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GRANULATION OF PHARMACEUTICAL POWDERS BY COMPACTION
AN EXPERIMENTAL STUDY

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ABSTRACT

Among technological which improve properties of powder before tabletting, dry granulation has been studied with a new compactor-granulator. An experimental study was carried out to understand the influence on powders of the adjustment of speeds and pressure during roll-compaction. The results obtained on an active substance are detailed in this article.

INTRODUCTION

A lot of pharmaceutical substances cannot be directly compressed on a tabletting machine. To solve this problem, one of the possible techniques is to densify the fine powders into granules which have a better flowability and a better compression capacity (1). Among the processes of densification, dry granulation is a very interesting technique. In a previous paper (2), we presented a new compactor-granulator, specially developed for pharmaceutical technology, according to good manufacturing practices. The aim of this work is to study the influence of the different adjustments of the machine according to the properties of the powder.

MATERIAL AND METHODS

Description of the equipment and its regulations

This study was carried out on a SAHUT CONREUR Compactor Pharma 250 (3)(Figure 1). One of the main objectives of this new compactor-granulator was to develop an equipment which could be very close to the Good Manufacturing Practices, i.e to have a machine which could be cleaned easily and quickly, which would be adapted to a variety of different products and which would enable an easy access to the working parts. On a roll compactor, the shape of the flakes or compacts obtained depends on the type of wheels. For example, wheels with little sticks give compacts, shallow pockets give flakes.Flakes are also obtained with little engravings (knurling). The other different possibilities of adjustments of the equipment are :

- the speed of the force-feeder (from 22 to 100 Rpm),
- the speed of the moulding wheels (from 3.3. to 27 Rpm),
- the pressure applied (from 2.5 to 60 kN/cml).

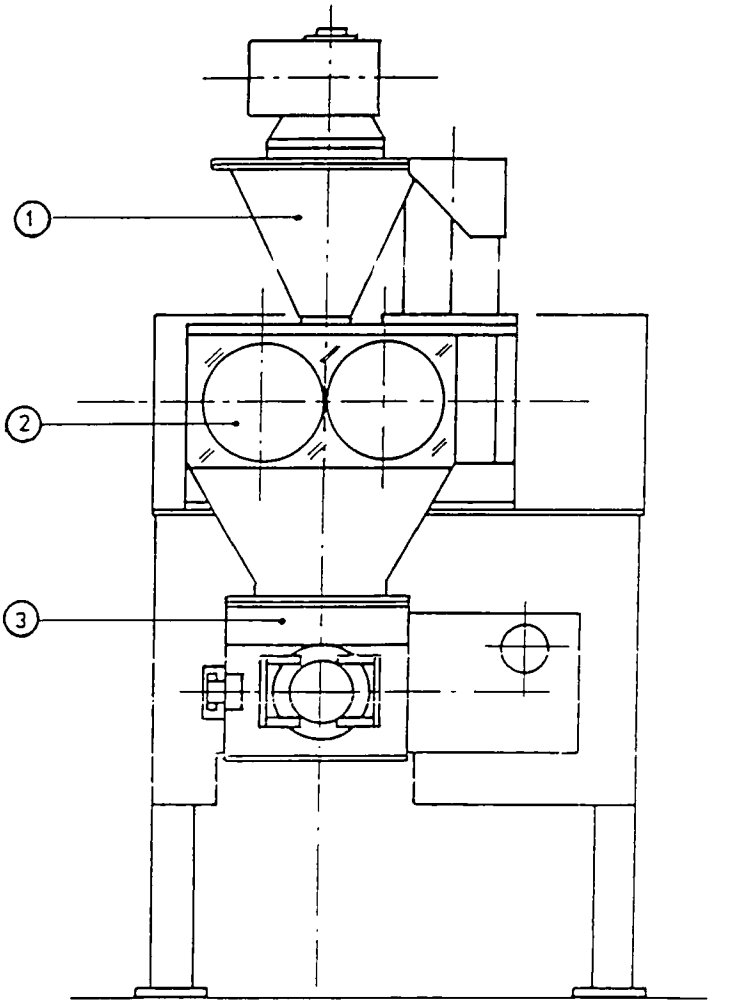

FIGURE 1 : Figure of the Compactor Pharma 250

1. Hopper with feeder screw
2. Compactor - two wheels
   - possibility to apply pressure on the moving wheel
3. Granulator (FREWITT MG 333)

Under the compactor, a Frewitt MG 333 oscillating granulator (4) is used to carry out the granulation. The different possibilities of adjustment on this granulator concern :

- the mesh size of the screen,
- tension of screen,
- the speed of the oscillating movement.

