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Aqueous-based Film coating of Tablets: Study the Effect of Critical Process Parameters

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Abstract : The aim of the present work was to study the effect of various process parameters on an aqueous-based film coating process of tablets performed in a side-vented perforated pan-coating apparatus. Results of preliminary trials indicate that spray rate, inlet air temperature, percentage solid content, atomizing air pressure and speed of rotation affected characteristics of coating. A 3^3 full factorial design was employed to study the effect of independent variables; spray rate (X_1), inlet air temperature (X_2) and rotating speed of pan (X_3) on dependent variables: coating uniformity, coating process efficiency, surface roughness and percentage loss on drying. The best batch exhibited spray rate of coating solution 8 gm/min, inlet air temperature 55°C and rotating speed of pan 12 rpm. The surface characteristics of the aqueous-based film-coated tablet were studied under a scanning electron microscope.

Keywords: Aqueous film coating, 3^3 full factorial design, process parameters.

Introduction

Aqueous film coating is applied as a thin polymeric film to the surface of a tablet. Film coating can protect the tablet from light, temperature and moisture, mask undesirable taste or odor, improve the appearance, provide tablet identity, facilitate swallowing and control or modify the release of the drug (1-2). Aqueous coating of oral solid dosage forms has rapidly replaced solvent-based coatings for safety, environmental and economic reasons. However, since tablets may contain moisture-sensitive drugs or excipients, the use of water raises concerns about the physical and chemical stability of the coated tablets (3). Film-coating of tablets is a multivariate process, with many different factors, such as coating equipment, process conditions, composition of the core tablet, shape of tablets, coating liquid etc., which affect the pharmaceutical quality of the final product. The side-vented, perforated pan coater is the most commonly used coating device of tablets. So process parameters are highly affecting the quality of final product. High quality aqueous film coating must be smooth, uniform and adhere satisfactorily to the tablet surface and ensure chemical stability of a drug(4). Atomizing air pressure is also affecting the surface property of coated tablets (5-6). The spray rate is an important parameter which affects the moisture content of the formed film and subsequently, the quality and uniformity of the film (7-9). The inlet air temperature affects the drying efficiency (i.e. water evaporation) of the coating pan and the uniformity of coatings. In the aqueous film coating process, tablets are exposed to wide temperature range and humidity variations that may promote undesired water penetration into the tablet core during coating or storage. Penetrated water can cause changes in the structure of the film core interface, core expansion and increase the risk of degradation of a moisture-labile drug. Wide variations in the amount of coating received by individual tablets within a batch may also have some effect on the dissolution rate of drug even from immediate-release tablets (9). It also affects the amount of moisture content of the core tablets. And moisture content increase the degradation of drugs (9-10). Rotating speed of pan affect the surface property and coating uniformity (11-13). Percentage solid content generally affects the tablet surface and coating efficiency (14).

The aim of the present work was to study the effect of various process parameters on an aqueous-based film coating process of tablets performed in a side-vented perforated pan-coating apparatus.

Experimental

Materials

Opadry II 31 (G 51557) was obtained as gift sample from Colorcon (Mumbai, India). The core tablet composed of colloidal silicon dioxide was obtained as gift sample from Cabot Sanmar Ltd. Dibasic calcium phosphate dihydrate was procured from Canbera Chemical. Hydroxyl Propyl Methyl Cellulose-K4M wase procured from Dow Chemicals. All other ingredients were analytical grade.

Methods

Preparation of coating solution

Three hundred milligrams of accurately weighed Opadry II 31 G 51557 was added in 100 mL of distilled water to obtained 3 % w/v of solution and stirring was carried out using a propeller stirrer (Remi, Mumbai, India) at 1000 rpm for 45 min.

Coating of tablets

The tablets were film-coated using a side-vented, perforated neocota pan coating machine (Neo Machine Mfg. Co. Pvt. Ltd. Calcutta, India). Inlet air spray-rate and exhaust air spray-rate were kept constant at 150 f^3/m and 200 f^3/m, respectively. First fixed quantity (2 kg) tablets were kept in the pan which was pre adjusted at 50° C temperature for 10 min. Then actual weight of tablet was determined. Then, various parameters like spray rate, inlet air temperature and rotating speed of pan were adjusted and studied with different levels (**Table 1**). After finishing of the coating tablets were kept in the pan at 60° C and 2 rpm for curing. Then tablets were removed from the pan and evaluated.

Coating uniformity

Coating uniformity was measured as the variation in weight gain of coated tablets within a coating trial. The reported standard deviation (SD) was calculated as

$SD = \{ \ [(wt_{ai} - w_{tb}) - x]^2/(n-1)\}^{1/2}$ **[1]**

where wt_{ai} and wt_{bi} are the weights of tablet i after and before coating, respectively, corrected for moisture content by drying to final weight; n is the number of tablets measured; and x is the average weight gain of the n measured tablets from the coating trial.

