DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 20(9), 1535-1554 (1994)

EFFECT OF AQUEOUS FILM COATING CONDITIONS ON WATER REMOVAL EFFICIENCY AND PHYSICAL PROPERTIES OF COATED TABLET CORES CONTAINING SUPERDISINTEGRANTS

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ABSTRACT

Few studies have examined the effect of aqueous film coating process conditions on the physical integrity of the final coated product. Characterization of the aqueous film coating process was previously carried out by selecting water removal efficiency as the response variable to detect and monitor moisture accumulation in the tablet bed [1]. In this study, regression techniques were utilized to obtain the relationship between some physical characteristics of aqueous film coated tablet cores that contained superdisintegrant and several process parameters such as inlet air temperature, spray rate, and pan speed. Tablet response variables measured included residual moisture content, tensile strength and percent porosity. Predicted values of these properties were plotted as a function of the inlet air temperature and the coating solution spray rate. The correlations between the coated tablet response variables and the water removal efficiency of the coating process indicated that coated tablet properties such as residual moisture content, tensile strength, and porosity were linearly correlated with the water removal

efficiency of the coating process, which is indicative of the environmental coating conditions present in the coating pan.

INTRODUCTION

Few studies have sought to determine the effect of various environmental conditions in aqueous film coating process on the integrity of the final coated product. Ebey [2] used energy and mass transfer parameters of evaporative systems to derive an environmental equivalency factor that was used to determine how a certain quality of coating could be reproduced in a variety of process environments. Previous investigations by Pourkavoos and Peck [3, 4] indicated that the extent of moisture sorption by film coated tablet cores containing superdisintegrants was sufficient to result in significant changes in some of the tablet physical characteristics such as residual moisture content, tensile strength, pore volume–size distribution, and the glass transition temperature of the tablet matrix.

In this study, the drying efficiency of the film coating process was determined in terms of its water removal capacity at several levels of the process parameters, including inlet air temperature, coating solution spray rate and the pan speed. A computer program for the thermodynamic analysis of aqueous coating (TAAC) was acquired from Thomas Engineering (Hoffman Estates, Illinois). The calculated values of the environmental equivalency factor [2] corresponding to different coating conditions were analyzed for their correlations with the experimentally determined values of water removal efficiencies.
Surface response methodology was utilized to obtain the relationship between some physical properties of aqueous film coated tablet cores containing superdisintegrants and several coating process parameters. In addition, correlations amongst the various coated tablet characteristics (such as residual moisture content, tensile strength, and porosity) and the water removal efficiency of the film coating process were examined.

MATERIALS AND METHODS

The formulated tablets consisted of the following components : dibasic calcium phosphate, dihydrate, USP (Di-Tab) from Rhone-Poulenc (Westport,

TABLE 1
Tablet Formulation Composition

	Formulation Code (% w/w)		
Tablet Ingredient	A_{II}	P_{II}	CP_{II}
Ac-Di-Sol	10		
Primojel		10	
Polyplasdone-XL			10
Avicel PH 101	20	20	20
Di-Tab	68	68	68
Cobalt Chloride	1	1	1
Magnesium Stearate	1	1	1

Connecticut); microcrystalline cellulose, NF (Avicel PH 101) and croscarmellose sodium, type A, NF (Ac-Di-Sol) from FMC Corporation (Philadelphia, Pennsylvania); sodium starch glycolate, NF (Primojel) from Generichem Corporation (Little Falls, New Jersey); crospovidone, NF (Polyplasdone-XL) from ISP Chemicals Corporation (Wayne, New Jersey); magnesium stearate and cobalt chloride hexahydrate from Mallinckrodt Inc. (Paris, Kentucky). The aqueous film coating solution consisted of hydroxypropyl methylcellulose 2910,USP (Methocel E-5) from Dow Chemical Company (Midland, Michigan); polyethylene glycol 3350 NF from Ruger Chemical Company (Irvington, New Jersey); and polyethylene glycol 8000 from Union Carbide Corporation (Danbury, Connecticut). All excipients were used as received from the suppliers, with the exception of Avicel PH 101 and cobalt chloride hexahydrate which were pre-dried for 21 hours at 80 °C.

Tablet Formulation and Preparation

Table 1 shows the percentages of excipients used in the manufacture of the various tablet formulations, each denoted by an appropriate code name. Tablets were prepared by using a standardized blending procedure and compression of the powdered ingredients. The powder mixture was passed through a 40 mesh stainless steel hand screen and was blended for 10 minutes in a small laboratory size V-blender. Magnesium stearate was passed through a 60 mesh screen and was added to the powder mixture followed by three minutes of blending. Five hundred milligram samples of the mixed powder ingredients were weighed and directly placed in a 12.7 mm flat faced punch and die set and compressed at a compression load of 6,000 pounds (211 MPa) at a constant rate of loading using a standard hydraulic laboratory press (Carver press, Menomonee Falls, Wisconsin).

