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EFFECTIVENESS OF LUBRICANTS AND LUBRICATION MECHANISM IN TABLET TECHNOLOGY

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ABSTRACT

A method for quantitative evaluation of the effectiveness of the lubricant used in tablet technology has been recentey proposed by the authors. It was based on the ejection force determination expressed as relationship between the force on the lower punch and the time (ejection curve).

The proposed methodology allows now quantitative analysis of the tablet ejection, considering that the lot of the parameters linked to the conditionning, tooling and operative procedure that can negatively affect the measurement, were optimized.

During the methodology development, series of ejection curves, relative to different type of diluent and a variety of lubricants, were collected.

Certain relationship between the form of ejection curve and the capacity of lubricant to reduce frictions was observed.

Starting from these observations, the aim of this work was to analyze quantitatively the ejection curves obtained with the proposed methodology, in order to have a measure of the effectiveness of the lubricant in the formulation.

The ejection curve must be considered as an effective means for this type of analysis, mainly because its pattern modifies according to formulative parameters such as compression force and lubricant amount.

Moreover, the product of ejection peak value and area under the ejection curve gives a dependent parameter that appears to be very sensitive to the conditions affecting tablet manufacturing in terms of lubrication. Because of its informative quality, this lubrication index could be profitably be used in the optimisation procedures for formula preparation.

INTRODUCTION

In tablet technology, lubrication is a crucial problem. Recently, we proposed a methodology in order to evaluate lubrication in tablet technology, based on the determination of the upper force level value at which problems occur during compression (1). Considering that the parameters linked to conditioning, tooling and operative procedures, negatively affecting the force measurement, were standardised, a quantitative analysis of tablet ejection can be done. To develop the methodology, numerous ejection curves, expressed as force on lower punch versus time, for various diluents and lubricants, were collected. Evident relationships between the shape of the ejection curve and the capacity of the lubricant to reduce friction were observed. Then the ejection curves obtained could be assigned to two different types of behaviour.

Starting from these observations, the aim of this work was to quantitatively analyse the ejection curves collected with the proposed methodology, in order to obtain a measure of lubricant effectiveness and information about lubrication mechanism.

Series of ejection curves, from mixtures prepared using two different diluents and various lubricants, were collected. Ejection curves were recorded at increasing amounts of the same lubricant and at several compression force levels.

MATERIALS AND METHODS

The following pharmaceutical excipients were used for mixture preparation :

- as diluents : Lactose Fast Flo (SEPPIC Paris F) Em compress (SPCI, La Plaine St. Denis F)
- as lubricants : magnesium stearate (Cooper, Melun F), Compritol 888 (Gattefossé, Saint Priest, F), Precirol atomisé (Gattefossé, Saint Priest, F).

The diluent was mixed with the lubricant using the successive portions technique (1). Ejection curves were recorded on a single punch tablet machine (OA Frogerais, F) instrumented for upper and lower forces and displacement measurements. The operative procedure applied for standardised compression consists of four steps, namely a) preliminary adjustments, b) tool cleaning, c) measurement standardisation and d) powder compression. The four steps summarised in Table I have already been described.

RESULTS AND DISCUSSION

Numerous ejection curves, obtained by plotting the force on the lower punch versus time during ejection of the tablet prepared by compressing binary mixtures of the two diluents and the various lubricants in the reciprocating tablet machine, were collected. An exhaustive analysis of the total ejection curve has previously been presented (2). In this study we only consider the three first parts. (Figure 1) corresponding to the different lower punch positions.

In the first part of the ejection curve, during the withdrawal of the upper punch, the lower punch does not move and the height of the flat part of the curve corresponds to the residual force value (T1).

Table 1 : Method for quantitative evaluation of the effectiveness of tablet lubricants

1. PRELIMINARY ADJUSTMENTS
Room air conditionning Speed of the machine
2. TOOL CLEANING
Compression of a cleaning mixture for 4 minutes in standardised conditions
3. STANDARDIZATION
Compression of a standard mixture and comparison of the answer obtained with standardized values.
If the values obtained are not inside the standardized values, go to point 2 for a new tool cleaning
4. MEASUREMENT
Compression of 30 tablets in standardized conditions under a low upper punch displacement
If no ejection problems occur, increasing of the upper punch displacement in order to determine the "limit of industrial workability", that is the maximum upper punch force that makes it possible to compress for 3 minutes without ejection problems

Then, the lower punch moves upwards and the force on it suddenly increases, giving rise to the appearance of the typical ejection force peak.
After the peak, the force can stay constant, or it can drop, to varying levels, showing different patterns. This second part of the curve can be divided into two subparts in dependence on the location of the tablet : in the first (T2a), the tablet is completely inside the die and, in the second (T2b), the tablet starts to emerge from the die.

