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DISINTEGRATING FORCE AND TABLET PROPERTIES

P.Colombo,C.Caramella,U.Conte.A.La Manna (*)
Dipartimento di Chimica Farmaceutica,Università di Pavia,Viale Taramelli 12.27100 PAVIA-Italia

A.M.Guyot-Hermann,J.Ringard (**)
Faculté de Pharmacie,Laboratoire de Pharmacie Galenique,2.Rue du Professeur Laguesse
59045 LILLE Cedex-France

ABSTRACT

The development of a disintegrating force inside the tablet due to the liquid/solid contact depends on a proper wetting of the material and occur according to saturation kinetics.

The aim of the present work is the evaluation of such a force development in relation to the characteristics of the tablet in particular to the compression force.

For this purpose.the disintegrating force of diffe-rent tablets formulations has been measured by means of a previcusly described apparatus.

The results obtained show that a new evaluation of a compact disintegration characteristics may be obtai-ned through the determination of such parameters as

(*) to whom all correspondence should be addressed

(**) present address:

Laboratoires Bottu,52-58, Avenue du Maréchal Joffre.92024 NANTERRE-France

the maximum force developed (y_0) and the time of the half maximum force development (b).

INTRODUCTION

The disintegration of a compressed tablet into granules or individual particles is a rate limiting step for the dissolution of drugs. Therefore a rapid disintegration process is the prerequisite for a good bioavailability.

For this purpose, it is necessary that the liquid penetration into the tablet activates the development of a force capable of separating the particles.

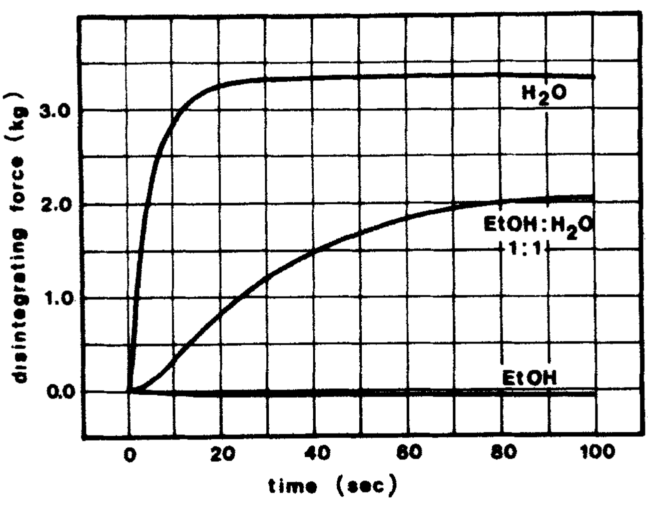


Fig. 1 – Disintegrating force pattern in different liquids.

Such a force activation is an essential moment: in fact, as shown in figure 1, tablets rapidly disintegrating in water, when submerged in ethanol, are quickly penetrated by the liquid but do not disintegrate because ethanol does not activate the disintegrating force. On the contrary when the liquid/solid contact is capable of causing a disintegrating force, a direct relationship can be observed between liquid penetration and force development rate. Such a relationship, previously verified by us (1), would indicate among the factors involved in force development those appearing in the Washburn equation describing the capillary penetration process of a liquid, i.e. (γ) surface tension, (θ) contact angle, (R) pores radius and (η) liquid viscosity. Consequently the mechanisms by which the disintegrating force develops depend on these factors; they may be grouped, on the basis of dinamic considerations, in the following manner:

a) the pressure exerted by the air entrapped in pores structures due to a hydrodinamic process (2) or to the heat of wetting (3)

b) the swelling of the disintegrating agent (4)

c) the repulsion among particles caused by the contact between solid and liquid (5) (6).

This would indicate that the development of a disintegrating force, and therefore a disintegration process, depend on a proper wetting of the tablet.

Such a force develops inside the tablet according to a saturation kinetics expressed by a hyperbolic equation written in the semplified form:

$$\frac{x}{y} = \frac{x}{y_o} + \frac{b}{y_o}$$

where x represents the time. y the force and y_o, b are constants. From the slope and intercept values of the straight line the parameters y_o, i.e. the maximum force developed, and b, i.e. the time needed to develop half maximum force can be calculated. The aim of the present work was the evaluation of such a disintegrating force inside the tablet and the definition of the meaning of the above mentioned parameters in relation to the characteristics of the tablet, in particular to the compression force.

For this purpose, the disintegrating force of different tablet formulations has been measured by means of a previously described apparatus (1).

EXPERIMENTAL

- Disintegrating force measurements

  The disintegrating force development was measured using the apparatus previously described (1) and illustrated in figure 2.