Determination of the characteristics of powders and compacts

Technological properties of powders are measured before and after the compaction-granulation process. These properties are :

- flowability,
- bulk density,
- packing capacity,
- particle size,
- compression capacity which is determined by the calculation of the Cohesion Index using a computerized single punch machine and a specific software (5).

$$\text{Cohesion Index} = \frac{\text{Hardness of the tablets (N)}}{\text{Maximum upper punch Force (N)}} \times 10^5$$

The mechanical resistance of the compacts obtained is measured by using two original techniques : on one hand, the "hardness" of the compacts is measured with a dynamometric hardness tester (6), and on the other hand, the friability of the compacts is the percentage of powder lost by the compacts during a standardised test in a tubular mixer (7).

RESULTS AND DISCUSSION

The aim of this work is to study the influence of the different adjustments of the compactor-granulator on the properties of the powder obtained. The study was carried out on a powder with good rheological properties but a bad compression capacity to be improved. The properties of the powder before granulation are given in the table a.

TABLE a. : Properties of the original powder

Flowability	8 s
Bulk density	0.8 g/cm3
V10 -V500	10 ml
Size distribution	95 % over 250 µm
Cohesion index	350

TABLE b. : Experimental field

X1 Speed of the wheels	6 to 22 rpm
X2 Speed of the feeder screw	22 to 86 rpm
X3 Hydraulic pressure applied	80 to 200 bars

The aim of this work is the study of the influence of the three main adjustments of the compactor-granulator on the properties of the powder obtained. As a result, it was necessary to have a preliminary study. For the powder chosen as model for this study, the experimental field for the three variables is described in the table b.

In this experimental field, we have chosen to perform a Box Wilson Design (15 experiments). The table c. gives the experimental matrix.

The table d. gives the code of the answers.

The table e. gives the results obtained.

TABLE c. : Experimental matrix

Exp. Code	Exp. Nr	X1	X2	X3
A1	1	-1	-1	-1
	VR	7.7	32.4	100
A8	2	1	-1	-1
	VR	18.2	32.4	100
A9	3	-1	1	-1
	VR	7.7	76	100
A2	4	-1	1	1
	VR	7.7	32.4	160
A3	5	1	1	-1
	VR	18.2	32.4	100
A10	6	1	-1	1
	VR	18.2	32.4	160
A11	7	-1	1	1
	VR	7.7	76	160
A4	8	1	1	1
	VR	18.2	76	160
A12	9	-(a)	0	0
	VR	6.3	60	140
A13	10	0	-(a)	0
	VR	15.2	22	140
A5	11	0	0	-(a)
	VR	15.2	60	80
A14	12	(a)	0	0
	VR	22	60	140
A15	13	0	(a)	0
	VR	15.2	86	140
A6	14	0	0	(a)
	VR	15.2	60	200
A7	15	0	0	0
	VR	15.2	60	140

TABLE d. : Code of the answers

Answer R1	Friability of compacts in %
Answer R2	Average of hardness in daN
Answer R3	Flowability in seconds
Answer R4	Tap test in millilitres
Answer R5	Percentage of grain below 250 µ
Answer R6	Percentage of grain below 350 µ
Answer R7	Value of cohesion index at 1500 daN on upper punch, adimensional number

TABLE e. : Results of answers

N°	Code	R1	R2	R3	R4	R5	R6	R7
1	A1	17.80	30	10.5	10	13.78	55.83	523
2	A8	76	8.1	6	10	16.94	46.75	364
3	A9	32	–	–	–	–	–	–
4	A2	15.85	30	8.3	10	10.95	66.20	571
5	A3	20.66	28.3	10	10	9.13	69.40	497
6	A10	73	7.4	6	8	12.56	53.33	377
7	A11	30	–	–	–	–	–	–
8	A4	14.72	27.6	14.2	10	10.68	61.20	508
9	A12	31	–	–	–	–	–	–
10	A13	74.3	7.9	8.3	8	15.58	42.56	359
11	A5	17.73	22.4	13.7	10	10.09	65.68	490
12	A14	69	9.3	9.3	8	13.24	45.13	406
13	A15	17.75	35	11	10	9.54	66.60	554
14	A6	17.5	35	13.5	10	9.35	75.14	568
15	A7	17.25	24	11.6	10	11.31	62.78	506

