteristics, and its efficiency and accuracy in coat deposition. Spray rates were varied at standardized conditions to study the characteristics of coats formed at different wetting conditions or processing times.

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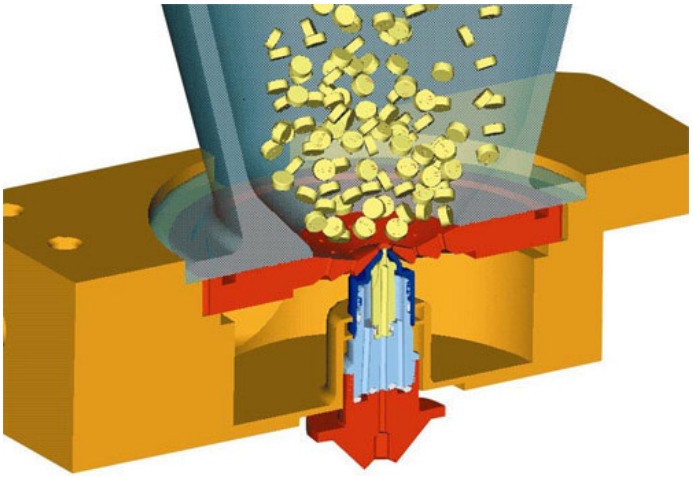

Figure 1. Three-dimensional simulated drawing of tablets suspended in the coating chamber of the Supercell coater during coating.

Materials and Methods

Characterization of core tablets

Circular normal convex tablets were used for coating. These tablets were made from direct compression using lactose, microcrystalline cellulose, starch, and polyvinyl pyrrolidone and were supplied by GEA, Aeromatic-Fielder, Eastleigh Hampshire, UK. Tablet weight was determined using a weighing balance (AJ50, Mettler-Toledo GmbH, Greifensee, Switzerland), thickness and diameter by a micrometer (Mitutoyo, Tokyo, Japan), hardness by a diametrical tablet hardness tester (HT1, Sotax, Basel, Switzerland), surface roughness by a scanning probe microscope (SPM-9500J, Shimadzu, Tokyo, Japan), and color by a tristimulus colorimeter (Chroma Meter CR-241, Minolta, Tokyo, Japan). At least 10 tablets were used for each test and results averaged. Tablet properties are reported in Table 1.

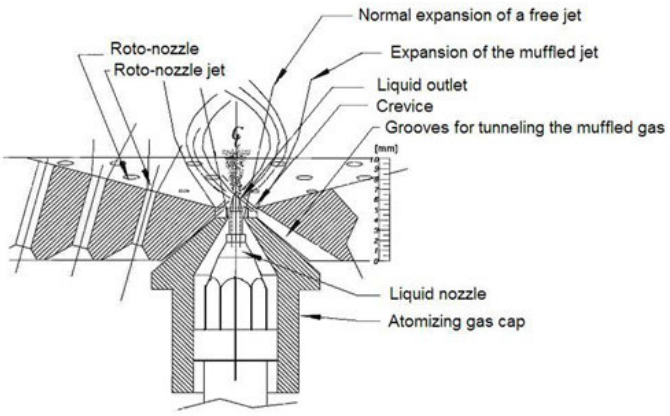

Figure 2. Cutaway diagram of the rotonozzle and liquid nozzle illustrating the muffling of the atomizing air.

Table 1. Properties of Tablets Used for Coating

Parameter	Values
Weight, mg	121 ± 1.30
Diameter, mm	6.04 ± 0.004
Thickness, mm	4.21 ± 0.021
Hardness, N	45.5 ± 6.73
Surface roughness, Ra, nm	206 ± 47.1
Color	L = 96.08 ± 0.58, a = –0.41 ± 0.38, b = 3.71 ± 0.26

L, a, b indicate CIELab units.

