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COMPUTER DETERMINATION AND COMPARISON OF THE COMPRESSION BEHAVIOUR OF POWDER MIXTURES

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ABSTRACT

The aim of this work is to analyse the forces measured and stored during compression by using a computer.
We propose to calculate a "tabletibility index" which is very useful to classify the materials according to their capacity to give proper tablets by direct compression.
We can also simulate the energy cycles in chosen experimental conditions, as it is not possible to compare cycles if the experimental conditions are not the same, which is very difficult to obtain.

In addition, this program calculates a "cohesion index" which is a dimensionless number. With this program and this cohesion index, it is possible to define the behaviour of different powder mixtures during compression very accurately. This is very useful to compare a batch to a reference as far as quality control, process control and formulation are concerned.

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INTRODUCTION

The formulation of tablets can be facilitated by the use of an instrumented tablet machine which allow the measurement of forces and of the displacement of the upper punch (1,2,3) It has often been mentioned that the forces measured during the compression are the resultant between the resistance of the product to compression, and the force applied by the upper punch which is dependent on the adjustment of the machine. As a result, the compression cycle (which is the upper punch force plotted against the displacement of this punch) is characteristic of a product if the conditions of the compression are strictly defined (diameter of the punches, depth of the compression chamber, speed of the machine, maximum displacement of the upper punch)(4).

If all these conditions are fulfilled, and only in that case, we have shown that powder mixtures can be compared with each other (5). We have particularly shown that the comparison of the cycles obtained under the same conditions allows the comprehension of the law of the behaviour of these powders and reveals the defects of these cycles ; our technique of qualitative optimization of tablet formulation is based on these notions and on the kwowledge of the hardness of the tablets (6).

But this technique is limited by the lack of precision of the oscilloscope that we use. So, it has been necessary to complete the instrumentation with equipment able to give exact values for a certain number of responses. Then it becomes possible to make finer comparisons either between batches of raw materials, or between nearly similar mixtures. These responses are given with standard deviations :

the value of the deviation of the displacement measures the error in the experimentation. Moreover, the data which are used for quality control are of interest in the field of research, for studying, for example, the shift between the maximum values of the forces and of the displacement plotted against time ; it can be related to the plastic flow of the product under compression (7,8). A significant difference between the deviations of the displacement and of the upper punch force

reveals a lack of regularity in the feeding of the tablet machine.
A significant difference between the deviations of upper and lower punch forces reveals a lack of regularity in the lubrication.

To obtain fine comparisons between different batches, all the measurements have to be made exactly under the same conditions. It is very long and difficult to obtain exactly the same maximum displacement on a single punch machine or the same hardness on a rotary press. In addition, to compare products with quite different densities, this technique is ineffective : some mixtures with a great resistance to compression cannot be compressed with the stated displacement because it produces tablets that are too hard. On the contrary some mixtures remain powder or produce tablets that are too soft.
We have proposed a technique using a constant measured force instead of a constant displacement: we have arbitrarily chosen 20 KN (9). The advantage is that we always obtain a 20 KN resultant. If we associate the value of the hardness obtained at 20 KN to the cycle we will have very helpful information for formulation. The drawback is that the adjustment is tedious and takes a long time. Moreover, the quality of a product under compression cannot be assessed by a single compression at a stated adjustment. The assessment requires the evolution of the force and of the hardness in relation with the adjustment of the machine (10).
Another possibility is to compress all the products so as to obtain the same hardness and to compare the responses of the measured forces and the cycles. But the drawback is that we cannot find a hardness value which can be used as a comparison value for all products. Besides, the adjustments still take much time. These obviously limit the techniques which have been proposed until now. It is the reason why we propose in the study a computerised technique to overcome these limits.

EQUIPMENT

1. Tablet machine

The trials have been made on a FROGERAIS OA eccentric tablet machine with punches of a 1.128 cm diameter. So the area of the punch is equal to 1 cm2. The depth of the chamber is set to 1 cm. Consequently all the experiments are carried out with a constant volume of 1 cm3.