Lubrication mechanism

The ejection curves obtained were divided into two main types of behaviour, having the shapes reported in Figure 2. Type I behaviour shows, after the ejection

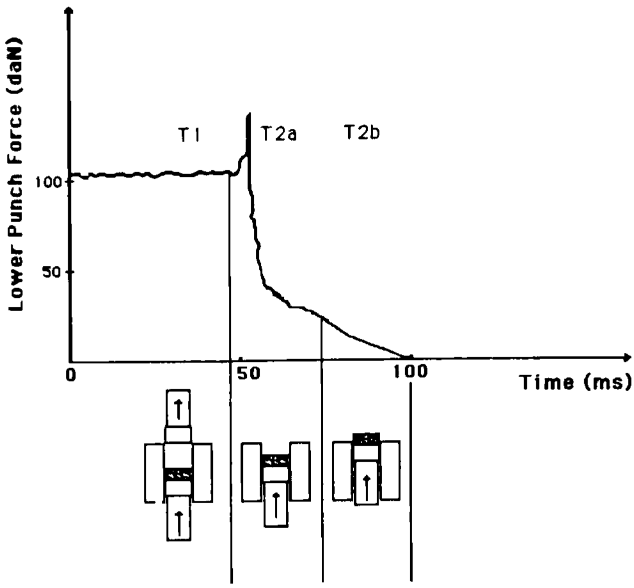

Figure 1. Ejection force curve time with respect to lower punch movement.

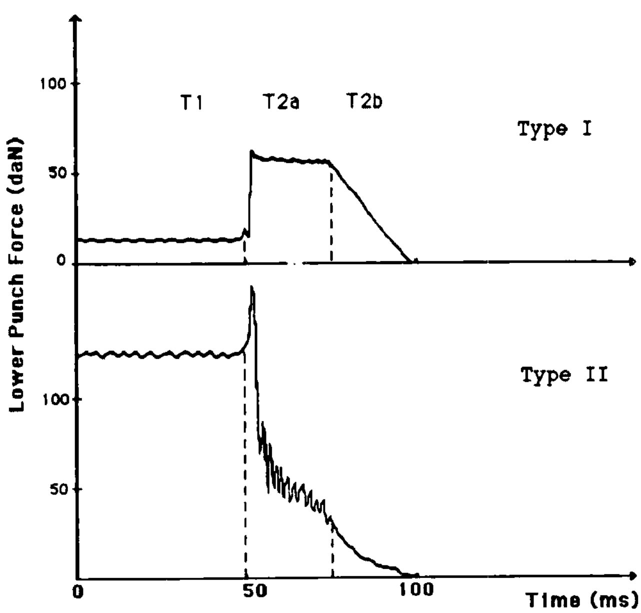

Figure 2. Typical ejection curves belonging to the Type I and Type II behaviours obtained at the same compression force level

peak, a steady ejection force value. This force decreases significantly as the tablet emerges from the die. Generally, no ejection problems occur during the manufacturing of tablets with a type I behaviour. The appearance of the tablet, particularly in relation to the lateral side, is smooth without any scraping or signs of indentation.

The main characteristic of the Type I curve, is the presence, after the ejection peak, of a steady resistance exerced by the tablet during its upward movement. Therefore, this curve can be interpreted, from a mechanical point of view, considering that the resistance from the tablet during ejection is like a secondary residual force. For example, magnesium stearate, with both the diluents and at all the concentrations used, shows Type I behaviour. Figure 3 shows a series of ejection curves obtained at increasing compression force levels with lactose lubricated with 1 % of Mg stearate. The shape of the curves indicates that this lubricant is capable of distributing the stresses during compression, but mainly during the ejection phase, quite possibly owing to its capability of spreading over the diluent particles. The lubrication mechanism evoked for magnesium stearate, as being capable of coating the diluent particles during mixing because of its crystallographic structure (4), agrees with the observation made in our experimental conditions.