Coating of core tablets

Coating application was performed using the Supercell tablet coater (GEA, Aeromatic Fielder). The coating material was fed using the syringe assembly of the coater. All coater actions were controlled and monitored in real time by a connected computer system. Tablets were coated in small batches using spray rates of 4, 6, 8, 10, and 12 mL/min, at standardized plenum pressure of 1500 mm water column (WC), batch load of 50 g, atomizing pressure of 3 bars, and inlet air temperature of 100°C. For each spray rate, tablets were coated to 1% or 3% wt/wt coating level (theoretical % increase in dry weight after coating), which corresponded to coat thickness of ~10 μm or 30 μm respectively, as derived from general surface area calculations. Processing time for 1% wt/wt coating level ranged from 15 seconds to 45 seconds and for 3% wt/wt coating level, 46 seconds to 139 seconds. Replicated runs were performed for each experimental condition. Under these processing conditions, there were no signs of tablet twinning or adherence to coater chamber surface.

The coating formulation consisted of an aqueous suspension of 12% wt/wt hypromellose (Methocel-E3, Dow Chemicals, Midland, MI), 2% wt/wt polyethylene glycol (PEG-3000, BASF, Ludwigshafen, Germany), 1% wt/wt red pigment (Red 30, BASF, Ludwigshafen, Germany), and 1% wt/wt chlorpheniramine maleate (Merck, Whitehouse Station, NJ).

Characterization of coat

The color (dE) of tablet surfaces were determined with a tristimulus colorimeter (Chroma Meter CR-241, Minolta, Tokyo, Japan) using *CIELab* units, *L*, *a* and *b* as described by Chan et al (2000)[16] in which

$$dE = \sqrt{(L_o - L_c)^2 + (a_o - a_c)^2 + (b_o - b_c)^2} \quad (1)$$

where the subscripts "*o*" refer to uncoated tablets and "*c*" refers to coated tablets. Color measurements were taken

over a 1.2-mm diameter spot at the middle of both convex front and back surfaces of each tablet. dE indicated the color intensity of the coat, and relative standard deviation (RSD) of dE was used as a measure of coat uniformity whereby a lower value signified better coat uniformity. Thirty tablets were randomly selected from each batch for analysis.

Pellet surface roughness was determined using a scanning probe microscope (SPM-9500J, Shimadzu, Tokyo, Japan). The probe consisted of a micro-fabricated cantilever with silicon tip (Pointprobe sensor type NCHR-20, Nanoworld Innovative Technologies, Wetzlar-Blankenfeld, Germany). Surface scans over 25 × 25-μm areas were obtained using the dynamic mode and a Z range of 10 μm. Ten tablets were randomly selected from each batch for analysis. The degree of surface roughness was expressed using the arithmetic mean height, Ra, whereby a higher value indicated a rougher surface.

Tablet surfaces were carefully sliced using a sharp razor to produce fragments of the tablet with coat attached. The fragments were mounted on aluminum studs and sputter coated with gold for 4 minutes. The coat surfaces were observed using a scanning electron microscope (JSM-5200, Jeol, Tokyo, Japan) at a magnification of ×5000.

Tablets were diametrically cut into halves from the cylindrical edge of the tablet (not the face) to give a cross-sectional view of the coat. Tablet cross sections were then examined under a stereomicroscope (BX61, Olympus, Tokyo, Japan) using a ×10 objective lens, with the cut surface facing up. Images were captured with a digital color video camera (DXC-390P, Sony, Tokyo, Japan) linked to the image analysis software (Micro Image version 4.5, Media Cybernetics, Silver Spring, MD). Measurement of coat thickness was performed manually using standard software functions. Coat thicknesses at 50 equally spaced spots along each face were measured for both convex faces of each tablet. Coat thicknesses of tablets coated to 1% wt/wt coating level were not measured because the coats were too thin to be accurately determined. Five tablets from each batch were analyzed.

Eight tablets from each batch of tablets were individually immersed in 2 mL of methanol and sonicated for 15 minutes to dissolve the coats. The supernatants were filtered through a 0.22-μm membrane filter before analysis using high performance liquid chromatography (LC-2010, Shimadzu, Tokyo, Japan) at 25°C using a 4.6 × 200-mm Agilent C-18 column. The mobile phase was methanol and acetic acid solution (1% vol/vol) in the ratio of 9:1 at 1.0 mL/min. The retention time of the drug, chlorpheniramine maleate, was found to be 1.75 minutes and detection was by UV at 264 nm. Drug content of tablets coated to 1% wt/wt coating level was too low to be accurately detected and only tablets coated to 3% wt/wt coating level were analyzed. The drug yield is the determined amount of drug from the tablet coat as a percentage of the theoretical amount of drug sprayed. The RSD of drug yield was also determined and used as an indicator of the uniformity of coat deposited onto the tablets.