Coating Solution Composition

The polymer coating solution was composed of the following : (a) Methocel E-5 (6% w/w); (b) polyethylene glycol 3350 (1% w/w); (c) polyethylene glycol 8000 (1% w/w); and (d) distilled water (q.s. 100% w/w).

Aqueous Film Coating Process and Equipment Description

A 24-inch Accela-Cota (Thomas Engineering, Hoffman Estates, Illinois) was used to conduct the aqueous film coating of tablets. The coating equipment instrumentation consisted of the following indicators : (a) inlet and exhaust air temperature (°C), (b) pan rotational speed (rpm), and (c) pressure drop across the tablet bed (inches of water).The temperature of the inlet drying air was controlled and maintained by a separate custom design air heating unit (Teko, Hoffman Estates, Illinois).

The amount of air flow through the pan was measured using an air velocity meter Model 1650 (TSI Inc., St. Paul, MN). The moisture content of the air in the system was monitored using a Solomat 455 thermohygrometer (Solomat Partners LP, Stamford, Connecticut). The thermohygrometer probe was inserted into the exhaust air stream through an opening (1/2 inch wide) in the exhaust air duct. The meter was connected to a strip chart recorder (Kipp & Zonen, Holland). A continuous record of the exhaust air percent relative humidity (% RH) was obtained for the duration of each coating experiment. The ultrasonic spray system consisted of the Sonicore nozzle, Model 052H (Sonic Development Corporation, Parsippany, New Jersey) attached onto separate stainless steel liquid and air feed lines. The coating solution was delivered to the spray nozzle assembly via a peristaltic flow meter (Cole Parmer Instrument Co., Chicago, Illinois).

Determination of Water Removal Efficiency

The water removal efficiency (WRE) of the aqueous film coating process was determined by a modified method previously described by Stetsko et al., [1].

It is defined as the percentage of the water sprayed onto the tablet bed per minute that is removed from the coating pan :

$$WRE = \frac{\text{lbs of water/minute (removed)}}{\text{lbs of water/minute (sprayed)}} \times 100 \quad \text{(Eq. 1)}$$

The rate at which water was sprayed was calculated from the spray rate multiplied by the fraction of water in the coating solution. The moist air density (lbs/cu ft) was obtained from air density tables [5] and from the wet and dry bulb temperature of the exhaust air at each set of process parameters. The air flow rate through the perforated pan was fixed at 423 cu ft/min. The percent relative humidity (% RH) of the inlet drying air could not be measured directly; instead, the equilibrium value of the exhaust air % RH was recorded at the beginning of each coating run (with the pan empty). The equilibrium values of the exhaust air percent relative humidities and temperatures before and after the spray application were used to determine the absolute humidities of the exhaust air in pounds of water vapor per pound of dry air from a psychometric chart [5]. The difference between the two exhaust air relative humidities (i.e., before and after spray application) was used to calculate lbs of water /minute removed.

Evaluation of the Environmental Equivalency Factor

The TAAC computer program utilizes thermodynamic principles together with heat and mass transfer rate equations to describe the coating process. These were combined into a single quantity named the environmental equivalency factor which governed the evaporation of water from the tablet surface [2]. The method of moisture evaporation involves both convective heat and mass transfer. Under steady conditions the rate of convective heat transfer is equal to the mass rate of evaporation multiplied by the change in enthalpy of water. Therefore,

$$H_h A_h (T_g - T_b) = H_m A_m (H_s - H_g) \times \lambda \quad \text{(Eq. 2)}$$

on rearranging

$$EEF = \frac{A_h}{A_m} = \frac{(H_s - H_g)}{(T_g - T_b)/\lambda} \times \frac{H_m}{H_h} \quad \text{(Eq. 3)}$$

where,

EEF = Environmental Equivalency Factor (typical range 1.5-5.2), A_h = Heat transfer surface area, A_m = Mass transfer surface area, H_h = Average heat transfer coefficient, H_m = Average mass transfer coefficient, T_g = Inlet air temperature, T_b

= Exhaust air temperature, H_g = Inlet air absolute humidity, H_s = Exhaust air absolute humidity and λ = The latent heat of vaporization of water

The experimental values of process parameters corresponding to different coating conditions were entered into the TAAC program operated on a microcomputer system. The program generated an output of calculated values of Environmental Equivalency Factor corresponding to any given set of process parameters. These values were analyzed for their correlation with the experimentally determined values of the water removal efficiencies.