2. Sensors

Upper and lower punches are instrumented with strain gauges. They have been calibrated against a reference device in a hydraulic press. The linearity of the response is guaranteed for the range of measurement used.
A linear variable differential transformer measures the displacement of the upper punch inside the die with an accuracy of 1/100th of mm. The calibration and the linearity have been controlled against a comparator with an accuracy of 1/100th of mm.

3. Electronics

The strain gauges and the displacement transducer are connected to wheatstone bridges selected according to the frequency of the phenomena to be measured.
The visualisation of the signals is obtained with a Y1, Y2/X oscilloscope.

4. Computers

The equipment used is an Apple IIE micro-computer with a 64K RAM central unit, 2 disk drives, a monitor, and an Imagewriter printer. An amplifier interface developed in our laboratory processes the signals which are fed into a multiplexor and then into an analogue digital converter. The programs developed in our laboratory allow the sampling of the signals with a frequency of 2KHZ. The digital values are stored by the central unit which converts them into Newtons for the forces and millimetres for the displacement ; at the beginning of the process, the values of calibration and sensitivity of the bridges are keyed in. The measurements can be made on a single tablet or on a sequence of two to ten tablets ; in that case the responses are the average of the results obtained for each compression. The masses, the thickness and the hardness of the tablets are keyed in. They are stored with the responses in a file on a floppy disk. The exploitation can be made at a later stage with a processing program.
A few adaptations enable the equipment and the program to be used for the measurement of forces on a rotary press. But in this case the measurement

of the displacement of the punches is not possible; no cycle of the force against the displacement of the punch can be obtained. As a result, the studies of formulation can be carried out on a single punch machine only.

RESULTS AND DISCUSSION

Instead of trying to adjust the machine to obtain either a definite force level or a definite tablet hardness, we propose to carry out at least five compression trials at different adjustments in order to cover all the interesting possibilities, that is to obtain tablets with hardness ranging from the minimum acceptable to meet industrial requirements to the maximum that can be obtained with the equipment. For each of these trials all the parameters of the experiment together with the values of masses, thickness and hardness of the tablets are stored on the disk with the values of forces and displacement required automatically. For each product, compressed with different displacements, we obtain a series of files that we are going to process with the program proposed according to the following schedule.

1. Screening

First, our program allows the display on the screen of the dots representative of the hardness of the tablets obtained against the maximum value of the force obtained during compression. For each adjustment there corresponds one dot.
The computer calculates and displays the regression coefficients and draws the regression line. This enables the operator to check if there is no aberrant experimental result ; in that case it is possible to eliminate those values. This will entail the calculation and the display of a new regression line. The positioning of the experimental dots, compared to the regression line, and the observation of the correlation coefficient enable us to realise if certain experimental conditions, which gave the hardest tablets, are not outside the limits of the hypothesis proposed, that is a linear relation between the measured force and the hardness of the tablets.
As figure 1 shows, it can often be noticed that the increase of the hardness is not linear, beyond a certain force level.

