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PROCESS CONSIDERATIONS IN REDUCING TABLET FRIABILITY AND THEIR EFFECT ON *IN VITRO* DISSOLUTION

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ABSTRACT

The tablet friability resulting from manufacturing process variations was studied for two differently sized tablets using the same formulation. Granulations containing lower moisture contents required higher compression and ejection forces to manufacture a tablet at a given hardness, although this did not influence friability. Increased tablet hardness (and to a lesser extent decreased tablet thickness) decreased the tablet friability of the larger tablet. An increase in the quantity of granulating fluid increased the granulation particle size and slightly improved compactibility without significantly affecting friability. Tablet dissolution increased as the quantity of granulating fluid was decreased. There was a strong interaction, with respect to dissolution, between moisture content and the amount of granulating fluid. Tablet hardness did not significantly influence dissolution. Doubling the quantity of magnesium stearate in the granulation in one tablet strength decreased the maximum tablet hardness that could be obtained, and for the other tablet strength increased friability. It also resulted in slower tablet dissolution.

INTRODUCTION

Obtaining a low friability for compressed tablets is important to formulators because it indicates that the tablets will withstand the rigors of handling during coating, packaging, shipping, and manufacturing operations in general. The most common method of testing friability is using a Roche friabilator (1), which provides both falling and frictional components, and thereby measures tablets' resistance to shock and abrasion. Although it is generally recognized that minimizing friability is desirable, variables affecting friability have not been fully explored; friability tends not to be the primary focus of most formulation studies. Of those studies that have focused on friability (2-9), only a single study (2) has examined some of the following characteristics of the granulation and related these parameters to friability: tapped density, particle size, and compression and ejection forces profiles. Additionally, there are relatively few investigations that report on the relationships of granulating fluid quantity (3), granulation moisture content (2-7), tablet hardness (3-6,8), and tablet thickness (2) to friability. A complete understanding of processing variables is essential if the friability of compressed tablets is to be minimized during the design phase of the solid dosage form. This paper reports the results of studies in which different quantities of granulating fluid were used so as to vary the characteristics of the granulation and thereby affect tablet friability. The impact of granulation moisture content and tablet hardness on friability was also investigated. In addition, the effect on friability of doubling the magnesium stearate concentration was assessed. The influence of these factors on *in vitro* tablet dissolution is also reported here.

MATERIALS AND METHODS

Formulation - The formulation was comprised as follows. All materials were USP/NF grade.

Ingredient	Mg Per Tablet	Mg Per Tablet
Naproxen (at least 99% pure, Syntex, Inc.)	250.00	500.00
Regular lactose, monohydrate (Foremost Whey Products)	73.56	147.11
Pregelatinized starch (Starch 1500®, Colorcon, Inc.)	38.00	76.00
Polyvinylpyrrolidone K-29/32 (PVP®, GAF Corp.)	10.00	20.00
Croscarmellose sodium (Ac-Di-Sol®, FMC Corp.)	7.60	15.20
Magnesium stearate (Mallinckrodt, Inc.)	0.76	1.52
D&C Yellow #10 (H. Kohnstamm, Inc.)	0.08	0.16
FD&C Yellow #6 (H. Kohnstamm, Inc.)	0.005	0.01
Purified water (Syntex, Inc.)	As required by the experimental design	

Granulation - The granulating solution was made by dissolving the dyes and polyvinylpyrrolidone in the water. The naproxen, pregelatinized starch, and lactose were mixed in a Littleford Lodige high shear mixer for 5 minutes, with the plows and choppers on. While mixing with the plows and choppers on, the granulating solution was pumped into the mixer over a 7 minute period (± 1 minute). Mixing was then continued for another 10 minutes. The resulting granulation was dried in a Glatt fluid bed dryer with an inlet air temperature of 55±5°C. The dried granulation, the magnesium stearate, and the croscarmellose sodium were passed through a Stokes Oscillator equipped with a #16 mesh screen, and then final blended in the mixer with the plows only, for 2 minutes. The batch size was 40 kg. For the batches with double the amount of magnesium stearate, 4 kg of granulation was blended with an additional 0.2% w/w magnesium stearate for 3 minutes in a Hobart planetary mixer.

Compression - The 250 mg strength tablets were compressed with an instrumented single punch machine (Stokes E) equipped with a round 7/16" diameter standard concave punch and die to the target hardness required (12, 16, or 20 Strong-Cobb Units, or SCU) and to a tablet weight of 380±10 mg. The 500 mg strength tablets were compressed with a single

punch machine (Stokes F-4) equipped with a 0.250" x 0.746" capsule-shaped, deep concave punch and die to the target hardness required (12, 16, or 20 SCU) and to a tablet weight of 760±20 mg.