Evaluation of Coated Tablet Characteristics

The determination of residual moisture content and tensile strength of coated tablet cores (polymer film layer removed) were carried out as previously described [3]. A microprocessor controlled Micromeritics Autopore II, Model 9220 (Norcross, Georgia) mercury intrusion instrument was used to measure the pore volume and pore volume-size distribution of coated tablets containing Polyplasdone–XL [3]. The mean geometric pore diameter was determined by plotting the percent cumulative pore volume oversize against pore diameter on a log probability paper. This plot yielded the pore diameter at 50% probability.Tablet porosity was calculated from the apparent solid densities obtained from mercury penetration data and from the tablet dimensions, weight, and the true solid densities of the individual tablet components.

Experimental Design

The independent variables manipulated in the coating process included the following : X_1 – inlet air temperature (°C), X_2 – coating pan rotational speed (rpm), and X_3 – coating solution spray rate (g/min)

The dependent or response variables measured included the water removal efficiency of the coating process:Y_1 – (WRE), and the coated tablet characteristics as follows : Y_2 – tablet residual moisture content (% w/w); Y_3 – tablet tensile strength (kg/cm^2); Y_4 – tablet mean pore diameter (CP_{II} only, µm), and Y_5 – tablet percent porosity (CP_{II} only).

The experimental design was a three factor central composite design [6]. The mathematical model was a second order response function shown below :

$$Y = b_0 + \sum_{j=1}^{k} b_j x_j + \sum_{j=1}^{k} \sum_{m=1}^{k} b_{jm} x_j x_m + \sum_{j=1}^{k} b_{jj} x_j^2 + E_{jm} \quad \text{(Eq.4)}$$

TABLE 2

Values Assigned to Experimental Levels Used in the Central Composite Design.

	Level				
Variable	-1.633	-1	0	1	1.633
Inlet air temperature (°C)	50	55	62.5	70	75
Pan rotational speed (rpm)	10	11	12.5	14	15
Solution spray rate (g/min)	75	79	85	91	95

where, Y is the response, x_j is the independent variable (j=1,2,3), x_jx_m is the interaction term (m=2,3), x_{jj} is the quadratic term, $b_0, b_1, \ldots b_k, b_{11}, \ldots, b_{kk}, b_{12}, \ldots, b_{k-1,k}$ are the unknown coefficient terms (k=3), and E_{jm} is the random error term.

Each variable was measured at five levels (i.e., -d, -1, 0, 1, and d, where d was the distance from the center point to each of the six extreme points in the central composite design). The assignment of real values to these experimental levels is shown in Table 2. A total of 15 treatment combinations were obtained for this design. The entire experiment was divided into three orthogonal blocks. The distance d was computed to be 1.633 [7]. The coating combinations assigned to each block were performed on the same day in a randomized fashion.

Coating Procedure and Data Collection

With the pan empty, the inlet and exhaust air temperatures and the exhaust air percent relative humidity were allowed to stabilize and were recorded accordingly. Fifteen marked tablets from each of the tablet formulations A_{II}, P_{II}, and CP_{II} (Table 1) were mixed with 2.0 kg of standard convex , red colored, lactose tablets (bulk up tablets) pre-coated with hydroxypropyl methylcellulose [8]. The tablet load was allowed to warm up to temperature for 10 minutes. Equilibrium values of air temperature and percent relative humidity were again recorded. The spray assembly was positioned inside the pan. The air pressure to the spray nozzle was set at 35 psig. The coating solution was applied using intermittent spraying with 0.7 minutes of spray per minute. Once a coating run was completed and the data collected, the process was stopped and the levels of the independent variables were changed for the next treatment combination. The film coated tablets were visually examined and found to be satisfactory in all cases.

RESULTS AND DISCUSSION

The Effect of Process Variables on the Water Removal Efficiency of the Coating Process

The SAS statistical software program (Cary, NC) was utilized for the regression analysis of the data and the graphical presentation of the predicted response surface over the experimentally defined levels of factors . Table 3 shows the results of the regression analysis. The F-value at the 5% significance level indicated that the second order regression model (Eq.4) was significant. The model fitted the experimentally obtained values of WRE, and adequately accounted for the variability in the data ($R^2 = 0.8570$). From the estimates of the parameter coefficients in the regression model, shown in Table 4, it was concluded that the only significant terms in the model were the linear and quadratic terms for the effect of inlet air temperature.