In contrast, the other lubricants studied show mainly Type II behaviour, particularly when they are present at a low concentration. The Type II is characterised by a sharp ejection peak and an immediate steep decrease in the ejection force just after the ejection peak.

But the shape of the curves, after the ejection peak is different with the different mixtures, corresponding to different behaviour during manufacturing (Figure 4) :

- for the Type IIa, obtained for example with lactose fast flow mixed with 0.75 % of Precirol, the shape of the curve is characterised by an immediate decrease in the force necessary to move the tablet inside the die.

There is no ejection problem during the manufacturing of these tablets if the ejection peak level is not too high, as a consequence of a too high compression force level.

- but, for the Type IIb, obtained for example with a mixture of lactose fast flo with 0.75 % of Compritol, a series of rise and fall sequence in the ejection signal is observed.

The cause of this special signal is the binding of the tablet in the die wall, and its gliding during ejection is characterised by a "stop and go" sequence.

As a consequence, the tablet, which produces this result on the curve, shows evident signs of indentation on the lateral side, and its manufacturing often provokes anormal noise in the tablet machine and a binding in the die.

Looking at the mechanism described, it must be considered that in this case the distribution of the lubricant over the diluent is less favoured than with the previous lubricant. The coverage of diluent particles requires more lubricant in order to obtain a constant gliding of the tablet during ejection.

Mechanically, this curve can be interpreted, as the inability of the tablet to accommodate the internal stresses, owing to insufficient lubrication, which affects the flow between the particles of the compressed powder bed.

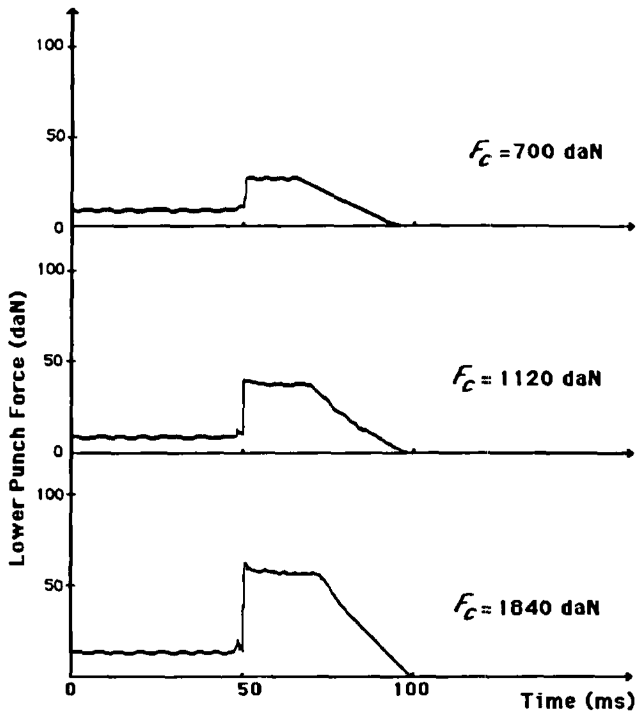

Figure 3. Ejection curves obtained at increasing compressior force using Lactose Fast Flo 1% Magnesium stearate mixture.

This is neatly demonstrated by observing the change in curve behaviour for the same lubricant according to its amount in the mixture. Figure 5 shows the evolution at a constant compression force level of the ejection curve in relationship to the concentration of lubricant. It can be easily seen, for example, that using Precirol the ejection curve behaviour moves from Type II to Type I according to the increase in lubricant content. The same was observed also with Compritol lubricant.

On the figure 6, the same mixture of lactose fast flo with 1 % of Precirol is compressed at different compression forces.

We can observe an increase in the residual force and in the ejection peak with the increasing in the compression force. But the pattern of the curve is in between the classical Types I and IIa.

It is interesting to note that it would not be possible to compress with a higher compression force level with this percentage of lubricant owing to ejection problems.