Granulation Moisture Content - Moisture content was determined by the loss on drying (LOD) technique using a Cenco moisture balance.

Granulation Size Distribution - Size distribution was determined with 200 g of granulation using an Allen Bradley Sonic Sifter, with the settings adjusted as follows: sift, 7; pulse, 9; time, 5 minutes.

Granulation Tapped Density - Tapped density was determined by dropping 50 cc of untapped granulation a distance of 0.5 cm at a rate of 100 taps per minute for 10 minutes. Compressibility (an indicator of powder flow characteristics) was calculated as per Carr (10) using the equation:

$$\frac{\text{Tapped density - Bulk density}}{\text{Tapped density}} \times 100 = \% \text{ Compressibility}$$

Tablet Hardness - Tablet hardness was determined immediately after compression, using a motorized hardness tester (Model 2E, Dr. K. Schleuniger and Co.). Fifteen tablets were tested for each batch and the mean and standard deviation were calculated. Hardness was measured in SCU (1.4 SCU = 1 kilopond = 9.8 newtons).

Tablet Thickness - Tablet thickness was determined by measuring the thickness of ten tablets using a vernier caliper (Model 120M, Starret).

Tablet Friability - Tablet friability was determined by subjecting 20 tablets from each batch to 100 revolutions in a Roche-type friabilator over a 4 minute period.

***In Vitro* Dissolution** - Dissolution of the tablets was performed according to USP XXI using Apparatus II. Six tablets were tested for each

TABLE 1 - The Formulation Variables and the Levels Evaluated in this Investigation

Variable	Levels Investigated		
Quantity of granulating fluid	14.00%	14.875%	15.75%
Granulation moisture content	1.0%	2.0%	3.0%
Tablet hardness	12 SCU	16 SCU	20 SCU

batch, and the mean and standard deviation were calculated. The medium was 900 ml of deaerated phosphate buffer (pH = 7.4) with a temperature of $37^{o}C \pm 0.5^{o}C$. The paddle rotated at 50 rpm. Automated sampling equipment removed the samples through a filter and analyzed them spectrophotometrically at 254 nm.

Experimental Design and Analysis - To design the experimental regimen, a modified computer optimized experimental design (COED, CompuServe, Inc.) was utilized for the variables listed in Table 1. The COED determined that 13 tablet batches of each strength would allow a statistically significant characterization of the variables being examined. It was found during the experiment that two of the 250 mg strength tablet batches (lowest amount of water, 1% LOD, 20 SCU, and intermediate amount of water, 1% LOD, 20 SCU) were impossible to manufacture, due to an inability to reach the target hardness. This significantly lowered the chances of accurately detecting correlations for the 250 mg strength tablets, so multiple linear regression analysis was not used to analyze the 250 mg strength data. A multiple linear regression analysis was used to analyze the 500 mg strength data. A computer program, (Microsoft Excel® version 4.0, Microsoft Corp.) was utilized. The procedure determined the parameters of a general quadratic equation utilizing the data produced during the

experiments, and then response surfaces were generated with the equation via the same program to illustrate the influence of the factors in the model. The general quadratic equation used to model the response surface was:

$$Y = b_0 + b_1X_1 + b_2X_2 + b_3X_3 + b_4X_1X_2 + b_5X_1X_3 + b_6X_2X_3 + b_7X_1^2 + b_8X_2^2 + b_9X_3^2 + \text{Error}$$

where Y represents the dependent variable (dissolution or friability), X_1, X_2, and X_3 are the independent variables (X_1 represents the amount of granulating solvent, X_2 is the granulation moisture content, and X_3 represents the tablet hardness), and the coefficients b_0, b_1, b_2 ... b_9 are the least square regression coefficients.

RESULTS AND DISCUSSION

Table 1 gives the levels that were investigated for the quantity of granulating fluid as a percent of the formulation, the granulation moisture content, and the tablet hardness. The experimental design that was used to investigate the above variables is illustrated in Table 2. Table 3 shows the actual granulation moisture contents, tablet hardnesses, weights, and thicknesses achieved, and the tablet friability and dissolution characteristics of these batches.