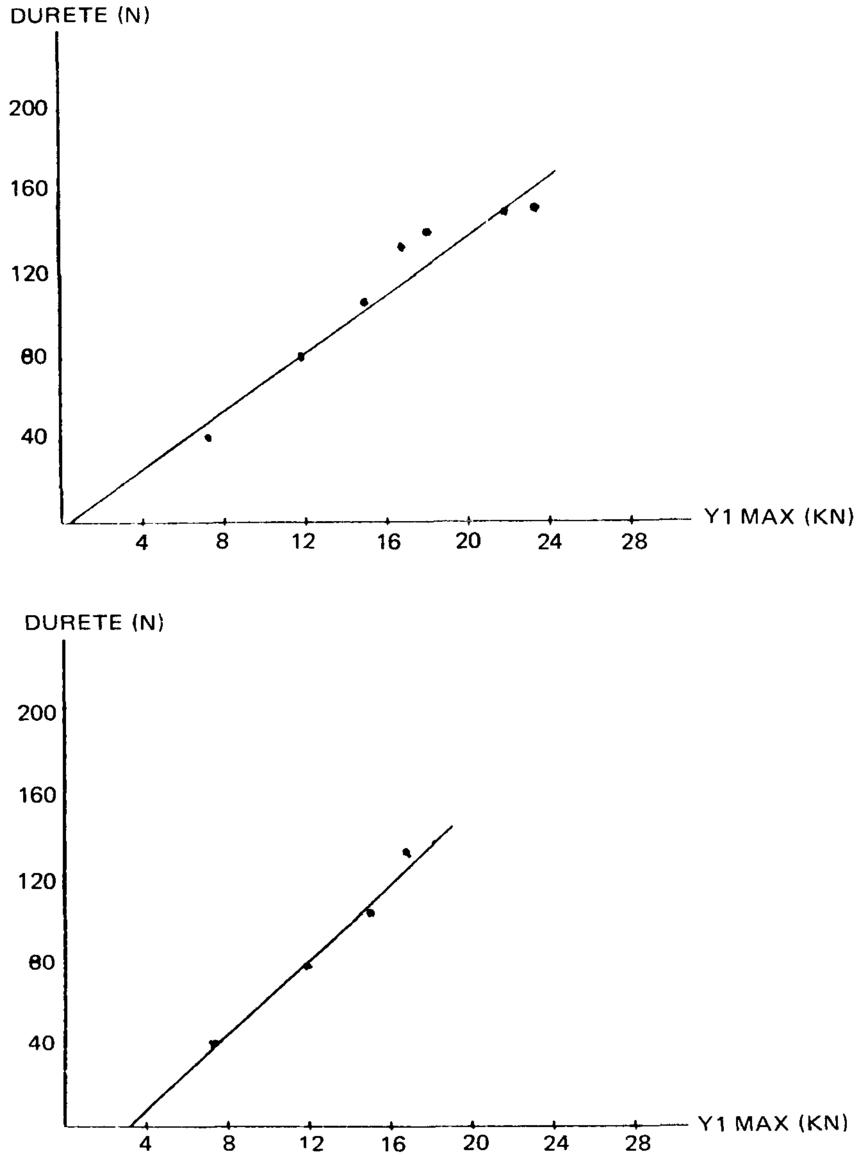

FIGURE 1 : Hardness of the tablets against the force measured-left : without screening right: after screening

It is obvious that for such products, we must remain within this force level as the "technological efficiency" is lower and the conventional consequences of an excess of energy consumption are capping, sticking and ejection problems. As a consequence, it is necessary to eliminate all the dots out of the linear zone ; the extreme experiments which are taken into account constitute the limits of the zone inside which the linearity hypothesis is verified ; the production must be carried out within these limits.

2. Cohesion index

When the screening is over, the computer gives the table of the characteristic values for the experiments taken into account. (Table 1).
Among those values, we propose the ratio PS/TS of the maximum pressure measured on the upper punch to the tensile strength (11) of the tablets. This ratio quantifies the technological efficiency of the compression operation for the product concerned under the mechanical conditions stated. Indeed, PS is the ratio of the force measured to the area of the punch ; this force is the resultant between the mechanical force determined by the adjustment of the machine and the resistance of the product. The tensile strength is the ratio of the force opposed by the tablet to the crushing to the diameter and the thickness of the tablet. Therefore the ratio of these two pressures is a number without dimensions which characterises the cohesion capacity of the product.
But it can be noticed that this index varies according to the mechanical conditions of the trial.
This problem will be settled by the continuation of the program.
After the table of the characteristic values of the different files, the computer draws the regression line of the tensile strength against the pressure measured on the upper punch. The slope of this line is a generalisation of the cohesion index PS/TS.
This graphic representation and the value of the slope are particularly helpful to compare products which are nearly similar as far as then compression capacity is concerned.