The fitted second order response function enabled values of water removal efficiency to be predicted for the various levels of process parameters. These predictions were utilized to generate a graphical illustration of the response function, characterized by the predicted response surface over the region of the two independent variables X_1 (inlet air temperature) and X_3 (coating solution spray rate).

The response surface, shown in Figure 1, possessed a rising slope with increase in air temperature and reached the maximum (i.e., 100% water removal efficiency at the high range of the temperature scale). The region of maximum efficiency extended over an inlet air temperature range of 69–75°C and the entire range of the coating solution spray rates.

Determination of the Predicted Values of Environmental Equivalency Factor

The environmental equivalency factor (EEF) was defined by Ebey [2] as the ratio of the surface areas over which heat was transferred by convection from the drying air to the tablet bed surface, to that which mass (i.e., moisture) was transferred from the liquid film at the tablet surface into the passing air stream

TABLE 3

Analysis of Variance for the Multiple Regression Model for the Effect of Inlet Air Temperature (X1), Pan Rotation Speed (X2) and Spray Rate (X3) on the Water Removal Efficiency of the Aqueous Film Coating Process.

Source	df	SS	MS	F-Value	$F_{(\alpha=0.05)}$
Model	9	4094.82	454.98	6.66 *	3.02
Linear	3	3670.67	1223.56	17.91 *	3.71
Quadratic	3	414.07	138.02	2.02	
Crossproduct	3	10.08	3.359	0.05	
Residual	10	683.09	68.31		
Lack of Fit	7	470.064	67.15	0.946	3.14
Pure Error	3	213.027	71.01		

R-Square = 0.8570
Coefficient of Variability = 9.78%

* Significant at $\alpha = 0.05$ level

TABLE 4

Results of the Estimates of Coefficients of the Mathematical Model for the Water Removal Efficiency

Variable	df	Estimate	T-Ratio
Intercept	1	90.508	26.87
X1	1	15.756	7.02*
X2	1	-2.651	-1.18
X3	1	-3.938	-1.75
X1X1	1	-5.056	-2.29*
X2X2	1	-1.63	-0.74
X3X3	1	-2.15	-0.97
X1X2	1	0.085	0.03
X1X3	1	-0.678	-0.23
X2X3	1	-0.889	-0.3

$T_{(.975),\,10} = 2.228$

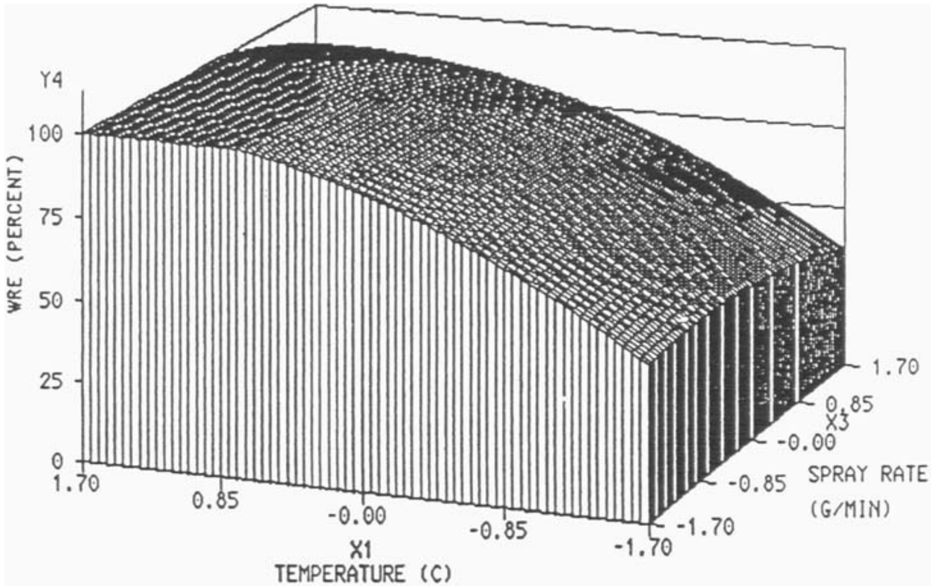

FIGURE 1

The Predicted Response Surface for the Water Removal Efficiency of the Aqueous Film Coating Process as a Function of Inlet Air Temperature from 50°C to 75°C and Coating Solution Spray Rate from 75 to 95 g/min.

(given by Equation 3). In this approach, prior testing was required to determine a given set of coating conditions that produced film-coated tablets of acceptable quality. The appropriate values for the process parameters thus established were utilized to calculate a typical production range for the term environmental equivalency factor. This range was shown to generally fall between 1.0 and 5.2 with 3.3 being a typical production value [2 and TAAC computer user's guide]. A value of 1.0 for the EEF indicated that the tablet bed was completely saturated with coating solution, whereas high values indicated a dry tablet bed or low spray rates.