Figure 1 clearly shows that granulation particle size distributions were principally determined by the amount of granulating fluid utilized. The greater the quantity of solvent employed, the coarser the granulation produced. Varying the amount of fluid by 0.875% w/w of the formulation resulted in dramatically different particle size distributions. The relationship between granulating fluid quantity and tablet friability and dissolution will be discussed later. Table 4 demonstrates that the granulation tapped density and the percent compressibility (10) tend to increase as the amount of granulating fluid is increased. This indicates that, within the range studied in this investigation, the flow properties of the granulation improved as the quantity of granulating fluid decreased. This trend is likely due to the

TABLE 2 - The Experimental Design Utilized for this Investigation for Each Tablet Strength

Granulating Fluid (% w/w)	% Granulation Moisture Content	Tablet Hardness (SCU)
14.0	1.0	12
		20
	2.0	16
	3.0	12
		20
14.875	1.0	12
		20
	2.0	12
	3.0	12
		20
15.75	1.0	12
	2.0	20
	3.0	16

TABLE 3 - Mean Tablet Friability and Dissolution Characteristics of the 24 Experimental Batches, with the Actual Granulation Moisture Content, Mean Tablet Hardness, Mean Tablet Weight, and Mean Tablet Thickness of Each Batch

Tablet Strength (mg)	Granulating Fluid (%)	Granulation Moisture Content (%)	Tablet Hardness ±SD (SCU)	Tablet Weight ±SD (Mg)	Tablet Thickness ±SD (mm)	Tablet Friability (%) or No. of Broken Tablets	% Dissolved ±SD (Avg. of Six Tablets) 10 min	20 min	30 min
250	14.0	1.0	12.0 ± 1.0	381 ± 1	3.902±0.011	0.25	44 ± 6	91 ± 4	97 ± 0
250	14.0	1.0	Target hardness (20 SCU) not obtainable						
250	14.0	2.0	16.0 ± 0.7	375 ± 2	4.016±0.017	0.25	53 ± 4	94 ± 2	97 ± 1
250	14.0	3.0	12.1 ± 0.5	387 ± 2	4.009±0.011	0.30	68 ± 10	98 ± 1	99 ± 0
250	14.0	3.0	20.3 ± 0.7	382 ± 3	4.022±0.012	0.22	46 ± 5	92 ± 4	100 ± 0
250	14.875	1.0	12.0 ± 0.6	388 ± 2	3.944±0.015	0.22	31 ± 4	69 ± 7	97 ± 4
250	14.875	1.0	Target hardness (20 SCU) not obtainable						
250	14.875	2.0	12.0 ± 0.6	380 ± 4	3.954±0.015	0.26	25 ± 3	58 ± 6	90 ± 2
250	14.875	3.0	11.8 ± 0.6	387 ± 3	4.026±0.015	0.30	29 ± 3	72 ± 6	96 ± 2
250	14.875	3.0	19.3 ± 1.2	379 ± 4	3.994±0.041	0.25	32 ± 3	71 ± 6	95 ± 2
250	15.75	1.0	12.1 ± 0.5	387 ± 2	3.995±0.012	0.22	24 ± 2	55 ± 6	87 ± 4
250	15.75	2.0	19.8 ± 1.0	381 ± 4	4.015±0.025	0.22	23 ± 2	52 ± 3	80 ± 3
250	15.75	3.0	16.0 ± 1.0	380 ± 5	4.088±0.040	0.28	21 ± 1	47 ± 3	73 ± 2
500	14.0	1.0	12.2 ± 0.5	750 ± 3	7.052+0.009	4 broken	89 ± 4	98 ± 1	98 ± 1
500	14.0	1.0	20.2 ± 0.6	747 ± 3	6.664+0.016	0.00	59 ± 2	95 ± 1	98 ± 1
500	14.0	2.0	15.5 ± 0.8	753 ± 5	6.982+0.019	0.11	90 ± 3	98 ± 1	98 ± 1
500	14.0	3.0	12.2 ± 0.6	757 ± 4	7.231+0.012	0.24	94 ± 4	98 ± 1	98 ± 1
500	14.0	3.0	20.3 ± 0.9	756 ± 5	6.870+0.032	0.15	86 ± 6	98 ± 1	98 ± 1
500	14.875	1.0	12.1 ± 0.8	761 ± 8	7.170+0.034	5 broken	56 ± 5	93 ± 3	98 ± 1
500	14.875	1.0	20.0 ± 0.9	762 ± 5	6.834+0.013	0.00	39 ± 1	76 ± 3	97 ± 1
500	14.875	2.0	11.9 ± 0.9	762 ± 7	7.241+0.009	7 broken	57 ± 4	94 ± 3	98 ± 1
500	14.875	3.0	11.9 ± 0.6	753 ± 4	7.196+0.006	0.25	62 ± 3	94 ± 2	98 ± 1
500	14.875	3.0	20.2 ± 1.1	758 ± 6	6.837+0.032	0.09	42 ± 4	78 ± 5	97 ± 1
500	15.75	1.0	12.4 ± 0.8	762 ± 7	7.195+0.082	4 broken	46 ± 5	85 ± 5	96 ± 3
500	15.75	2.0	20.0 ± 1.5	748 ± 6	6.790+0.022	0.08	28 ± 1	62 ± 3	87 ± 1
500	15.75	3.0	15.8 ± 1.0	773 ± 5	7.189+0.014	0.14	35 ± 6	70 ± 5	91 ± 3