TABLE f. : Influence of the speed ratio on the compact friability and cohesion index

Codes	Speed Ratio	Compact Friability	Cohesion Index
A 1	0.237	17.8	523
A 2	0.237	15.95	571
A 3	0.239	20.60	497
A 4	0.239	14.72	508
A 5	0.253	17.73	490
A 6	0.253	17.50	568
A 7	0.253	17.25	506
A15	0.176	17.50	554
A 8	0.561	76	364
A10	0.561	73	377
A13	0.691	74.3	359
A14	0.366	69	406
A 9	0.101		
A11	0.101		
A12	0.105		

The answers received were mathematically assessed according to parameters X1, X2 and X3. From the results obtained, our conclusions are the following ones :

At the beginning, the speeds X1 and X2 play an important role on the answers, and the pressure X3 is a modulating factor only as far as the experiments on this powder are concerned. This is particularly true for the hardness of the compacts and the cohesion index which increases from 350 to over 490 in 8 experiments, and have an optimum value of 571. The flowability of the product is also connected to the wheel speed but influenced by the pressure.

A second very interesting result is that the friability index develops in the same way as the cohesion index; the relation can be checked with a correlation of 0.93. On the other hand, a low friability index corresponds to a good compact

hardness with a correlation coefficient of 0.98. This obviously shows the interest of the tests proposed on the compacts so as to predict the characteristics under compression of the powder obtained by grinding of the compacts.

In the table of the results obtained, we can notice that we have no answers for 3 experiments A9, A11 and A12, because for these adjustments of the compactor, the compacts obtained looked like china, the product heated up considerably and it was necessary to stop the machine. For these experiments, we can notice that the speed of the screw feeder is high whereas the speed of the wheels is low. And this is the reason why problems occur during compaction : if the speed of the screw feeder is too high in correlation with the speed of the wheels, clogging occurs. If we calculate the ratio between the two speeds, we obtain a value near 0.100, and we can notice that this ratio is always higher for all the other experiments. As we can see in the table f., the good cohesion index are obtained with compact friability near 20 %, and for these experiments, the speed ratio is near 0.200.

In the second part of the table, the cohesion indices are low, the compact friability is high and the speed ratio is high. This is obvious since the feeding is too low in correlation with the speed of the wheels, and no densification occurs.

CONCLUSION

With the powder chosen for this study, we have demonstrated that on this compactor-granulator :

The adjustments of the speeds are more important than the usual adjustment of the pressure. It is necessary to keep a ratio between the speed of the screw feeder and the speed of the wheels. The screw feeder has a very important role of predensification. On the other hand, the in process test proposed to measure the compact hardness and friability is very interesting. It enables to predict the characteristics of the

powder obtained under compression through this technique of dry granulation.

REFERENCES

(1) LIEBERMANN H. and LACHMAN A.
Pharmaceutical dosage forms : Tablets
DEKKER New York 1980

(2) F.DEHONT, P. HERVIEU, E. JEROME, A. DELACOURTE, JC. GUYOT
Briquetting and granulation by compacting ; a new granulator-compactor
Drug Development and Industrial Pharmacy
1989 (15) 2245-2264

(3) SAHUT CONREUR
BP 49 F-59590 RAISMES (FRANCE)

(4) FREWITT, Fabrique de machines SA
CH-1700 FRIBOURG/GRANGES-PACCOT

(5) JC. GUYOT, A. DELACOURTE, P. LETERME, P. BILLARDON
L'aide du Génie Pharmaceutique dans la recherche et le développement des comprimés - Utilisation de l'informatique et des plans d'expérience
STP PHARMA
1989 (5) 168-175

(6) SODEXIM, Huizon
F-51140 JONCHERY SUR VESLE

(7) E. JEROME
Etude des paramètres de l'opération de granulation sèche par compactage
D.E.A. de Pharmacie industrielle et Génie Pharmaceutique
Lille 1986