Statistical analysis

Statistical tests were performed using MINITAB Release 14, whereby independent-sample *t*-test was used to compare 2 sample sets and 1-way analysis of variance (ANOVA) with Tukey's test as the post hoc analysis was used to compare more than 2 sample sets. Sample means were significantly different if P was less than .05.

Results and Discussion

Surface characteristics of tablet coats

Surface morphology and surface roughness

At the lowest spray rate of 4 mL/min, the coat appeared to be covered by distinctly shaped structures (Figure 3a). As uncoated core tablet surfaces were devoid of these structures, these were presumed to be dried coat droplets that were deposited onto the core tablets. At this low spray rate, rapid drying caused even drying of spray droplets before or soon after impingement on the surface. Hence, the droplets were not well fused and spread out, giving rise to the rough surface (Figure 4). At the spray rate of 6 mL/min, coat quality was smoothest (Figure 4) indicating well-coalesced spray droplets (Figure 3b). The conditions were ideal for coat formation. At higher spray rates of 8, 10, or 12 mL/min, the magnified dried spray droplets took on unusual shapes consisting of branching arms and scale-like structures (Figure 3c, d, e), which made the coats rougher than those obtained at a spray rate 6 mL/min (Figure 4). Higher spray rates caused wetter conditions, which resulted in longer drying times. As such, the converging airflow at the spray zone caused distortions in the shapes of the impinged droplets, and tablet-tablet impacts spread out the adhering droplets before they dried completely on the surfaces. This phenomenon in Supercell coating associated with high drying efficiency and intense mixing allowed impinged spray droplets to "flatten out" during drying and enabled higher spray rates to be used. Also, mass transfer of coating material between tablets occurred in wet conditions at higher spray rates where wet coats were impacted onto one another, leading to flattened surfaces, as seen in Figure 3d. These effects occurred at spray rates higher than 6 mL/min, and similar surface roughness values were obtained (Figure 4). The impact and spreading of coat materials were able to smooth irregularities, even with the larger spray droplets formed when using higher spray rates.

The differences in the appearance of coats with different spray rates suggested that a different physical environment