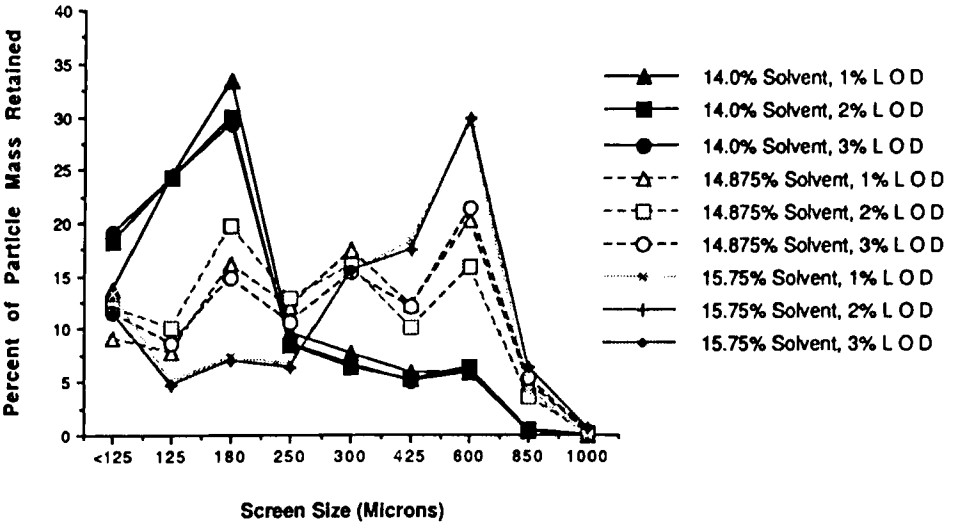

FIGURE 1

Graph of particle size distributions for granulations manufactured with three different quantities of granulating fluid and dried to three different moisture contents

TABLE 4 - Bulk and Tapped Density of the Granulation, and the Calculated Percent Compressibility, at Different Levels of Granulating Fluid

Granulating Fluid (%w/w)	Bulk Density ± SD (gm/cc)	Tapped Density ± SD (gm/cc)	% Compressibility
14.000	0.626 ± 0.027	0.710 ± 0.010	11.8
14.875	0.658 ± 0.003	0.777 ± 0.008	15.3
15.750	0.655 ± 0.006	0.785 ± 0.017	16.6

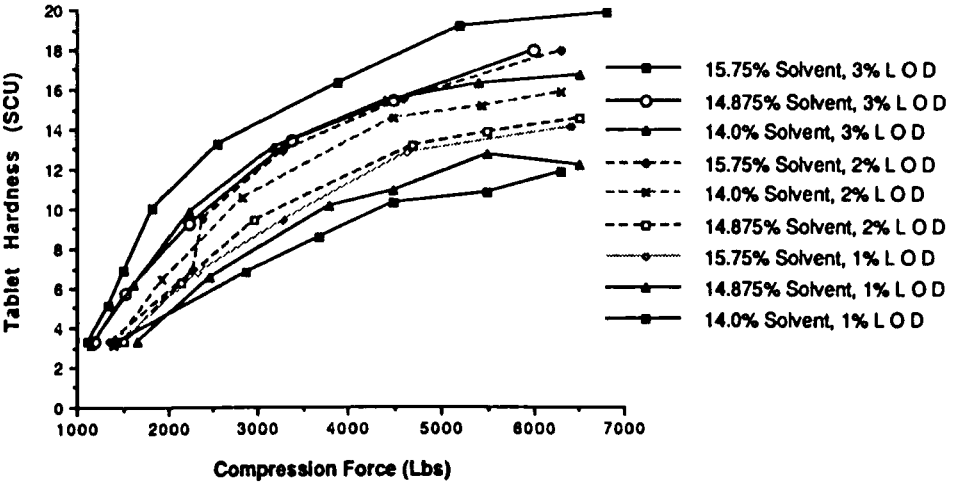

FIGURE 2

Graph of compression force versus tablet hardness for granulations manufactured with three different quantities of granulating fluid and dried to three different moisture contents, and compressed into 250 mg strength tablets

increased amount of solvent forming denser, as well as coarser, more irregularly shaped granules.

