The Influence of Coating Parameters on The Transparency of Semipermeable Membrane Coating of Push-Pull Osmotic Pump Tablets

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Introduction

Cellulose acetate (CA) is commonly used as a semipermeable membrane coating on controlled release osmotic pump tablets. The transparency of the semipermeable membrane coating of CA on the push-pull osmotic pump tablets is very important for identification of the drug layer and the push layer during laser drilling, so that the drug release orifice is drilled on the correct side of tablets.

During the process of semipermeable film coating, the film may become opaque if the coating parameters are not used optimized. The purpose of this study was to evaluate the effect of different coating parameters on the transparency of a semipermeable membrane coating (Opadry® CA) applied to push-pull osmotic pump tablets.[1,2]

Methods

Design of experiment (DOE) was used to carry out the random customized experimental design with 12 experiments, including one central point. Spray gun to bed distance (5 cm), atomizing air pressure (1.2 bar), pattern air pressure (1 bar) and pan speed (20 rpm) were kept constant in the study. Variables included: inlet temperature (30-60℃), inlet air volume (50-70 m^3/h), liquid spray rate (10-30 g/min), coating weight gain (3-5%) and environmental humidity (49-80%). The product bed temperatures in different experiments were collected for further analysis (Table 1).

Push-pull osmotic pump tablets were replaced by placebo tablets coated with Opadry brown and further coated with Opadry CA according to DOE experiment conditions (Fig. 1).

The brown placebo tablets without Opadry CA coating were chosen as reference for color difference analysis. Coated tablets from different experiments were measured by Datacolor 600 spectrophotometer to get delta E (DE) values to quantify the transparency of semipermeable membrane.

Data was analyzed using DOE software to identify the key parameters influencing film transparency. The tablets from different experiments were cut in half and cross sections of the film coat were examined using scanning electronic microscopy (SEM) to observe any structural differences of the film following different coating conditions.

Results

The results showed that liquid spray rate, inlet temperature and their interaction significantly influenced the transparency of the semipermeable membrane. Product bed temperature and its interaction with inlet air humidity were also significant factors to film transparency (Figure 2). SEM pictures showed that the film structure of Opadry CA was different when coating parameters were changed (Figure 3).

Table 1. DoE of Coating Parameter and Response Results

Run	Inlet Temp. (°C)	Inlet Air Flow (m^3/h)	Spray Rate (g/min)	Relative Humidity (%)	Weight Gain (%)	DE Value (n=20) (X±SD)	Bed Temp. (°C)
1	30	50	10	49	5	0.50 ± 0.13	27
2	30	50	30	68	3	36.91 ± 5.41	12
3	60	50	10	64	3	6.42 ± 1.56	44
4	30	70	30	57	3	28.33 ± 10.53	12
5	60	70	10	65	5	13.97 ± 1.03	46
6	60	70	30	61	5	1.10 ± 0.64	31
7	45	60	20	57	4	1.37 ± 0.17	22
8	30	50	10	80	5	1.51 ± 0.82	22
9	60	50	30	79	3	1.63 ± 1.19	25
10	30	70	10	79	3	1.33 ± 0.47	23
11	30	70	30	80	5	39.54 ± 1.41	13
12	60	70	10	80	3	3.49 ± 0.50	45