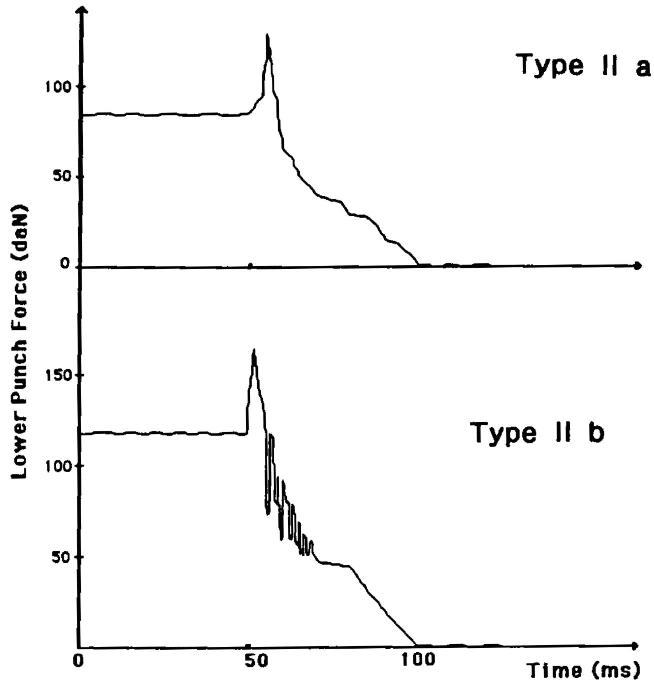

Figure 4. Ejection curves obtained at compression force of 1100 daN with Lactose Fast Flo mixed with 0.75% of Precirol (Type II a) and Compritol (Type II b).

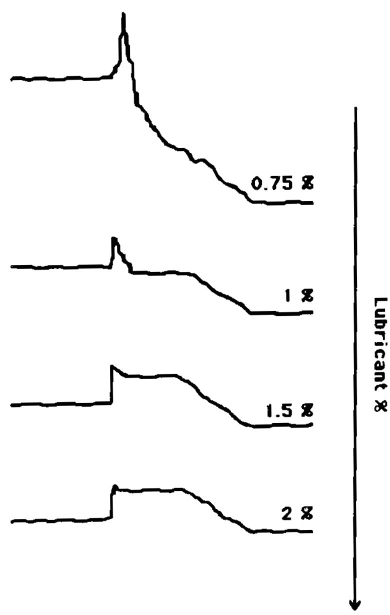

Figure 5. Ejection curves obtained at compression force of 1100 daN with Lactose Fast Flo mixed with increasing percentage of Precirol.

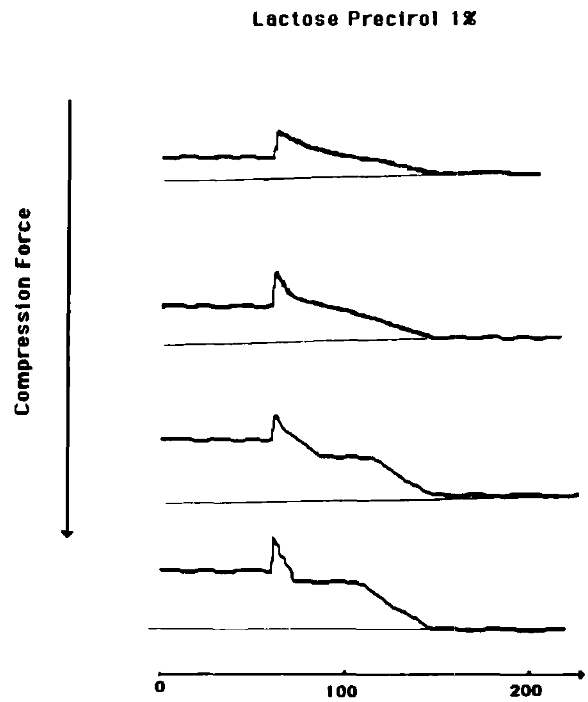

Figure 6. Ejection curves obtained at different compression forces with Lactose Fast Flo mixed with 1% Precirol

Figure 7, is a schematic representation of the curves obtained, with the Lactose fast flo and the lubricant Precirol with different percentages of lubricant and at different compression force levels. We can observe that the Type of the curves is always IIa (or in between Types I and IIa) when the amount of Precirol is under 1.5 % and of Type I when it is above however high the level of compression force.