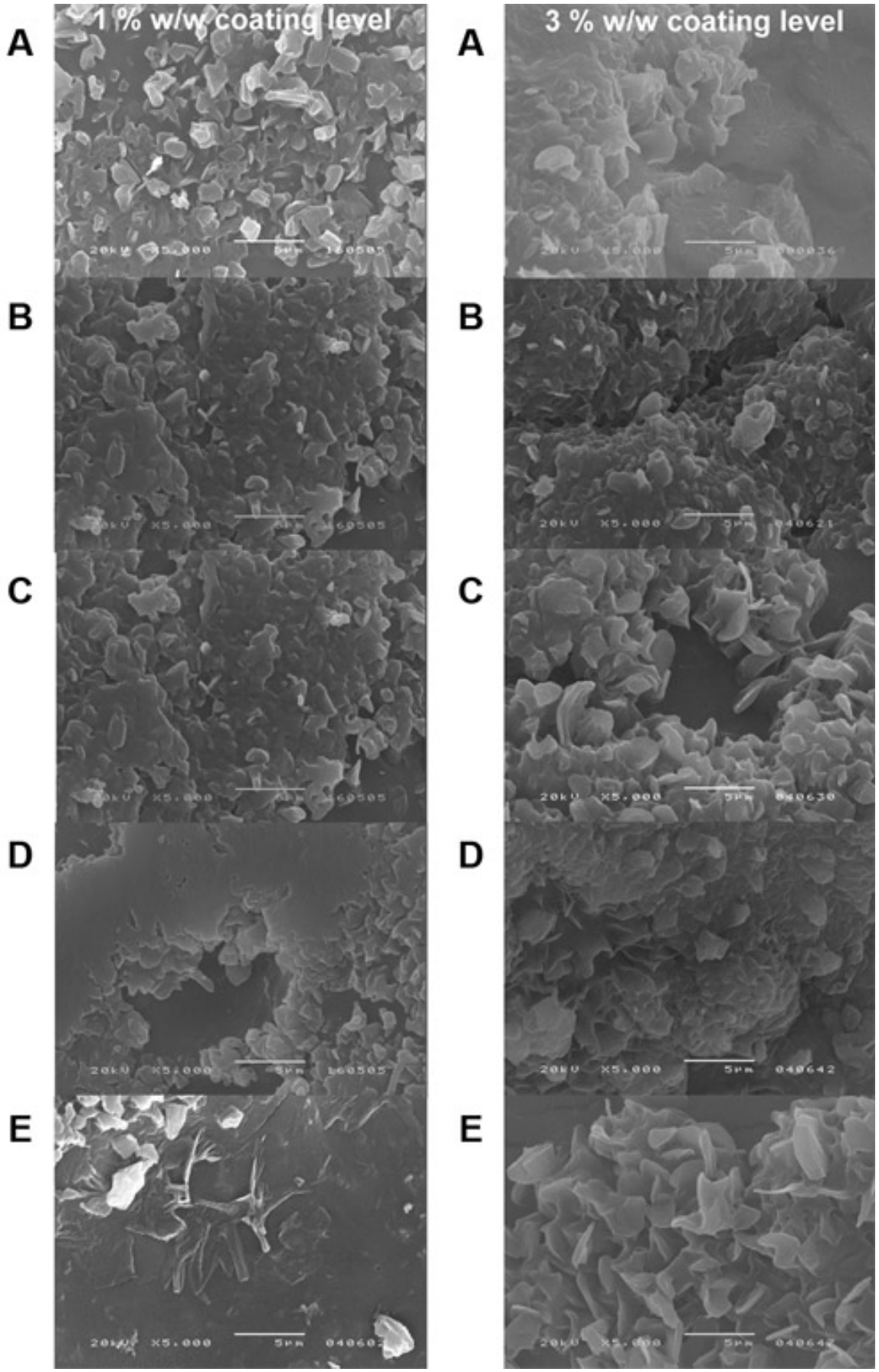

Figure 3. Scanning electron micrographs of tablet surfaces formed at spray rates of (A) 4, (B) 6, (C) 8, (D) 10, and (E) 12 mL/min to 1% wt/wt coating level and 3% wt/wt coating level (×5000).

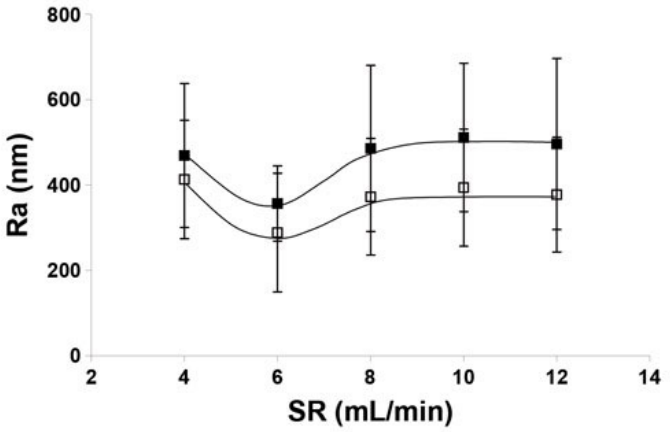

Figure 4. Influence of spray rate (SR) on surface roughness (Ra) of tablets at 1% wt/wt coating level (white squares) and 3% wt/wt coating level (black squares).

existed for different spray rates. For example, under the formulation and processing conditions studied, spray rate of 6 mL/min formed the smoothest coat, suggesting that coalescence was optimal and would be most suitable for producing a coat for functional purposes such as providing barrier properties. Coats formed in drier conditions would dissolve or disintegrate fastest as the film would not be as continuous because of the spray-drying effect. However, this is acceptable and suitable for a nonfunctional or decorative coat where fast release is desired. The coat made up of branching scale-like structures appeared to be more rigid and as such may have higher tensile strength. Mass transfer at higher spray rates may also encourage polishing of tablet coats making them glossier. However, these characteristics would differ with different polymeric materials and hence actual experiments are needed to relate each specific coating material to the properties of coat formed.