Coating process efficiency

Coating process efficiency (CPE) was measured as the actual percent weight gain relative to the theoretical percent; a theoretical 100% transfer of coating to the tablets would mean no lost coating. Coating process efficiency was determined by the following equation.

$CPE = (\%wg_a / \%wg_t) \times 100\%$ **[2]**

where wg_t is the theoretical percent weight gain, which in this experiment was 3% in every coating trial, and wg_a is the actual percent weight gain, which is computed as

Processing $\% \ wg_a = [(wt_a - wt_b)wt_b] \times 100\%$ **[3]**

Where wt_b and wt_a are the total batch weights before and after coating, respectively.

Percentage loss on drying

Percentage loss on drying (% LOD) is the moisture content of the coated tablet expressed as percent weight. The tablets were weighed, dried at 60 °C for 24 h, and then reweighed. All uncoated tablet cores used in this study had an initial moisture content of 3% and %LOD was determined by the following equation.

$\%LOD = [(wt_b - wt_a) / wt_b] \times 100\%$ **[4]**

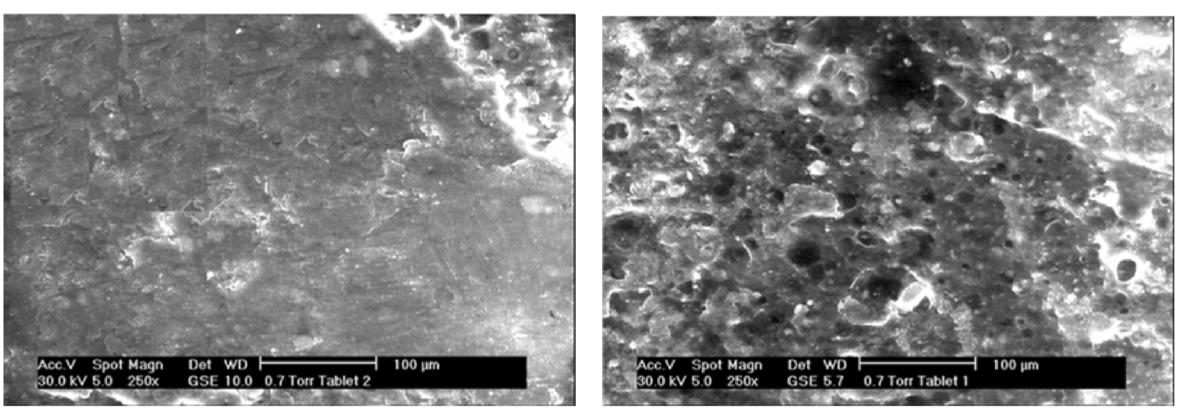
where wt_b and wt_a are the coated tablet weights before and after drying, respectively.

Scanning electron microscopy

Scanning electron photomicrograph of surface of coated-tablets was taken. A coated-tablet was taken on glass stub. Afterwards, the stub containing the tablet was placed in the scanning electron microscope (JSM 5610 LV SEM, JEOL, Datum Ltd, Tokyo, Japan) chamber. A scanning electron photomicrograph was taken at the acceleration voltage of 20 KV, chamber pressure of 0.6 mm Hg, at different magnification. The photomicrographs of coated tablets with different conditions are depicted in Fig **1**.

Surface roughness

Surface roughness was checked visually and was graded from 1 to 10 as better to best.



A B

Figure 1: SEM micrographs of aqueous-based film-coated tablet surface.

Table 1: 3^3 full factorial design layout

Batch No.	Variable level in coded form			Standard deviation (mg)	Coating process efficiency (%)	Surface roughness	Percentage LOD
	X_1	**X_2**	**X_3**				
1	-1	-1	-1	3.2	95.21	8.5	1.58
2	-1	-1	0	2.5	96.46	8.6	1.8
3	-1	-1	1	1.2	94.97	8.6	2.01
4	-1	0	-1	3.3	87.33	6.7	1.36
5	-1	0	0	2.4	86.56	6.8	1.51
6	-1	0	1	1.1	86.78	6.7	1.64
7	-1	1	-1	3.3	79.32	5.1	0.95
8	-1	1	0	2.6	80.45	5.1	0.99
9	-1	1	1	1.3	78.87	5	1.12
10	0	-1	-1	3.4	95.23	7.6	3.5
11	0	-1	0	2.3	94.46	7.6	3.65
12	0	-1	1	1.2	95.11	7.7	3.88
13	0	0	-1	3.3	91.23	7.6	1.6
14	0	0	0	2.4	91.56	7.6	1.79
15	0	0	1	1.1	92.13	7.5	2.02
16	0	1	-1	3.2	85.22	6.5	0.98
17	0	1	0	2.6	84.98	6.5	1.2
18	0	1	1	1.6	84.79	6.6	1.32
19	1	-1	-1	3.4	91.12	7.7	4.73
20	1	-1	0	2.6	90.24	7.6	4.82
21	1	-1	1	1.5	90.15	7.8	4.9
22	1	0	-1	3.3	95.23	8.8	1.9
23	1	0	0	2.5	95.64	8.8	1.92
24	1	0	1	1.4	96.18	8.7	1.92
25	1	1	-1	3.4	91.23	7.5	1.5
26	1	1	0	2.6	91.65	7.6	1.46
27	1	1	1	1.4	92.08	7.6	1.59