The TAAC computer program enables the researcher to investigate how changes in the coating process variables affect the value of EEF and the quality of the final coated product. In this study, the values of the independent process variables (i.e., X_1, X_2, and X_3), together with the experimentally measured values of the exhaust air temperature and absolute humidity were entered into the TAAC computer program to generate predicted values of the EEF for the various coating conditions in the experimental design. In addition, the program output listed predicted values of the exhaust air temperature and absolute humidity.

From the results shown in Table 5, it can be seen that the predicted values of EEF were indeed within the range of 1.0-5.5. This indicated that the coating conditions obtained from the different treatment combinations in the central composite design were within the normal production limits as specified by the TAAC program specifications. The difference between the predicted and the measured values of the exhaust air temperature ranged from 0°C to 12.7°C. The same difference for the exhaust air humidity ranged from 0.75 to 16.72 grains of water/lb of dry air (gr/lb). However, it was observed that there was good agreement between the measured and the predicted values of exhaust air temperature at low levels of EEF and WRE, signifying that the tablet bed had become overwet.

Figure 2 shows the positive linear correlation ($R = 0.8516$) between the experimentally obtained values of the water removal efficiency and the predicted values of the environmental equivalency factor obtained for each set of coating conditions in the experimental design. These results demonstrate that the approach undertaken here to model the film coating system using a simple empirical polynomial equation can closely predict process behaviour obtained by the application of standard thermodynamic relationships.

TABLE 5

Results of the Predicted and the Measured Values of Environmental Equivalency Factor, Water Removal Efficiency, and Exhaust Air Temperature and Humidity Obtained from the TAAC Program and by Experimentation Respectively.

				Measured Exhaust Air		Predicted Exhaust Air			
Treatment Combination	Inlet Air Temp. (°C)	Pan Speed (rpm)	Spray Rate (g/min)	Temp. (°C)	Humidity (grains of water/lb of air)	Temp. (°C)	Humidity (grains of water/lb of air)	Predicted EEF	Measured WRE (%)
1	55	11	79	38	39.2	41	52.5	2.628	65.067
2	70	11	79	47.5	64.26	57.5	63.2	3.933	100
3	55	14	79	38	36.75	41.3	52.4	2.676	58.304
4	70	14	79	48	51.45	60.7	42.6	5.427	100
5	55	11	91	37	40.18	39.2	56.9	2.325	61.364
6	70	11	91	47	56.14	57.8	53.3	4.091	100
7	55	14	91	38	39.48	38.7	58.5	2.251	57.465
8	70	14	91	46	55.86	55.4	58.8	3.416	90.023
9 [1]	62.5	12.5	85	43.8	52.39	49.12	55.02	3.229	90.23
10	75	12.5	85	49	66.15	61.7	66.9	4.048	100
11	50	12.5	85	36	36.75	36.0	51.9	2.339	60.543
12	62.5	15	85	43.5	55.44	48.6	50.1	3.065	85.194
13	62.5	10	85	44.5	56.7	48.9	57.5	3.142	94.38
14	62.5	12.5	95	40.5	53.2	45.6	63.5	2.538	76.685
15	62.5	12.5	75	45	57.12	52.9	50.5	4.435	100

[1] Average values of 5 replications at the center point

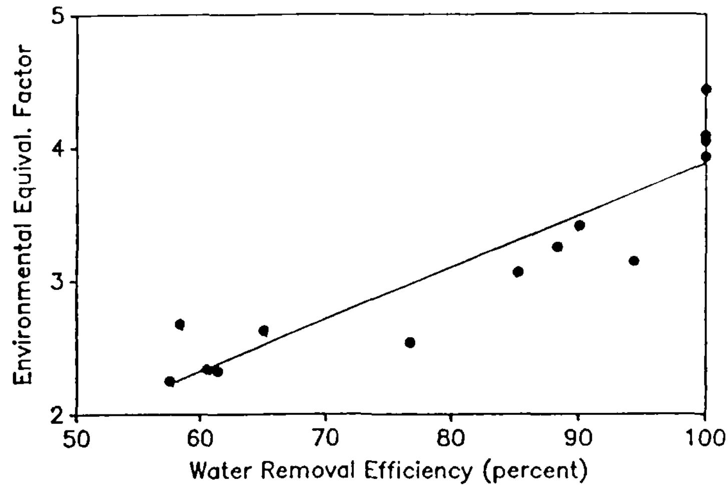

FIGURE 2

The Relationship of Environmental Equivalency Factor to Water Removal Efficiency of the Aqueous Film Coating Process.