Color intensity and color uniformity

The color intensities of coats formed at the different spray rates were close, with dE values in a narrow band of 63 to 67 (Figure 5A). The trends obtained for the 2 coating levels were, however, dissimilar.

At 1% wt/wt coating level, color intensities decreased (Figure 5A) and color uniformity increased with the spray rate (Figure 5B). The greater uniformity was attributed to better mass transfer and spreading of spray droplets at higher spray rates, which allowed distribution of the coating material among the tablets. This distribution of coat materials caused overall thinner coats to form, making the coat less able to conceal the base white color of the core tablets, hence resulting in the lower color intensities. Despite having shorter coating times and hence fewer passes through the spray zone, tablets coated at higher spray rates had more uniform coats (Figure 5B), showing that spreading of tablet coats by mass transfer and the converging airflow were more important factors than the number of passes through the spray zone for color uniformity. Nevertheless, the RSD of dE was found to be less than 4%, which indicated that all the tablets were very uniform in color even at the low coating level of 1% wt/wt.

In contrast, at the 3% wt/wt coating level, color intensity was found to increase with spray rate (Figure 5A). This was due to a higher amount of light scattering for coats formed with lower spray rates, as they were observed to be dull compared with coats formed at higher spray rates that were glossier. As discussed earlier, the higher spray rates enabled a greater degree of surface coat remodeling, producing better-compacted surfaces. Cumulative loss of coating materials by attrition or spray drying at lower spray rates also resulted in the lower color intensity as substantiated by the lower drug yield for tablets coated at a spray rate of 4 mL/min (Figure 6). With a high coating level, variations in color were less pronounced as the color coat was already very uniform because of the thicker coat layer deposited (Figure 5B).

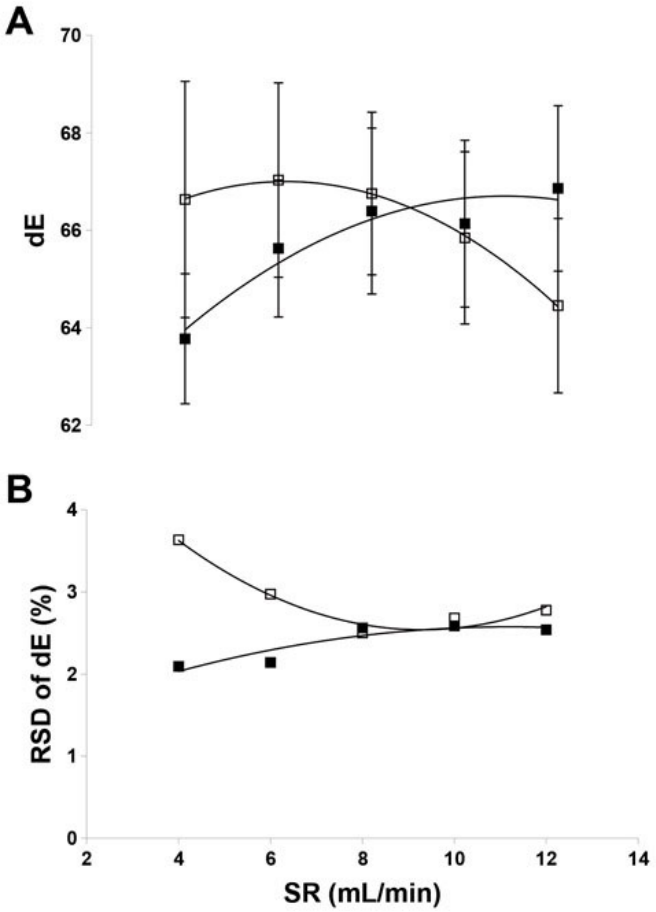

Figure 5. Influence of spray rate (SR) on (A) color intensity (dE) and (B) RSD of dE of tablets at 1% wt/wt coating level (white squares) and 3% wt/wt coating level (black squares).