Figure1: Appearance of Placebo Tablets and Semipermeable Membrane Coated Tablets

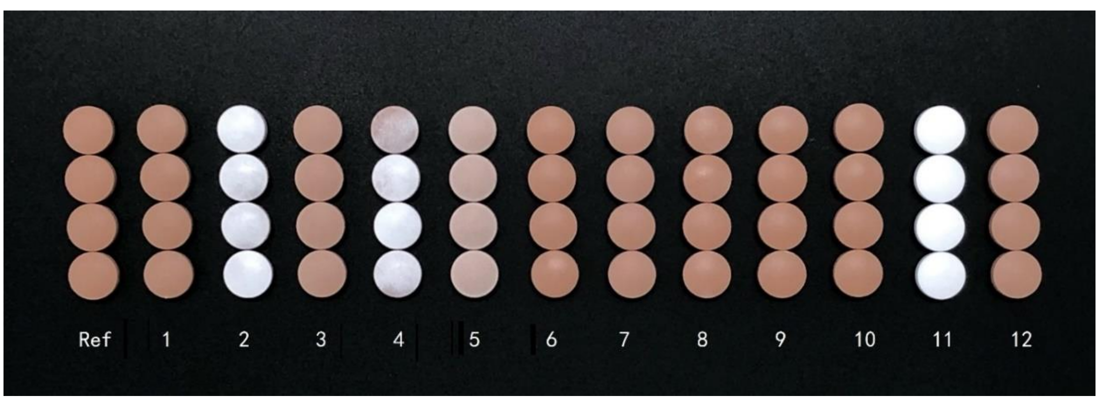


Figure 2: Influence of Coating Parameters on DE Value

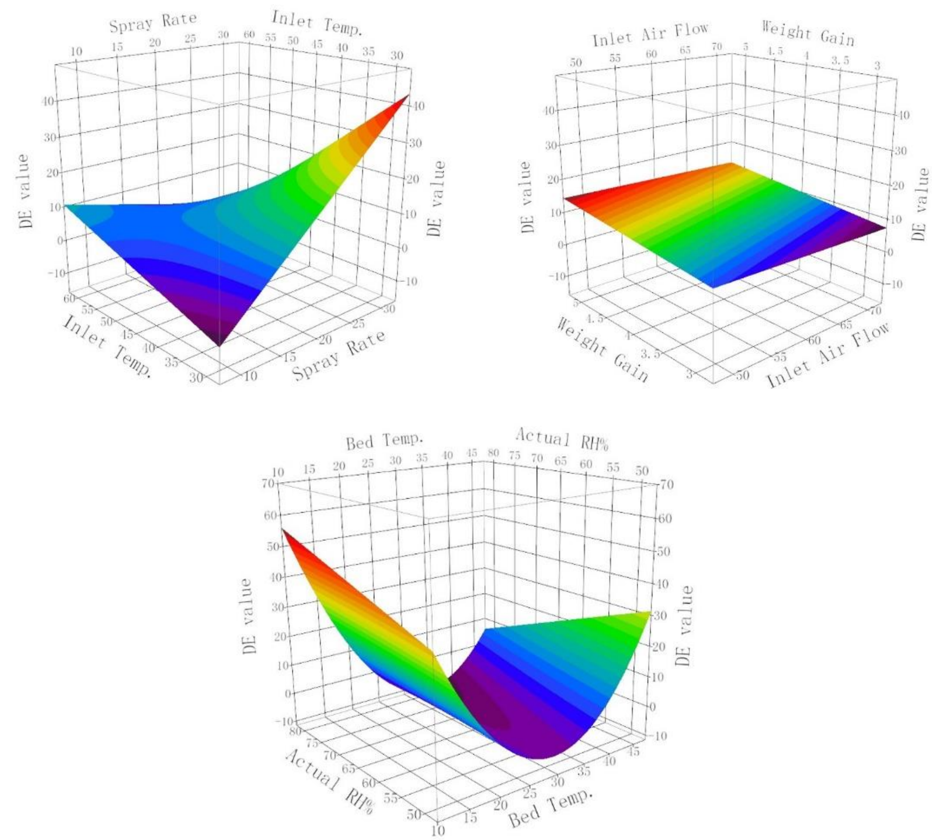
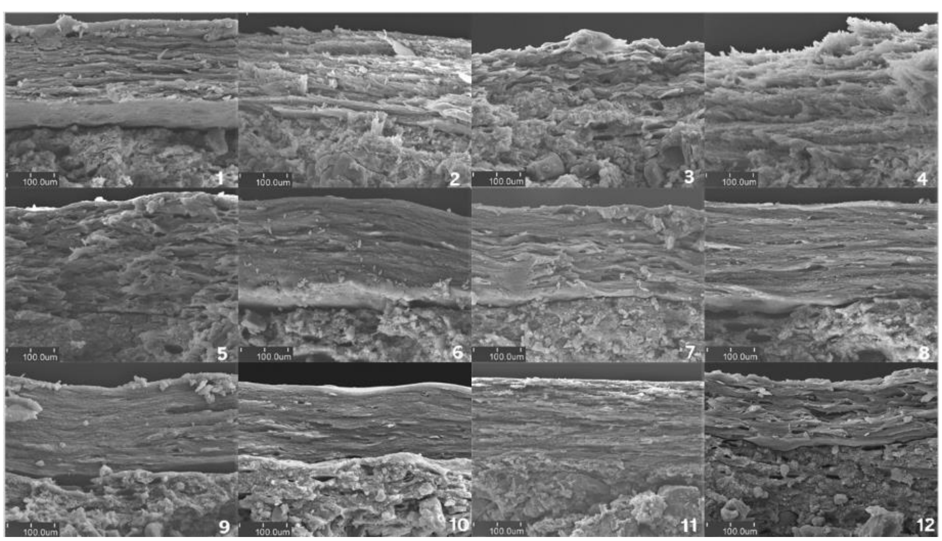


Figure 3: SEM of Cross Section of Tablets from Twelve Trials



Conclusions

Two reasons could be responsible for membrane transparency of the semipermeable membrane coating of push-pull osmotic pump tablets.

First, spray drying occurring in coating process; a small amount of the droplets is dried as fine powder before being deposited on the tablet surface and distributed on the coating pan and the surface of the core tablets. Then the powder adhered to and solidified in the film, unable to merge with other liquid droplets to form a transparent film resulting in film transparency. As a result, subsequent droplets cannot merge with the previous and the film has a loose and porous texture. Light scatters as it passed through the porous film, affecting transparency. Based on the general understanding of the coating process, the occurrence of spray drying is usually related to coating conditions such as low spray velocity, high inlet air temperature, high atomizing air pressure, long distance from the gun to tablet bed, and high product bed temperature.

Secondly, film whitening (loss of transparency) is related to the solvent. Evaporation of the acetone and water solvent mix can remove a lot of heat in the drying process, especially at high spray rate. This lowers the bed temperature, sometimes even below dew point. Additionally, the dew point of the environment is relatively high in high humidity environment. When the bed temperature is close to dew point, water may condensate on the surface of the core. As acetone has a lower boiling point (56°C) than water, the evaporation efficiency of water and acetone may vary under such conditions. The different evaporation rates of the two solvents may eventually lead to a change in the solvent ratio in droplets on the surface of the core and failure to meet the solubility requirements of the polymers, resulting in flocculation and film whitening. It could be more serious under high humidity condition. Based on this view, lower solid content or lower water content in solvent mix may be beneficial to improve the transparency of semipermeable membrane. In this case, altering the coating parameters such as decreasing the spraying speed, increasing the inlet air temperature, increasing coating temperature or decreasing the coating environment humidity can also be useful to solve film whitening problems.

References

1. Martin L, et al. Investigation of Critical Process Parameters for Coating Push-Pull Osmotic Pump Tablets with Opadry CA. AAPS Annual Meeting and Exposition, 2012.
2. Martin L, et al. Investigation of Cellulose Acetate Polymer Viscosity and Coating Solution Concentration on Performance of Push-Pull Osmotic Pump (PPOP) Tablets. CRS 39th Annual Meeting and Exposition of Controlled Release Society, 2012.