Figures 2 and 3 show that the amounts of compression force and ejection force required to produce a tablet at a specific hardness are mainly influenced by granulation moisture content, with granulating fluid quantity exerting a minor influence on compressibility. Higher LODs usually required less compression pressure to obtain a given tablet hardness, and less ejection force to eject the tablet from the die. Larger quantities of granulating solvent also caused a weak trend towards less compression force being necessary to obtain a particular tablet hardness.

When tablet thickness was examined (shown in Table 3), it was found for the 500 mg tablets that there was a loose rank order correlation between thickness and friability, with thicker tablets tending to exhibit higher

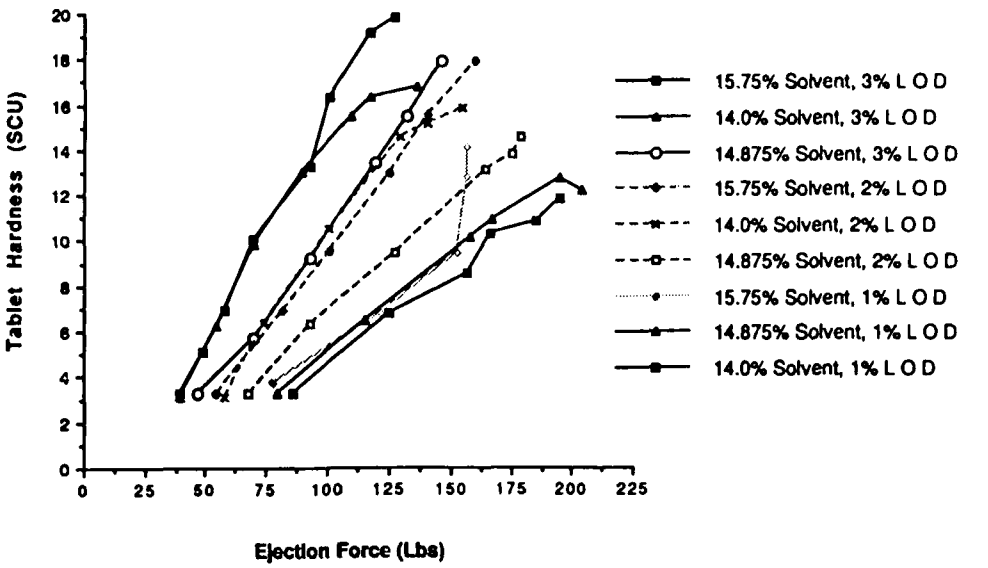

FIGURE 3

Graph of ejection force versus tablet hardness for granulations manufactured with three different quantities of granulating fluid and dried to three different moisture contents, and compressed into 250 mg strength tablets

friability. This is likely incidental to the strong rank order relationship between tablet hardness and tablet thickness; lower tablet hardnesses resulted in higher thickness values, and lower hardnesses also caused higher friability values. For the 250 mg tablet, no correlation between thickness and friability or hardness was demonstrated.

As was noted in the Experimental Section, two tablet batches that were included in the original experimental design for the 250 mg tablets turned out to be impossible to manufacture. Due to the loss of the data from these two batches, quadratic equations were not generated for the 250 mg tablets because the resultant predictive accuracy of the equations would be low. However, for the 500 mg tablets, all of the batches required by the experimental design were manufactured, and so reliable quadratic equations

TABLE 5 - Analysis of Variance for the Regressions, and R^2, for Tablet Friability and Dissolution

Item	F Value	Significance of F	R^2
Regression for friability	24.6780	0.0116	0.987
Regression for dissolution	32.7310	0.0077	0.990

could be generated. The coefficients for the quadratic equation describing the model for tablet friability were generated for the 500 mg tablets, and the significance of the model's terms was evaluated. Table 5 shows that the friability model for the 500 mg tablet was significant at the $p = 0.01$ level, and it had good predictive characteristics ($R^2 = 0.987$).

Table 6 demonstrates that for the friability model, tablet hardness, the cross-term tablet hardness x moisture content, and tablet hardness squared were significant terms in the equation at the $p<0.05$ level. In order to further describe the behavior of the tablet friability, contour surface plots were generated. The resulting contour surfaces (Figures 4-6) clearly show the impact that varying the amount of granulating solvent, the granulation moisture content, and tablet hardness had on tablet friability. Figures 4-6 demonstrate that as hardness increased, friability decreased. On the other hand, moisture content did not significantly influence friability. Because compression and ejection forces were dependent on moisture content, this indicated that a granulation's compression and ejection force requirements to obtain a specific tablet hardness did not affect tablet friability. Varying the quantity of granulating fluid, and the correspondingly large differences in particle size distribution, had little influence on friability.