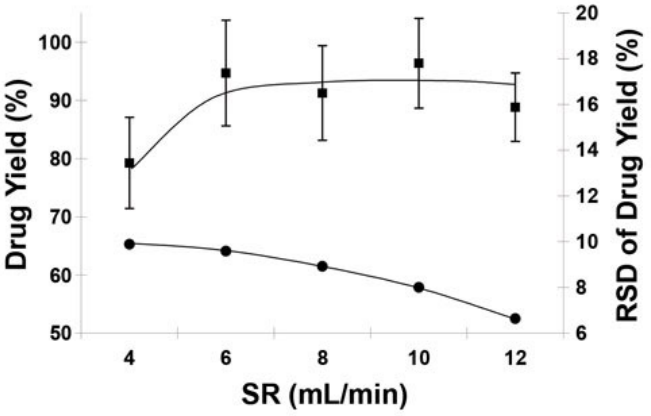

Figure 6. Influence of spray rate (SR) on drug yield (black squares) and RSD of drug yield (black circles) of tablets at 3% wt/wt coating level.

Internal characteristics of the coats

Drug yield and uniformity

The drug yield was used as a measure of the relative amount of coating material deposited onto each tablet. With the increase in spray rates, the drug yield ranged from 80% to 96%. Drug yield of tablets coated using the spray rate of 4 mL/min was significantly lower than the other spray rates, which have reached a plateau (Figure 6). The higher loss of coating materials at the spray rate of 4 mL/min was likely due to spray drying.

The RSD of drug yield between tablets ranged from 6.6% to 9.9% over all the spray rates studied showing that high coat uniformity could be achieved even at short tablet-coating times of 46 seconds to 139 seconds per tablet batch. The RSD of drug yield between tablets was found to decrease with increasing spray rates. The more uniform drug yield at higher spray rates could be again attributed to the efficient spreading environment whereby deposited coats that were wetter could undergo mass transfer when sliding pass one another and hence enhance the redistribution of the coating material among the tablets.

Coat thickness and uniformity of coat thickness

There was a decreasing trend observed between coat thickness and increase in spray rate (Figure 7). From the determination of drug contents (Figure 6), it could be concluded that the amount of deposited coating material was similar for all batches coated at different spray rates except when a low spray rate of 4 mL/min was used. Knowing the amount of coat deposited, the thickness of coats could provide some inferences about the densities of coats formed. The increased coat thickness at lower spray rates despite the lower amount of coat deposited indicated that coats present were less dense. This could be attributed to the rapid drying of the spray droplets, causing semi-dried spray droplets to be fused to form the tablet coat, with greater entrapment of air in the coat. As a result, dull-looking coats were formed. At higher spray rates, the wetter conditions allowed better spreading of spray droplets on impact onto tablet surfaces. The converging airflow allowed some attritive tablet-tablet friction and mass transfer of coating materials between tablets. Collectively, the wetter coating environment and rapid drying contributed to denser and thinner coats. This resulted in the glossier tablet coats as observed visually.

In contrast to uniformity of drug yield between tablets (Figure 6), the RSD of coat thickness increased with spray rate showing that there were higher variations in coat thickness at higher spray rates. This was likely caused by the wetter coating conditions that allowed some involvement of the tablet surfaces in mass transfer. Coating materials can also dissolve tablet core surfaces at wetter regions, thus making the baseline of coats more undulating, resulting in a higher RSD of coat thickness. Under dry conditions, coats built up and dried in more uniform and well-defined layers giving rise to lower RSD for coat thickness.

Mechanisms of coat impingement in Supercell coating and possible applications

From the experimental results, small differences in the mechanisms of coating could be observed for Supercell coating as coating and coat formation depended on the spray rates used. These are diagrammatically represented in Figure 8.