The Effect of Process Variables on the Coated Tablet Characteristics

Tables 6 and 7 show that the regression model for the moisture content (percentages of weakly bound-unbound water determined by thermogravimetric measurement) of coated tablets A_{II} and P_{II}, was significant at the 5% level (R^2 = 0.9073, and 0.8366 respectively). With respect to tablet cores containing Ac-Di-Sol (i.e. A_{II},) all main effects due to the process parameters as well as the quadratic term due to the inlet air temperature (X_1) and the two–way interaction term between spray rate and pan speed (X_3X_2) were found to be significant ($P < 0.05$). The detection of a significant quadratic term indicated the existence of curvature in the response surface and a significant interaction term indicated that the effect of either spray rate or pan speed on the tablet moisture content cannot be judged independently (this implied that the effect of change in the level of one factor i.e., spray rate or pan speed on the tablet residual moisture content was dependent on the level of the other factor).

Figure 3 shows the predicted response surface for tablet P_{II} moisture content (% w/w) as a function of inlet air temperature and spray rate. An increase in the spray rate and a decrease in air temperature served to increase the availability

TABLE 6

Analysis of Variance for the Full Regression Model for the Effect of Process Parameters on the Percent w/w Weakly Bound–Unbound Water for Tablet A_{II}.

Source	df	SS	MS	F-value	$F_{(\alpha=0.05)}$
Model	9	11.019	1.224	10.87 *	3.02
Linear	3	9.084	3.028	26.89 *	3.71
Quadratic	3	1.230	0.41	3.64	
Cross product	3	0.705	0.235	2.09	
Residual	10	1.126	0.113		
Lack of Fit	7	0.946	0.135	2.53	3.14
Pure Error	3	0.180	0.060		
R-square = 0.9073					
Coefficient of variability = 6.869%					

TABLE 7

Analysis of Variance for the Full Regression Model for the Effect of Process Parameters on the Percent w/w Weakly Bound–Unbound Water for Tablet P_{II}.

Source	df	SS	MS	F-value	$F_{(\alpha=0.05)}$
Model	9	7.019	0.779	5.12 *	3.18
Linear	3	2.674	0.891	5.85 *	3.86
Quadratic	3	3.601	1.200	7.88 *	
Cross product	3	0.744	0.248	1.63	
Residual	9	1.370	0.152		
Lack of Fit	7	1.170	0.167	1.672	19.35
Pure Error	2	0.200	0.100		
R-square = 0.8366					
Coefficient of variability =7.971%					

* Significant at $\alpha = 0.05$ level.

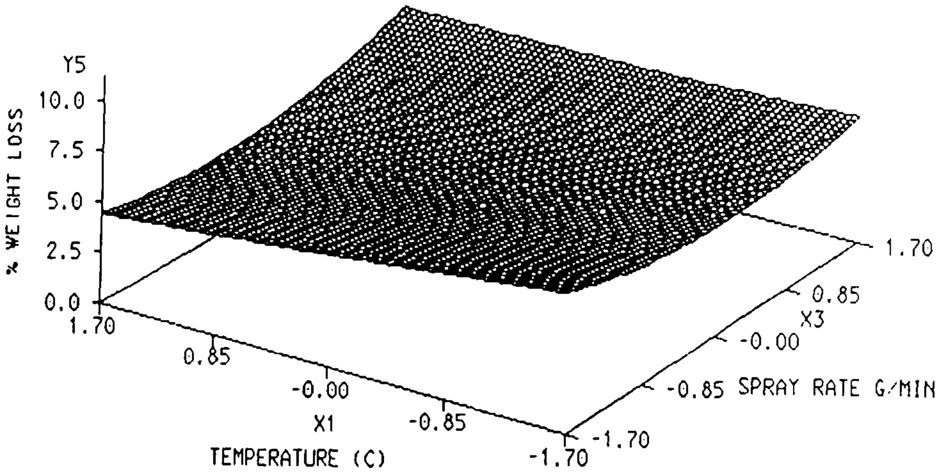

FIGURE 3

The Predicted Response Surface for the Percent (w/w) WeaklyBound-Unbound Water for the Aqueous Film Coated Tablets Containing Primojel as a Function of Inlet Air Temperature from 50°C to 75°C and Coating Solution Spray Rate from 75 to 95 g/min.

of moisture (both in the liquid and the vapor state) in the coating pan, which in turn increased the extent of moisture sorption by the tablet cores from the applied polymer coating solution. Table 8 shows the regression analysis of data for percent weight loss on oven drying for polyplasdone–XL containing tablets (CP_{II}). In this case the reduced regression model (containing terms only for the linear and quadratic effects of air temperature and spray rate) was significant at the 5% level ($R^2 = 0.7148$).