TABLE 1 : Comparison of the characteristic values of different files

XMAX (MM)	Y1MAX (KN)	Y2MAX (KN)	Y2/Y1	DUR (N)	EPAIS (CM)	MASSE (G)	PS/TS
FICHIER : V27CFS205STMG01							
538	14.91	14.04	.94	106.86	.487	.668	120
FICHIER : V27CFS205STMG03							
546	16.82	15.82	.94	134.38	.485	.669	107
FICHIER : V27CFS205STMG04							
488	7.15	6.7	.93	40.21	.534	.669	168
FICHIER : V27CFS205STMG05							
519	11.72	11	.93	78.97	.505	.671	132
FICHIER : V27CFS205STMG07							
551	18.04	16.94	.93	141.25	.481	.67	108

If we superimpose the different regression lines, the compared qualities of the products appear very clearly (figure 2).

The interest of the program is in the fact that the results are obtained after a screening which has eliminated the aberrant trials and particularly the dots out of the zone of application of the linear model, in opposition to previous studies.

3. Simulation

The continuation of the program enables the computer, by using the regression equation to calculate the values of the maximum of the forces which would be measured if the machine was adjusted to obtain a determined value of the average hardness of the tablets. Vice-versa, it enables the computer to calculate the hardness of the tablets which would be obtained if the machine was adjusted to measure a determined value of the maximum force on the upper punch.
This can be achieved on a rotary press as well as on a single punch machine, but the use of a single punch machine will, in both cases, provide the supplementary indication of the corresponding value of the maximum displacement. The interest of this simulation technique is

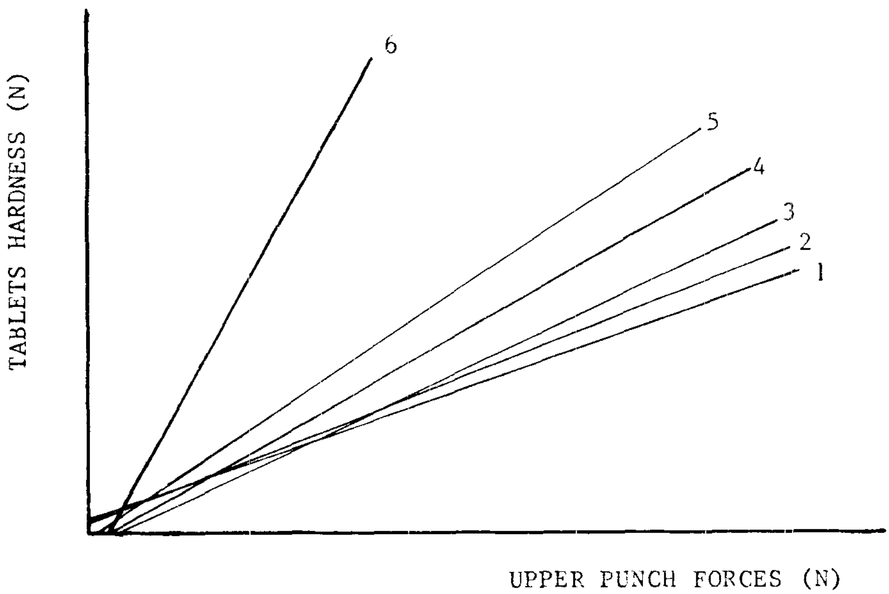

FIGURE 2 : Comparison of the compression capacity of different products by the use of the regression lines.

obvious : suppose we have to compare a mixture obtained after modifying the process to the reference mixture. With the conventional technique, we try to compress the new mixture under experimental conditions as near as possible to the conditions under which the reference mixture was compressed. It is well known that it is practically impossible to obtain exactly the same adjustment or, at least, that it would be very tedious and would take a long time. As a result, in case of nearly similar products, it is difficult to ascertain if the difference in the response is due either to the difference in adjustment or to the products, and consequently it is very difficult to draw a conclusion.
With our technique, we propose the following procedure : a series of trials, a screening and the calculation by the computer, for example, of the upper punch maximum force for exactly the hardness value obtained with the reference mixture. But it is absolutely necessary to remain within the limits defined beforehand.