The figure 8 is exactly the same, but with Compritol

We have seen that with the mixture of lactose fast flo with 0.75 % of compritol we obtain a curve of Type IIb if the compression force level is above 1.000 daN, with a lot of ejection problems. We can see here that with the same percentage, but a compression force level for under 1.000 daN, we obtain a Type II a curve, and no ejection problems.

With 1 % of Compritol, the curve is of Type I for a low compression force level, and Type II a above 1.000 daN.

But it is interesting to note that we don't observe Type IIb, even if the compression force level is high, in our experimental conditions.

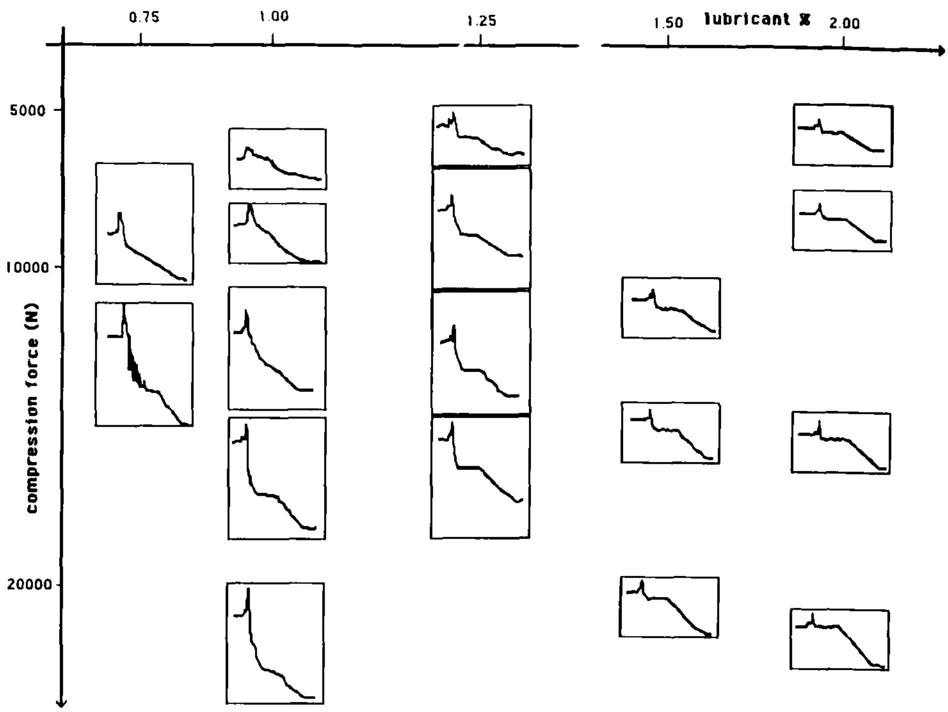

Figure 7. Ejection curves obtained at different compression forces with Lactose Fast Flo mixed with Precirol at different percentages.

With the increase in the percentage of lubricant, the limit of the compression force level between the Type I and the Type IIa is higher.

Lubricant effectiveness

From ejection curves a quantitative evaluation of the lubrication capacity can be obtained. A common method for assessing the lubricant performance is the measure of the ejection peak in relation to the compression force value. However, in consideration of the two types of lubricant behaviour observed, this value does not demonstrates exhaustively the performance of the lubricant. A more informative approach might be the measurement of the area under the ejection curve, i.e. the impulse made for tablet ejection. The measurement of the area gives an evaluation of the total resistance exhibited by the tablet to the recovering movement of the lower punch. However, for the two types of lubricant behaviour, the area under the curve for Type II lubricant, at the same compression force level possesses a value lower than the Type I lubricant, even if the evidence of critical situation in ejection is obtained with Type IIb behaviour. Thus considering that for