The inlet air temperature was also the significant factor ($P < 0.05$) in the reduced quadratic regression model for the tensile strength of coated tablet core A_{II}. Figure 4 shows that the response surface possessed a negative slope. The reduction in tablet cohesion was attributed to the effect of penetration and sorption of water from the applied polymer coating solution into the coated tablet cores. The resulting hydration and expansion of Ac–Di–Sol and microcrystalline cellulose particles in the tablet matrix exerted a swelling pressure on the surrounding tablet components which in turn resulted in weakening of the tablet internal structure.

TABLE 8

Analysis of Variance for the Reduced Regression Model for the Effect of Process Parameters on the Percent Weight Loss on Oven Drying for Tablet CP_{II}.

Source	df	SS	MS	F-value	$F_{(\alpha=0.05)}$
Model	5	8.391	1.678	7.02 *	2.96
Linear	2	7.788	3.894	16.29 *	3.74
Quadratic	2	0.600	0.3	1.26	
Cross product	1	0.002	0.001	0.01	
Residual	14	3.347	0.239		
R-square = 0.7148					
Coefficient of variability = 7.143%					

* Significant at α = 0.05 level.

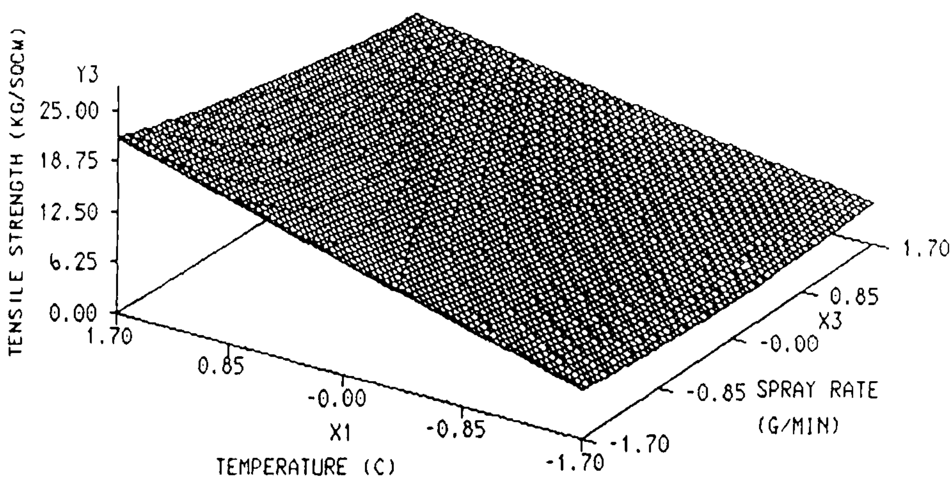

FIGURE 4

The Predicted Response Surface for Tablet Tensile Strength for the Aqueous Film Coated Tablets Containing Ac-Di-Sol as a Function of Inlet Air Temperature from 50°C to 75°C and Coating Solution Spray Rate from 75 to 95 g/min.

TABLE 9

Analysis of Variance for the Full Regression Model for the Effect of Process Parameters on Tablet CP_{II} Percent Porosity.

Source	df	SS	MS	F-value	$F_{(\alpha=0.05)}$
Model	9	300.533	33.393	9.63 *	3.18
Linear	3	270.607	90.202	26.02 *	3.86
Quadratic	3	14.059	4.686	1.35	
Cross product	3	15.868	5.289	1.53	
Residual	10	34.671	3.467		
Lack of Fit	7	31.894	4.556	4.923	8.84
Pure Error	3	2.776	0.925		
R-square = 0.8965					
Coefficient of variability =7.988%					

* Significant at $\alpha = 0.05$ level.

TABLE 10

Equations of Best Fit for the Linear Regression Relationships Between the Tablet Response Variables Containing 10% w/w Superdisintegrant and the Water Removal Efficiency of the Coating Process.