Translation of coded levels in actual units

Variables level	**Low (-1)**	**Medium(0)**	**High (1)**
Spray rate (gm/min)X_1	8	12	16
Temperature(°C) X_2	55	65	75
Pan speed (rpm) X_3	8	10	12

*All the batches were performed at constant 2 bar atomizing air pressure and 12 % solid content

Table 2. Summary of results of regression analysis

Coefficient	b0	b1	b2	b3	b12	b23	b31	b123	b11	b22	b33	R2
Coating Uniformity	2.40	0.066	0.038	-1	-0.033	0.041	0.033	-0.01	0.044	0.044	-0.18	0.9905
Coating Process Efficiency	91.84	2.642	-4.131	-0.003	4.28	0.108	0.172	0.253	-0.552	-1.874	-0.101	0.9466
Surface Roughness	7.59	0.611	-0.788	0.011	0.841	-0.016	0.0083	0.025	0.155	-0.511	-0.011	0.9318
% LOD	1.81	0.654	-1.097	0.127	-0.630	-0.031	-0.05	0.022	-0.121	0.5922	0.012	0.9460

Factorial design

A statistical model incorporating interactive and polynomial terms was used to evaluate the responses:

$Y=b_0+b_1X_1+b_2X_2+b_3X_3+ b_{12}X_1X_2+ b_{13}X_1X_3+ b_{23}X_2X_3+ b_{123} X_1X_2X_3+ b_{11}X^2{}_1+ b_{22}X^2{}_2+ b_{33}X^2{}_3$ **[5]**

where, Y is the dependent variable, b_0 is the arithmetic mean response of the 9 runs, and b_i is the estimated coefficient for the factor X_i. The main effects (X_1, X_2 and X_3) represent the average result of changing one factor at a time from its low to high value. The interaction terms (X_1X_2) (X_1X_3), (X_2X_3) and ($X_1X_2X_3$) show how the response changes when two or more factors are simultaneously changed. The polynomial terms ($X^2{}_1$), ($X^2{}_2$) and ($X^2{}_3$) are included to investigate nonlinearity. On the basis of the preliminary trials a 3^3 full factorial design was employed to study the effect of independent variables; spray rate (X_1), inlet air temperature (X_2) and rotating speed of pan (X_3) on dependent variables: coating uniformity, coating process efficiency, surface roughness and percentage loss on drying.

Results and Discussions

In this study an aqueous-based film coating process of tablets were performed in a side-vented perforated pan-coating apparatus. In the preliminary study, five process or apparatus parameters (spray rate, atomizing air pressure, inlet air temperature, rotating speed of pan and percentage solid content) of potential importance with respect to the final film quality were evaluated. The preliminary results revealed that spray rate, inlet air temperature and rotating speed of pan had a major effect on tablet coating performances. On the basis of the preliminary trials a 3^3 full factorial design was employed to study the effect of independent variables [spray rate (X_1), inlet air temperature (X_2) and rotating speed of pan (X_3)] on dependent variables coating uniformity, coating process efficiency, surface roughness and percentage loss on drying.

The results depicted in Table **1** are clearly indicate that all the dependent variables are strongly dependent on the selected independent variables as they show a wide variation among the twenty seven batches (1 to 27). The fitted equations (full models) relating the responses (i.e. coating uniformity, coating process efficiency, surface roughness and %LOD) to the transformed factor are shown in Table **2**. The polynomial equations can be used to draw conclusions after considering the magnitude of coefficient and the mathematical sign it carries (i.e. positive or negative). The high values of correlation coefficient **(Table 2)** for the dependent variables indicate a good fit. The equations may be used to obtain estimates of the response since small error of variance was noticed in the replicates.

Factorial equation for coating uniformity

The standard deviation (SD) decreases the coating uniformity increases and SD increases the coating uniformity decreases. The coating uniformity for coated tablets varied from 1.1 to 3.4 and showed good correlation coefficient (R^2 = 0.9905). Results of the equation indicate that the effect of X_3 (rotating speed of pan) is more significant than X_1 (spray rate). Moreover, rotating speed of pan had a negative effect on coating uniformity (i.e. rotating speed of pan increased the standard deviation decreased). This finding might be due to tablets spend equal time in fluid spray.