For the analysis where tablet dissolution was the dependent variable, the 10 minute dissolution time point was selected because no formulations had

TABLE 6 - Values of the Coefficients for the General Quadratic Equation that were Generated via the Multiple Linear Regression Analysis for the 500 mg Tablet

Coefficient (Corresponding Terms)	Dissolution		Friability	
	Coefficient	P-Value	Coefficient	P-Value
b_0 (Intercept)	34.5538	0.0066	1.8758	0.3024
b_1 (Granulating solvent)	-433.4018	0.0077	-17.1941	0.4573
b_2 (Moisture content)	118.5312	0.0193	-9.8266	0.2000
b_3 (Hardness)	-0.0206	0.8828	-0.0542	0.0332
b_4 (Granulating solvent x Moisture content)	-855.9334	0.0124	37.1576	0.4541
b_5 (Granulating solvent x Hardness)	0.8632	0.2488	-0.0890	0.4634
b_6 (Moisture content x Hardness)	0.6278	0.1886	0.5291	0.0001
b_7 (Granulating solvent x Granulating solvent)	1362.0421	0.0113	61.7837	0.4276
b_8 (Moisture content x Moisture content)	33.5004	0.9314	-111.5645	0.1013
b_9 (Hardness x Hardness)	-0.0044	0.1934	0.0015	0.0143

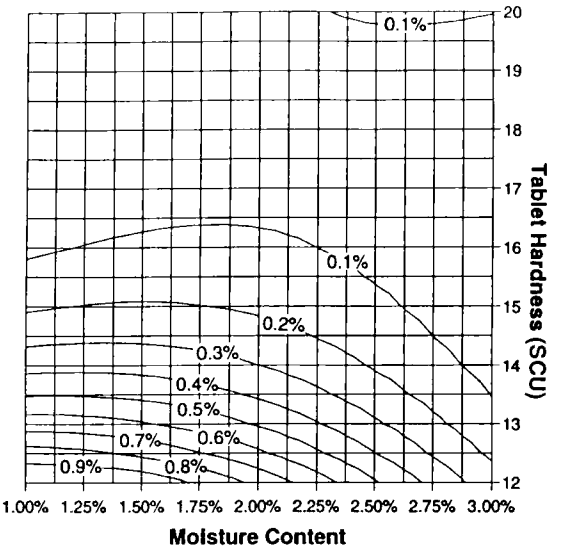

FIGURE 4
Contour surface plot for tablet friability with 14.0% granulating solvent