Functional Relationship	Equation of Best Fit	Correlation Coefficient (r)
Percent weakly bound–unbound water for tablet A_{II} versus WRE	Y = 9.067 - 0.0479 WRE	0.9719
Percent porosity for tablet CP_{II} versus WRE	Y = 40.987 - 0.2162 WRE	0.9480
Percent weight loss for tablet CP_{II} versus WRE	Y = 10.183 - 0.0400 WRE	0.9165
Percent weight loss for tablet P_{II} versus WRE	Y = 10.109 - 0.0413 WRE	0.8956

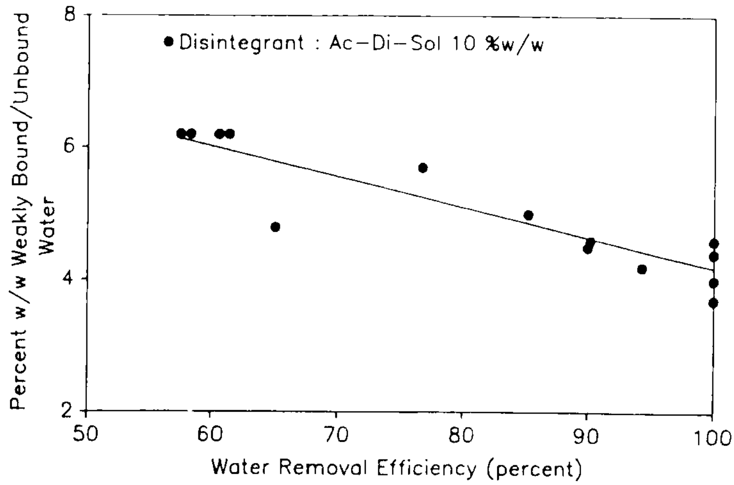

FIGURE 5

The Relationship of Water Removal Efficiency to Percent Weakly Bound–Unbound water Content for Aqueous Film Coated Tablets Containing Ac-Di-Sol at 10% w/w.

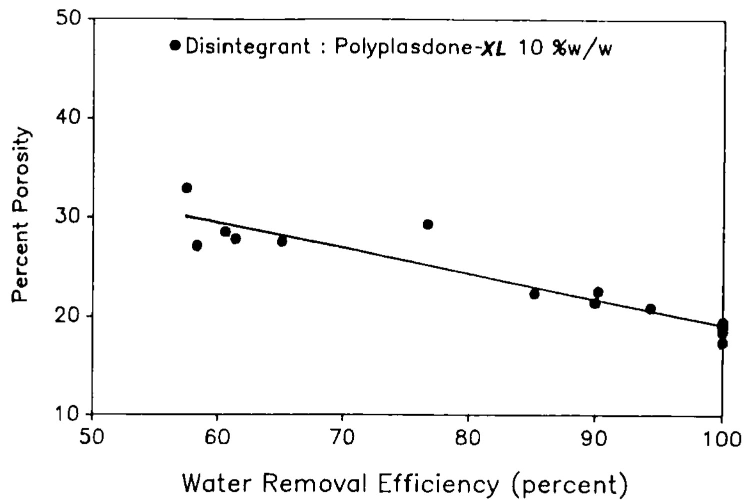

FIGURE 6

The Relationship of Water Removal Efficiency to Percent Porosity for Aqueous Film Coated Tablets Containing Polyplasdone-Xl at 10% w/w.

In the case of Primojel containing tablet cores when the mean value for all treatment combinations (8.649 ± 2.979 kg/cm^2) was compared to the value for the uncoated tablet tensile strength (20.202 ± 1.986 kg/cm^2), a significant reduction of tablet cohesion was obtained after the coating operation.

From data presented in Table 9 it was determined that the quadratic regression model was significant at the 5% level ($R^2 = 0.8965$). The model adequately described the changes in tablet porosity caused by exposure to the different coating conditions in the experimental design. Air temperature and spray rate significantly affected tablet percent porosity. The changes in coated tablet microstructure were caused by the penetration of water from the coating solution into the tablet matrix. The subsequent hydration and swelling of the polyplasdone-XL polymer lattice structure resulted in enlargement of the tablet inter – and intra – particle void space . These findings indicate that the coated tablet characteristics measured in this study were adequately accounted for by a 2nd order regression model based on several levels of coating process parameters.

Analysis of the Relationship Between the Water Removal Efficiency and the Coated Tablet Response Variables

For each set of coating conditions, tablet core response variables were plotted as a function of the corresponding values of the water removal efficiencies of the coating process. The equations of the best fit lines are presented in Table 10. Figures 5 and 6 show that the tablet residual moisture content and percent porosity for A_{II} and CP_{II} respectively were linearly correlated with the water removal efficiency of the coating process. This indicated that as the capacity of the coating process to remove moisture from the coating pan was increased, a corresponding decrease in the tablet residual moisture content was obtained. On the other hand, low values of WRE represented greater availability of moisture within the tablet bed, and a widening of the tablet pore size distribution was resulted from the penetration of moisture into the tablet matrix. The results of this study indicate that the water removal efficiency of the aqueous film coating process may be used to predict the impact of various environmental coating conditions on the integrity of the final coated tablet dosage form.

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