The difference noticed can only be due to the process modification. Therefore it is an extremely powerful tool which is proposed here to compare the compression capacities of the various products. With this simulated file, the computer gives a table of the characteristic values particularly the cohesion index.
This index, obtained with different products under exactly the same conditions, is very helpful. For formulation studies and quality control, as the products are nearly similar, the imposed value will be the hardness of the reference batch. But, to compare products with very different densities, the imposed value will be, for example, an upper punch force of 20KN. Then the cohesion index PS/TS allows the classification of the products. But we can go much further into this simulation and, by using the computer, calculate the coordinates of each dot of the curves of the upper punch force, and of the displacement (for a single punch machine only) against time. It is then possible, by using the computer, to draw the compression cycle which would be obtained for a given hardness. The comparison of the cycles is then made easier and is very useful for the formulation specialist (figure 3).

4. Modelisation

The last part of our program is to give an equation of the curve representing the force against the displacement of the upper punch in the die. This will be carried out by using the file obtained by simulation at 20KN or for a given hardness. The aim of this technique is to obtain supplementary parameters which could inform us on the compression capacity of a powder. Many authors have proposed equations to describe the deformation of the powder under compression (12). The best-known is HECKEL's equation (13) but we have chosen to consider the equation proposed by KAWAKITA and LUDDE in 1966 (14). According to these authors, the degree of reduction of the powder bed volume (c) is such as $c = \frac{Vo-V}{Vo} = \frac{abP}{1+bP}$

in which a and b are constants, P the pressure, V the powder bed volume under pressure P and Vo the apparent initial volume, hence $\frac{P}{c} = \frac{1}{ab} + \frac{P}{a}$.

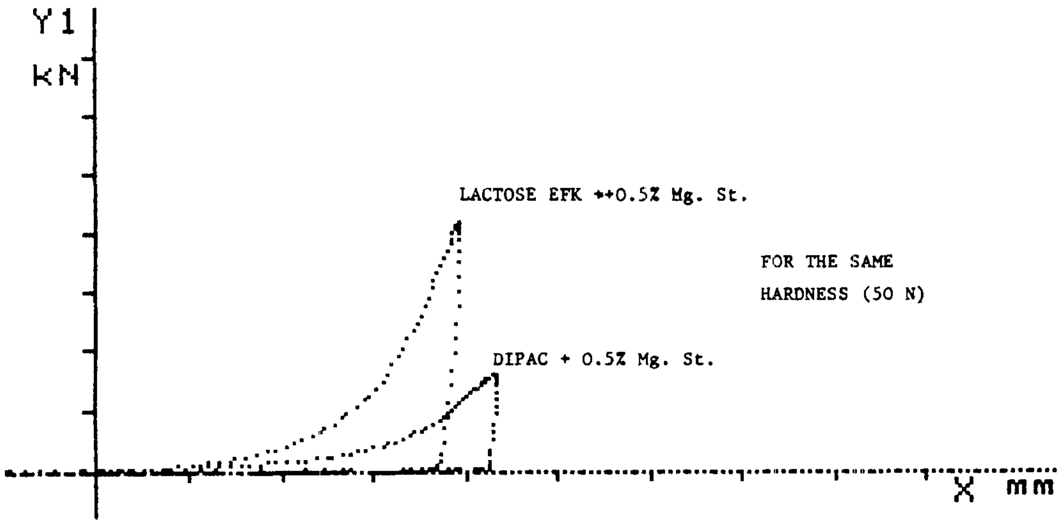

FIGURE 3 : Comparison of the cycles of two products simulated for the same hardness (50N).
1. Lactose EFK 2. Dipac

So, we obtain a linear model $\frac{P}{C}$ as a function of P which is valid when P is not too low. Since all our trials are carried out with the same diameter of the die, KAWAKITA's equation can be changed as follows : $\frac{Y}{\frac{ho-h}{ho}} = \frac{1}{ab} + \frac{Y}{a}$

in which Y is the force measured on the upper punch, h_o the depth of the compression chamber and h the height of the powder bed after compression (figure 4).

