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OPTIMIZING THE FRIABILITY OF A TABLET FORMULATION

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ABSTRACT

The impact on tablet friability caused by the loss-on-drying of the granulation, the granule-size distribution, the lubricant concentration, the compression force, and the pre-compression was scrutinized in a factorially designed experiment. A reduction of friability was obtained by reducing the deviation of the granulation loss-on-drying from approximately 4.6%; by decreasing the lubricant concentration; or by increasing the compression force.

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INTRODUCTION

Recently, the optimization of the disintegration time and crushing strength of a tablet formulation was published[1]. This investigation is now completed in that the friability has been tested.

MATERIALS AND METHODS

Materials

Tablets consisting of a freely soluble drug, lactose, corn starch, povidone, cellulose and magnesium stearate from an earlier test[1] stored ambiently, which means approximately 20°C and 50% relative humidity, for 18 weeks.

Test

Tablets in samples of approximately 6 g were tested by being subjected to 100 revolutions during 4 mins. in the Roche friabilator[2]. The loss due to abrasion was the measure of friability, and it was expressed as a percentage.

RESULTS AND DISCUSSION

It is known from previous experience that the friability of this formulation changes very little when stored at 25°C and less than 75% relative humidity. Consequently delaying the friability measurements did not entail any disadvantages.

The friability values were low, less than 0.35% in the whole investigated domain.

A multiple linear regression analysis resulted in the following model after reduction in a backward elimination procedure:

$$Y_3 = - 0.073X_1 + 0.180X_3 - 0.000095X_4 +$$

$$+ 0.008X_1^2 + 0.390 \qquad \text{Eq 1}$$

where Y_3 stands for the response variable friability and the investigated independent variables were: loss-on-drying of dried granulation (X_1), granule-size distribution of comminuted granulation (X_2), lubricant concentration (X_3), compression force (X_4) and pre-compression (X_5). This means that X_1, X_2 and X_4 exerted a significant - $P<0.05$ - influence on friability. The variable X_3 increased the response while X_1 and X_4 reduced it. The squared multiple correlation coefficient was 0.57.

When the ratio (Y_4) of mean tablet weight to mean tablet thickness was included as a co-variate, the multiple correlation coefficient was increased to 0.68. The following model was obtained after stepping down:

$$Y_3 = - 1.2 \cdot 10^{-3}X_1^2 - 0.2 \cdot 10^{-5}X_{2,150}X_4 -$$

$$- 0.1 \cdot 10^{-5}X_{2,300}X_4 + 0.2 \cdot 10^{-5}X_{2,300}X_5 +$$

$$+ 1.57 \cdot 10^{-4}X_3X_4 - 0.066Y_4 + 3.866 \qquad \text{Eq 2}$$

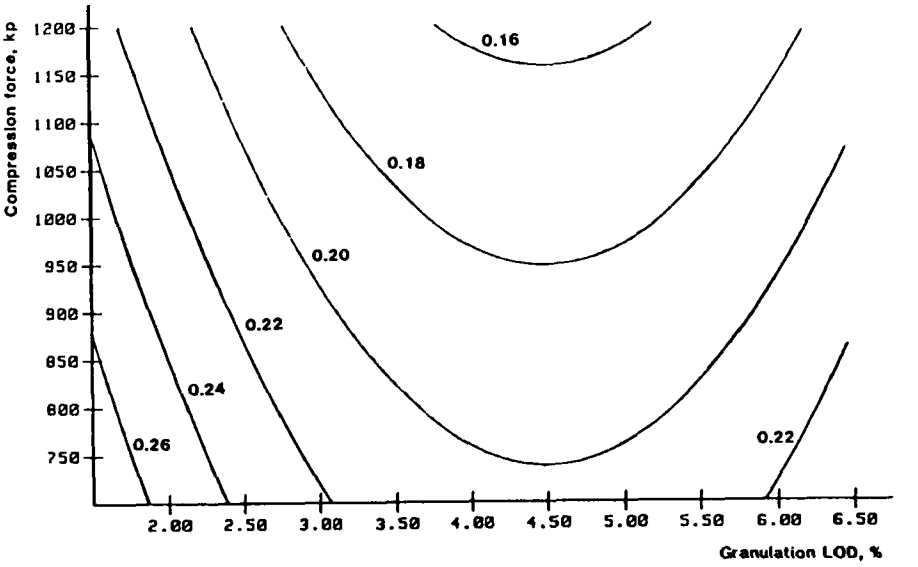

FIGURE 1

where $X_{2,150}$ denotes a granule fraction less than 0.150 mm and $X_{2,300}$ stands for a granule fraction larger than 0.300 mm. The model indicates that the ratio of mean weight to mean thickness exerts an important influence on tablet friability. This was not the case with regard to disintegration time and crushing strength[1].

Fig. 1 presents the response surface contour plot of friability at a fixed lubricant concentration with reference to the reduced model without co-variate. There was minimal tablet friability at a granulation LOD of approximately 4.6%. Thus the contour plot was very similar to that of crushing strength in the earlier report, but the crushing strength was maximal at 4.6% LOD. Higher compression forces reduced tablet friability.

Tablet friability, expressed as a percentage, versus compression force (Y-axis) and granulation LOD (X-axis) at a lubricant concentration of 0.25%.

CONCLUSIONS

Friability was low in respect to all the tablet variants.

As could be expected, the tablet friability of the investigated formulation increased when the deviation of the granulation LOD was increased from approximately 4.6%. Besides, friability was greater when the lubricant concentration was increased, whereas a higher compression force reduced the response.

The ratio of mean tablet weight to mean tablet thickness had an important influence on tablet friability.

ACKNOWLEDGMENTS

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