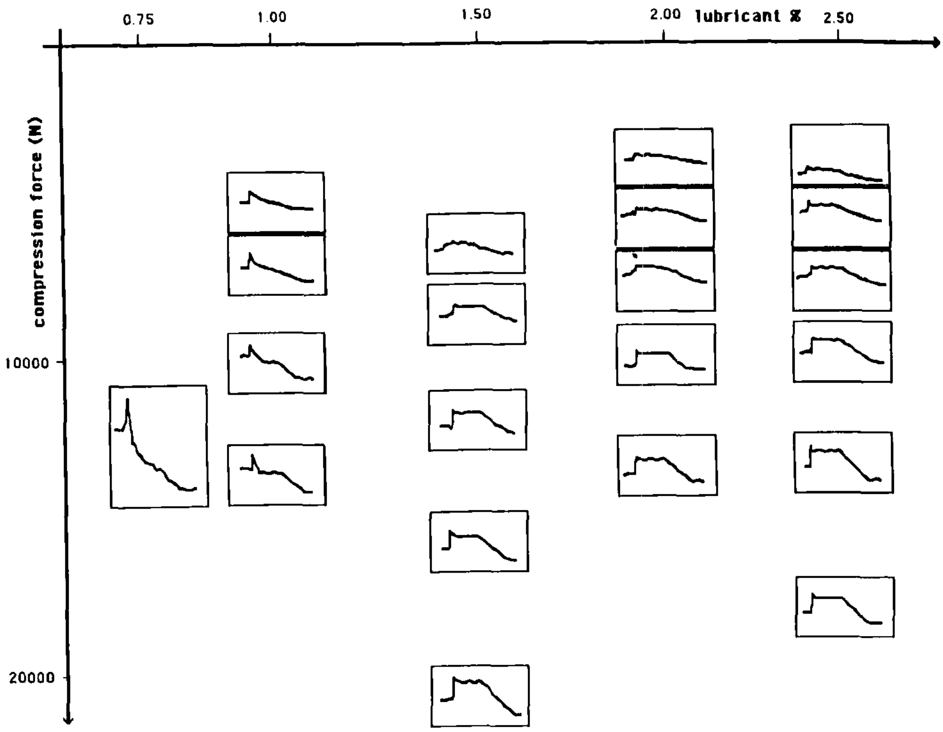

Figure 8. Ejection curves obtained at different compression forces with Lactose Fast Flo mixed with Compritol at different percentages.

lubrication analysis of the tablet both ejection peak and ejection area are partially informative, a lubrication index, obtained by multiplying the ejection peak value by the ejection area (A*EJ), was proposed. Physically, the new value illustrates both the immediate resistance shown by the tablet compressed in the die and the continuous resistance arising from the gliding along the die wall during the recovery of the tablet. Thus, this value was calculated from all the ejection curves recorded and used as dependent variable in an analysis for determining the optimal lubricant percentage in relation to the compression force level used for tablet preparation.

The figure 9 shows the evolution of the lubrication index in correlation with the compression force level and the percentage of lubricant with the mixture of lactose and magnesium stearate. It is clear that a percentage of 0.5 is necessary to obtain a low lubrication index. The correlation with ejection problems is clear : if the amount of magnesium stearate is not sufficient and the compression force not very low, the lubrication index increases very sharply.

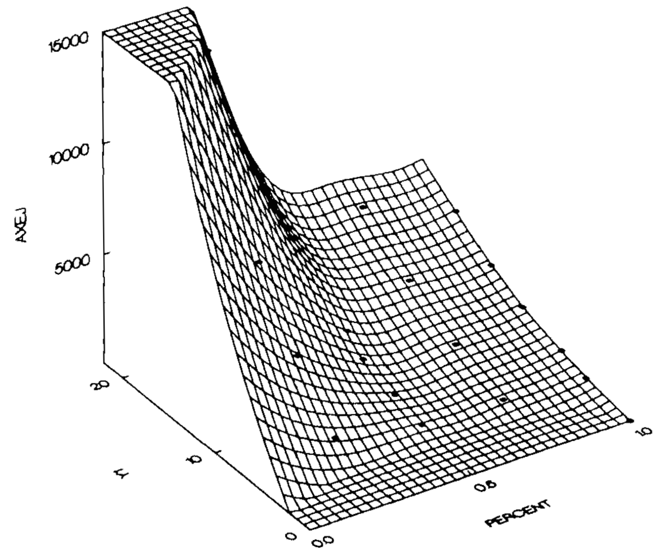

Figure 9. Smoothing surface plot of Lactose Fast Flo - Magnesium stearate mixtures.