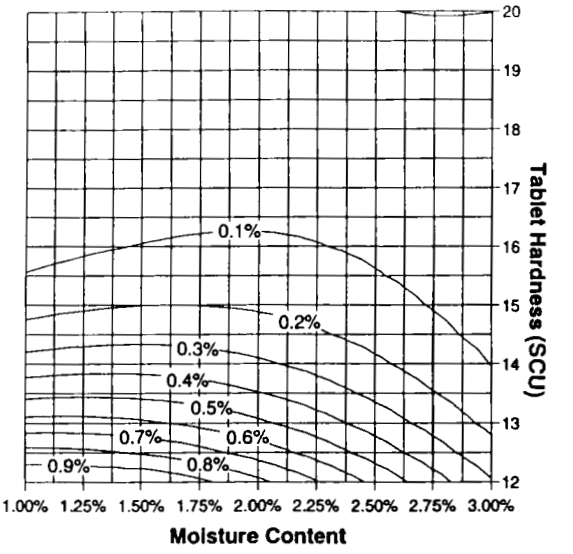

FIGURE 5

Contour surface plot for tablet friability with 14.875% granulating solvent

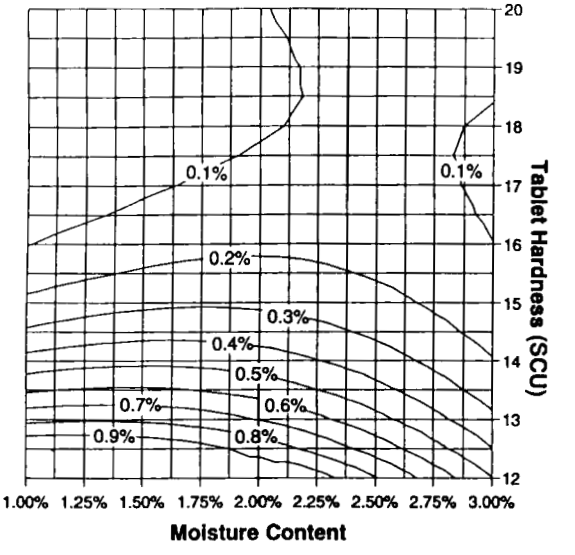

FIGURE 6

Contour surface plot for tablet friability with 15.75% granulating solvent

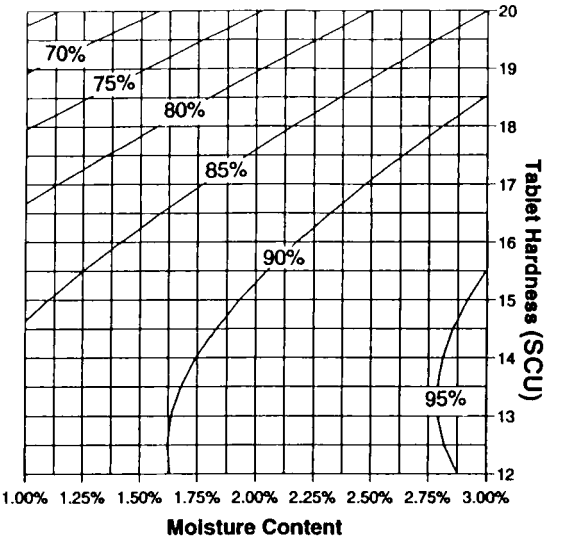

FIGURE 7
Contour surface plot for tablet dissolution with 14.0% granulating solvent

reached the upper limit of 100% dissolved at that time point. The model was significant at the $p = 0.01$ level (Table 5), and had good predictive characteristics ($R^2 = 0.990$). The results of the analysis (Table 6) illustrate that the terms granulating solvent quantity, granulation moisture content, the cross-term granulating solvent quantity x granulation moisture content, and granulating solvent quantity squared had a significant impact on tablet dissolution at the $p < 0.05$ level. Figures 7-9 demonstrate that the quantity of granulating fluid was the dominant determinant of tablet dissolution characteristics, with less solvent resulting in faster dissolution. When the amount of granulating fluid was controlled, the effect of moisture content was highly interactive with the quantity of granulating fluid, so that at the lower level of granulating fluid, higher granulation moisture content was found to result in faster dissolution. At the higher quantity of granulating fluid, the opposite effect was seen. Varying the tablet hardness had only a slight (and not statistically significant) influence on dissolution.

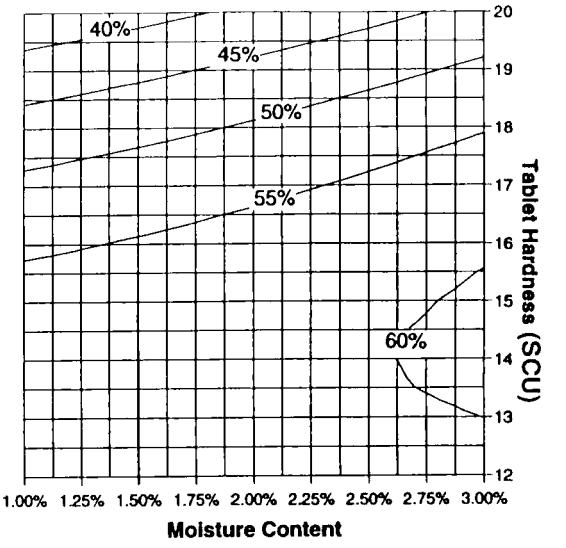

FIGURE 8

Contour surface plot for tablet dissolution with 14.875% granulating solvent

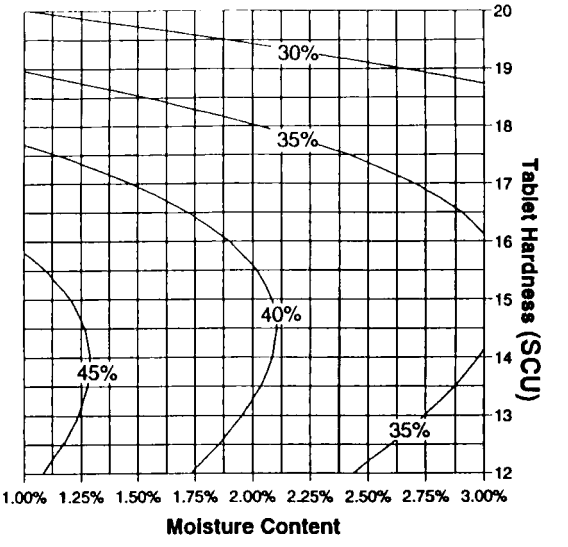

FIGURE 9

Contour surface plot for tablet dissolution with 15.75% granulating solvent

TABLE 7 - Friability and Dissolution for Tablets When the Amount of Magnesium Stearate in the Formulation is Doubled to 0.4%, with the Values for Corresponding Tablets Containing 0.2% Magnesium Stearate Included (Where Available) for Comparative Purposes