By changing the spray rates, different wetting conditions can be produced. At a low spray rate, the very high drying rate present enabled deposited droplets to rapidly dry and set, producing coat deposits with distinct shapes (Figure 8A). The rapid drying also resulted in greater loss of coating material by the spray-drying effect. In addition, entrapment of air in the coat led to greater coat thickness.

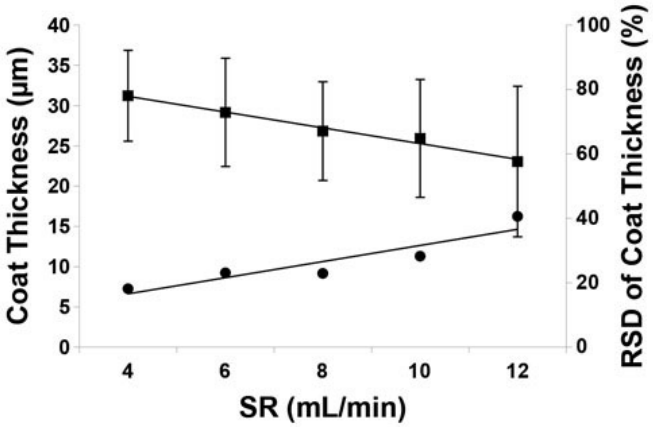

Figure 7. Influence of spray rate (SR) on the coat thickness (black squares) and RSD of coat thickness (black circles) of tablets at 3% wt/wt coating level.

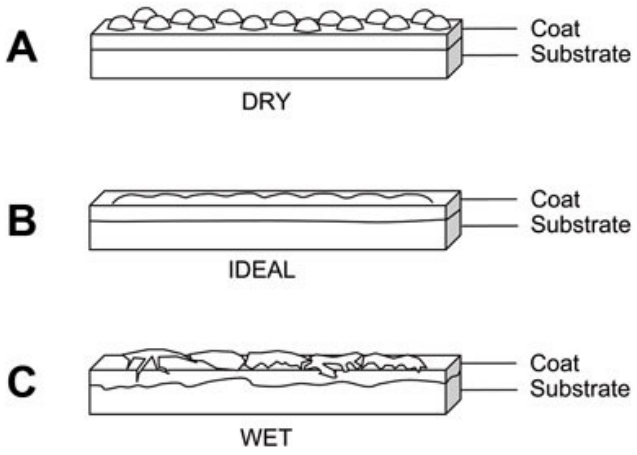

Figure 8. Diagrammatic representations of droplet impingement onto tablet surfaces in Supercell coating at (A) dry, (B) ideal, and (C) wet conditions.

An optimal or ideal wetting condition was identified at spray rate of 6 mL/min. This ideal spray rate enabled conditions ideal for coalescence of spray droplets and formed the smoothest coat surface (Figure 8B). This condition would be best for functional coating under the formulation and processing conditions used.

At higher spray rates, the wet conditions were favorable to mass transfer and less conducive for rapid drying, leading to transfer of wet impinged coating material between tablets. The wetter coats formed viscous intermediates before drying and the high shear forces imparted by the converging airflow led to branching arms and scale-like structures (Figure 8C). On the other hand, these effects contributed to the distribution of coat material among the tablets resulting in greater uniformity of drug yield and color between tablets. Coat thickness was more variable due to mass transfer of coat materials between tablets as well as difficulties to demarcate the baseline core surfaces. This would not favor functional coatings but may increase the efficiency in decorative coating by allowing a high spray rate and short coating times to be used. The mass transfer between tablets also formed tablet coats that appeared glossier. This could be attributed to the slippages of the wetted tablets during coating.

Conclusion

By controlling the spray application rate in the Supercell coater, coats of different qualities could be produced. High mass transfer of coat material at wetter conditions had beneficial as well as detrimental effects. Overall, the Supercell coater was found to be versatile, capable of quasi-continuous tablet coating in small batches (~50 g) at very short processing times (46 seconds to 139 seconds), yet producing high coat yields (80% to 96%) and uniform coat yields (RSD of 6.6% to 9.9%) over the large range of wetting conditions.

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