As the displacement X of the upper punch in the die is equal to (ho - h) we obtain :

$$\frac{Y}{\frac{x}{ho}} = \frac{1}{ab} + \frac{y}{a}$$

or $\frac{hoY}{x} = \frac{1}{ab} + \frac{Y}{a}$ or $\frac{aho\ Y - XY}{aX} = \frac{1}{ab}$

that is to say (aho - X) Y = $\frac{X}{b}$

and in our case where h_o is equal to 1 :

$$Y = \frac{X}{- bX + ab}$$

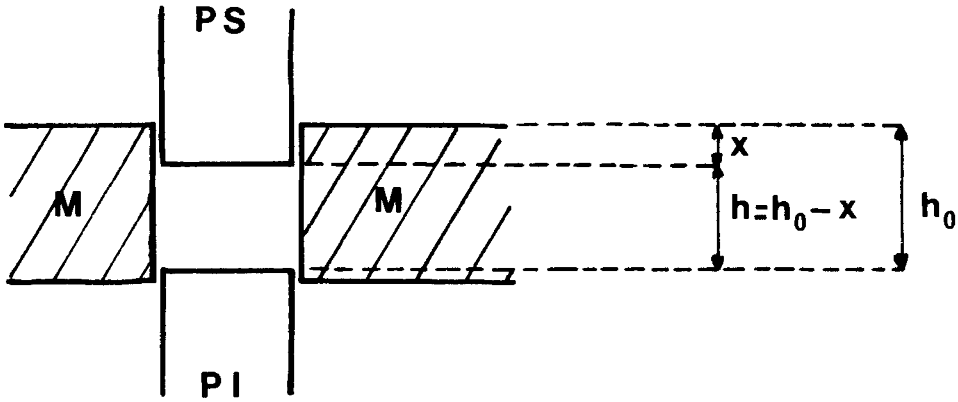

FIGURE 4 :Compression chamber of a single punch machine.

This is the equation of an equilateral hyperbola. (figure 5)

It can be linearized into Y by X as a function of Y : $\frac{Y}{x} = \frac{1}{ab} + \frac{Y}{a}$ (figure 6)

As KAWAKITA indicated that his equation is valid only when the forces measured are not too low, we considered that the linearization according to this equation can be verified only if we eliminate the dots corresponding to the values of Y which are too low. These values lead to a correlation coefficient which cannot be accepted. When these values are eliminated, from a certain displacement value onwards which we called "M", the correlation coefficient becomes satisfactory and the linearization is verified.

So, we have devised a program which allows, from an experimental or simulated file, the automatic calculation of :

- the value of the displacement M expressed in 1/100 of mm, for a depth of the compression chamber h_o = 1 cm, from which the dots are linearized according to the equation $\frac{Y}{X} = A + BY$ and for a linear correlation coefficient r equal or superior to 0.9990.
- the value of the intercept (A) and of the slope