Amount of Magnesium Stearate (%)	Tablet Strength (mg)	Granulation Moisture Content (%)	Tablet Hardness ± SD (SCU)	Tablet Weight ± SD (mg)	Tablet Friability (Avg.) (%)	% Dissolved ± SD (Avg. of Six Tablets) 10 min	20 min	30 min
0.4	250	2.0	12.3 ± 0.4[a]	379 ± 1	0.21	51 ± 7	94 ± 2	99 ± 0
0.2	250	3.0	12.1 ± 0.5	387 ± 2	0.30	68 ± 10	98 ± 1	99 ± 0
0.4	250	3.0	12.2 ± 0.5	381 ± 1	0.25	53 ± 4	97 ± 1	100 ± 0
0.4	250	3.0	15.3 ± 0.7[b]	381 ± 1	0.21	50 ± 3	93 ± 2	99 ± 0
0.4	500	2.0	12.4 ± 0.3	762 ± 2	6 broken	N.A.[c]	N.A.	N.A.
0.2	500	2.0	15.5 ± 0.8	753 ± 5	0.11	90 ± 3	98 ± 1	98 ± 1
0.4	500	2.0	16.2 ± 0.6	763 ± 3	5 broken	77 ± 4	98 ± 0	98 ± 0
0.4	500	2.0	20.0 ± 0.7	764 ± 1	0.14	62 ± 2	97 ± 1	98 ± 0
0.2	500	3.0	12.2 ± 0.6	757 ± 4	0.24	94 ± 4	98 ± 1	98 ± 1
0.4	500	3.0	11.8 ± 0.4	767 ± 2	2 broken	N.A.	N.A.	N.A.
0.4	500	3.0	15.8 ± 0.5	764 ± 1	0.12	90 ± 5	98 ± 0	98 ± 0
0.2	500	3.0	20.3 ± 0.9	756 ± 5	0.15	86 ± 6	98 ± 1	98 ± 1
0.4	500	3.0	20.0 ± 0.8	765 ± 3	0.12	67 ± 3	98 ± 1	98 ± 0

[a] Maximum hardness achievable for this granulation was 13.7 SCU (results reported are for 12.3 SCU)

[b] Maximum hardness achievable was 15.3 SCU

[c] N.A. stands for *Not Available*

The consequences of doubling the amount of magnesium stearate in the formulation can be seen in Table 7. The first effect found was that for the 250 mg tablet the granulations that contained the larger quantity of the lubricant were much less compressible. Although the 250 mg tablets were originally compressed from granulations manufactured with the lower quantity of magnesium stearate, with 14.0% granulating solvent, and with 2% and 3% LODs to hardnesses of 16 and 20 SCU, respectively, when the magnesium stearate level was doubled the maximum achievable hardnesses were 13.7 and 15.3 SCU, respectively. Increasing the amount of the lubricant did not have a notable effect on the friability of the 250 mg tablets at a given hardness; however, it had a large impact on the 500 mg tablets. The 500 mg tablets made with the lower amount of magnesium stearate, 14.0% granulating solvent, and having moisture contents of 2% and 3% never broke during friability testing. Tablets that incorporated the larger quantity of the lubricant failed friability testing due to tablet breakage at 2% LOD with hardnesses of 12 and 16 SCU, and at 3% LOD with a hardness of 12 SCU. This greater friability, combined with the lower compressibility seen for the 250 mg tablet, indicated that doubling the amount of magnesium stearate adversely affected intergranule binding. Increasing the quantity of magnesium stearate also caused slower tablet dissolution.

CONCLUSION

The results of this study show that tablet friability can be affected by process parameters. This study indicated that tablet hardness and, to a much lesser extent granulation moisture content (only as a component of a cross-term) had significant impacts on friability. The amount of compression and ejection force required to compress the granulations to a given hardness did not influence friability. Tablet thickness was loosely associated with friability, but only for the larger tablet. The relationship between thickness and friability was probably due to the effect that hardness had on these two factors. The amount of granulating solvent, which had a large impact on granulation particle size, had little effect on friability. The results suggest that a thorough understanding of the processing factors influencing tablet

friability is important in designing tablet formulations. The drug dissolution rate was also affected by these factors, although the relative importance of the factors was quite different. For dissolution, the most significant factor was the quantity of granulating fluid utilized, followed by granulation moisture content. Tablet hardness did not significantly impact dissolution. Doubling the amount of magnesium stearate in the granulation decreased the tablet hardness achievable for the smaller tablet; for the larger tablet it resulted in greater tablet friability. Tablet dissolution was affected less adversely than was friability by the use of the higher level of lubricant.

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