The linear model generated for coating uniformity was found to be significant with an *F*-value of 25.64 ($p<0.0001$) and R^2 value of 0.9905:

Coating uniformity = $2.4074 + 0.0666X_1 + 0.0388X_2 - 1X_3 - 0.0333X_1X_2 + 0.0416X_2X_3 + 0.0333X_1X_3 –$

$0.0125X_1X_2X_3 + 0.0444X^2_1 + 0.0444X^2_2 - 0.1888X^2_3$ [6]

Factorial equation for coating process efficiency

Coating process efficiency (CPE) is a measure of the actual amount of coating applied to the tablets relative to the theoretical quantity of coating applied. It can therefore be another indicator of over wetting or over drying. When over wetting occurs, material can potentially be transferred from the surface of the tablets to the walls of the coating pan, thus reducing CPE. Conversely, when over drying occurs, coating solution can dry prematurely in the air stream (commonly called spray drying) and be lost into the exhaust air stream instead of being transferred to the tablets (9,15). The Coating process efficiency for coated tablets varied from 79.32 to 96.18 and showed good correlation coefficient ($R^2 = 0.9466$). Results of the equation indicate that the effect of X_2 (inlet air temperature) is more significant than X_1 (spray rate). Moreover, inlet air temperature had a negative effect on coating process efficiency (i.e. inlet air temperature increased, the coating process efficiency decreased). This might be due to at high temperature water evaporation is very fast and particles get dried before reaching to the tablets.

The linear model generated for coating process efficiency was found to be significant with an *F*-value of 42.52 ($p<0.0001$) and R^2 value of 0.9466:

Coating process efficiency = $91.8403 + 2.6427X_1 - 4.1311X_2 - 0.0033X_3 + 4.2875X_1X_2 + 0.1083X_2X_3 + 0.1725X_1X_3 + 0.2537X_1X_2X_3 - 0.5527X^2_1 - 1.8744X^2_2 - 0.1011X^2_3$ [7]

Factorial equation for surface roughness

Surface roughness is an important parameter in pharmaceutical tablet dosage forms. It is well known that roughening the surface of solids could change many aspects of the surfaces including adhesion and bond formation (9). Figure **1** shows the surface roughness depending in the process variables. The surface roughness for coated tablets varied from 5.0 to 8.8 and showed good correlation coefficient ($R^2 = 0.9319$). Results of the equation indicate that the effect of X_1 (spray rate) and X_2 (inlet air temperature) is equal. Moreover, inlet air temperature had a negative effect on surface roughness (i.e. inlet air temperature increased, the surface roughness decreased).

The linear model generated for surface roughness was found to be significant with an *F*-value of 36.45 ($p<0.0001$) and R^2 value of 0.9319:

Surface roughness = $7.5925 + 0.6111X_1 - 0.7888X_2 + 0.0111X_3 + 0.8416X_1X_2 - 0.01667X_2X_3 + 0.0083X_1X_3 - 0.025X_1X_2X_3 + 0.1555X^2_1 - 0.5111X^2_2 - 0.0111X^2_3$ [8]

Factorial equation for percentage LOD

Percentage LOD is a measure of the moisture content of the tablet. It can be extremely important to both tablet core and drug stability. Percentage LOD is a process-driven property that expresses over wetting or over drying of the core during coating. The ideal circumstance is to have no net gain or loss of core moisture content due to coating.

The percentage LOD for coated tablets varied from 0.95 to 4.82 and showed good correlation coefficient ($R^2 = 0.9460$). Results of the equation indicate that the effect of X_2 (inlet air temperature) is more significant than X_1 (spray rate). Moreover, inlet air temperature had a negative effect on coating process efficiency (i.e. inlet air temperature increased, the percentage LOD decreased).

The linear model generated for surface roughness was found to be significant with an *F*-value of 67.12 ($p<0.0001$) and R^2 value of 0.9460:

Percentage LOD = $1.8125 + 0.6544X_1 - 1.0977X_2 + 0.1277X_3 - 0.6308X_1X_2 - 0.0316X_2X_3 - 0.05X_1X_3 + 0.0225X_1X_2X_3 - 0.1211X^2_1 + 0.5922X^2_2 + 0.0122X^2_3$ [9]

Conclusion

In this study an aqueous-based film coating process of tablets were performed in a side-vented perforated pan-coating apparatus. The preliminary results revealed that spray rate, inlet air temperature and rotating speed of pan had a major effect on tablet coating performances. The spray rate of coating solution 8 gm/min, inlet air temperature 55°C and rotating speed of pan 12 rpm considered as a optimum aqueous film coating of special shaped tablets in neocota coating machine.

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