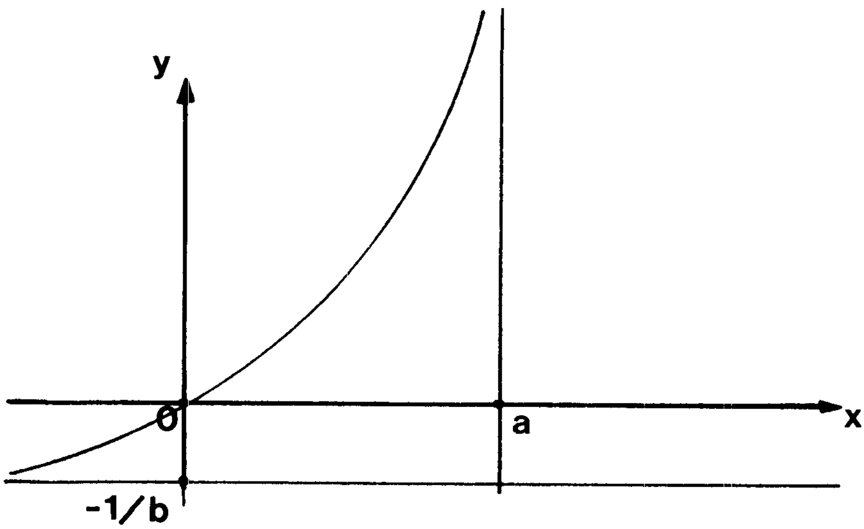

FIGURE 5 : The equilateral hyperbola of the Kawakita model.

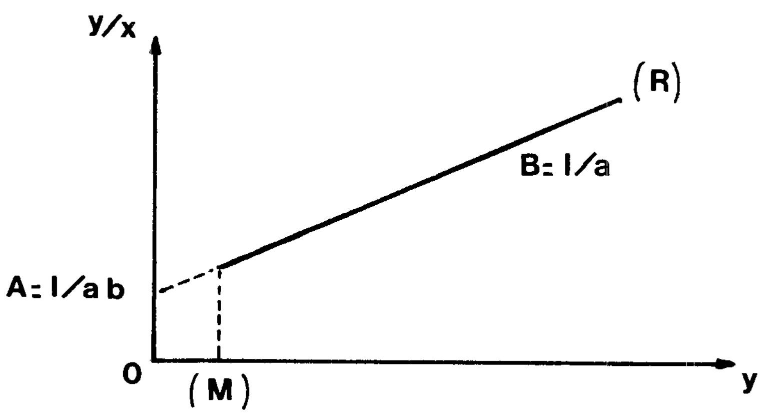

FIGURE 6 : Linearisation of the Kawakita model

(B) of this function in which Y is expressed in KN and X in mm.

- by inverting the slope (1/B), we obtain the value of the asymptote on the x-axis expressed in mm.

To validate this model, we used a program which displays the curve of Y against X using the values of A and B obtained and calculates every point and the area under the curve.

From the results it can be noticed that the curve obtained is very similar to the experimental one ; this is confirmed by the similarity of the values of forces and areas of both the calculated curve and the experimental one.

The interest of this program is evident as it allows, for the law of the behaviour of the powder under compression, the expression of three parameters which are very useful for industrial purposes :

- M is the value of the displacement of the upper punch just between the packing phase and the actual compression phase. From this value onwards the model is verified.

With a number of products, we compared the calculated values of M and the experimental value of F that we proposed before (12). As a reminder, the value F is the maximum displacement of the upper punch to obtain a tablet with zero hardness. We have shown that this value is very useful to compare the compression capacity of powders. We must point out that the value M does not take into account the notion of hardness of the tablet obtained. But if we classify the products according to the values of F or M, we notice that the products appear in the same order, which means that the automatic calculation of M seems to be as useful as the experimental determination of F.

- the second parameter is the slope B which characterises the aspect of the curve and could in a way allow the evaluation of the plasticity of the product.

- the third parameter is the assymtote on the x-axis obtained by calculating 1/B ; it is the second limit of the validity of the model. Then (1/B)-M can be deducted : it corresponds to the tabletibility range ; we have shown the interest of this notion on a practical level (15).

CONCLUSION

The study technique that we propose allows the pharmacist to save time during the experimental phase as it is no longer necessary to adjust the machine precisely to obtain a reference value of force or hardness.
The screening phase proposed is very important as it allows the pharmacist to limit himself to the range of forces leading to a technologically efficient response.
We propose a cohesion index to characterise a product and to compare different products finely.
The simulation and modelisation programs enable the pharmacist to obtain very helpful parameters for tablet formulation, scaling up and quality control.

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