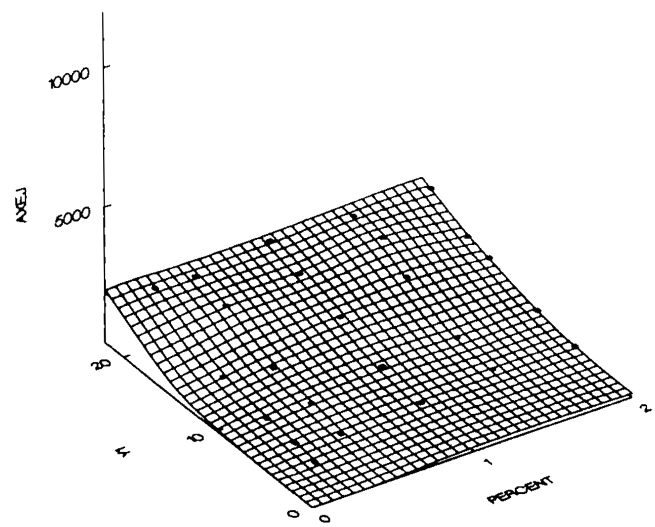

Figure 10. Smoothing surface plot of Emcompress - Magnesium stearate mixtures.

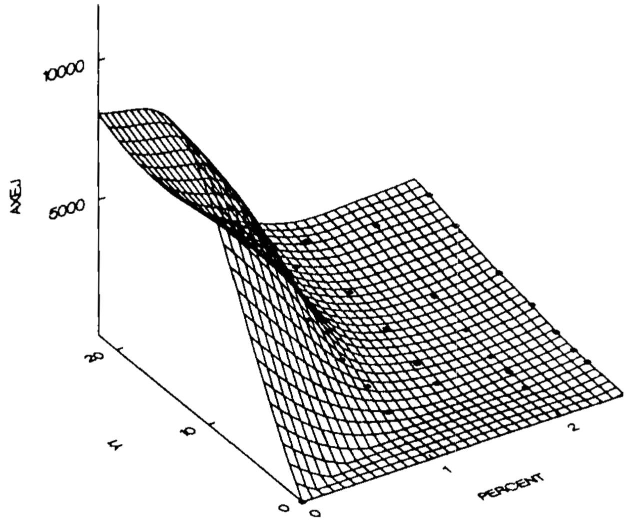

Figure 11. Smoothing surface plot of Lactose Fast Flo - Precirol mixtures.

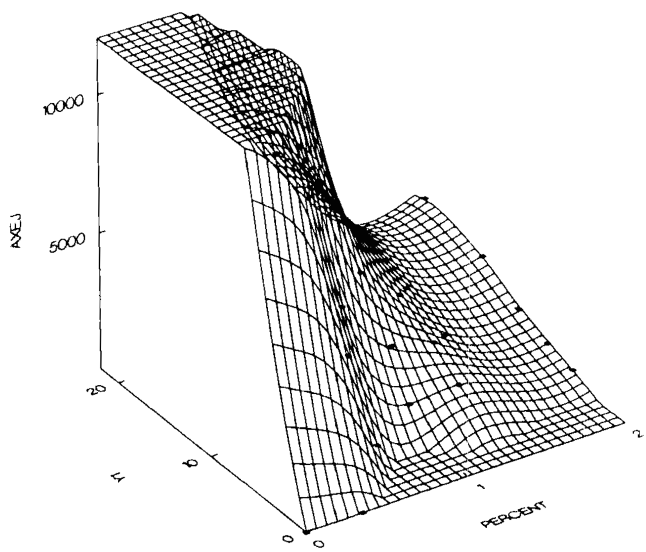

Figure 12. Smoothing surface plot of Lactose Fast Flo - Compritol mixtures.

But with the same magnesium stearate and the diluent : Emcompress, the shape of the response area is completely different (figure 10), in correlation with the industrial workability of the Emcompress/mixtures.
We have already seen the behaviour of the lactose/Precirol mixtures, with an ejection curve of Type IIa. The figure 11 confirms our previous findings.
Similary, figure 12 confirms the problems obtained with the lactose/ compritol mixtures, which gives curves of Type IIb and ejection problems, if the amount of lubricant is not sufficient even if the compression force is very low.

CONLUSIONS

From the data obtained it was revealed that the ejection curve gives the possibility to differentiate the lubrication mechanism. The capacity of the lubricant to spread over the diluent particles, or between particle and tooling, is seen to be an important quality for the product.
But the measurements have to be made in strict experimental conditions in order to obtain good reproducible information.

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