- Products employed

  Different series of tablets, prepared under controlled conditions, were studied. Their compositions are given in Table I.

The tablets were checked for porosity, hardness, disintegration time (USP XIX without disc), water penetration (7) and disintegrating force.

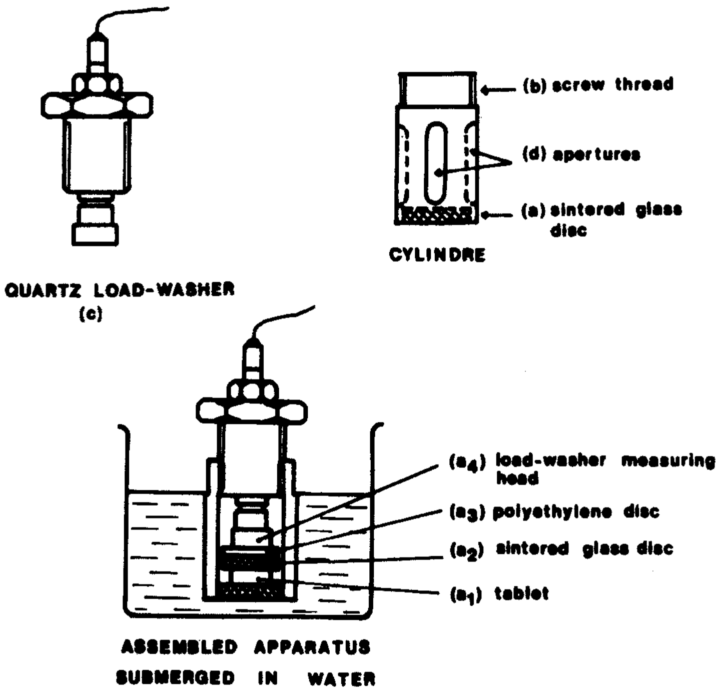


Fig. 2 — Apparatus for disintegrating force measurement.

RESULTS AND DISCUSSION

The example of GRAN series tablets, obtained at approximately the same compression force level, is significant to elucidate the relationship between y_0, b values and disintegration time of tablets: a rapid disintegration process requires the development of a significant force, but the rate at which this process occurs is important too. The examination of Table 2 shows that $GRAN_0$ tablets, which develop a high disintegrating force (83 N), disintegrate more slowly that the $GRAN_{100}$ tablets, which develop a smaller disintegrating force (28 N) but in a shorter time.

TABLE I

Composition of Tablets (Ø 11 mm)

ASA_5		Aspirin crystals Maize starch	0.500 g 0.025 g
ASA_{10}		Aspirin crystals Maize starch	0.500 g 0.050 g
ASA_c 3%		Aspirin coated Syloid[r] Explotab[r] Maize starch	0.500 g 0.016 g 0.015 g 0.015 g
ASA_c 15%		Aspirin coated Maize starch	0.500 g 0.075 g
ASA_c Avicel		Aspirin coated Avicel pH 101 Magnesium stearate	0.500 g 0.075 g 0.005 g
ASA_c Elcema		Aspirin coated Elcema G250 Maize starch Talc	0.500 g 0.070 g 0.030 g 0.010 g
ASA_c Sta-RX		Aspirin coated Sta-RX Talc	0.500 g 0.100 g 0.010 g
GRAN	(°)	Diluent (granular form) Nitrofurantoin Explotab[r] Magnesium stearate	0.450 g 0.050 g 0.015 g 0.005 g
STZ	(x)	Sulphathiazole granules Maize starch	0.500 g 0.050 g

(°) The diluent was obtained by wet granulation of mixtures of potato starch:lactose (7:3) and $CaHPO_4 \cdot 2H_2O$ in different proportion ranging from 0 to 100%. $GRAN_0$ means no $CaHPO_4 \cdot 2H_2O$. $GRAN_{25}$ 25% $CaHPO_4 \cdot 2H_2O$, $GRAN_{50}$ 50% $CaHPO_4 \cdot 2H_2O$, and $GRAN_{100}$ 100% $CaHPO_4 \cdot 2H_2O$.

(x) The granules were obtained by wet granulating with gelatin solution then slugging, milling and sieving to obtain a 18-70 ASTM fraction.

TABLE 2

GRAN Tablets Characteristics

	Porosity %	y_o N	b sec	USP XIX D.T. sec
$GRAN_0$	8.4	83	16"10	65"
$GRAN_{25}$	11.2	66	8"90	40"
$GRAN_{50}$	22.6	54	5"80	22"
$GRAN_{100}$	24.5	28	6"79	24"

This is in agreement with the results obtained comparing disintegration time and water penetration (12) which evidenced that the water penetration rate rather than the amount of water absorbed influences the disintegration time.

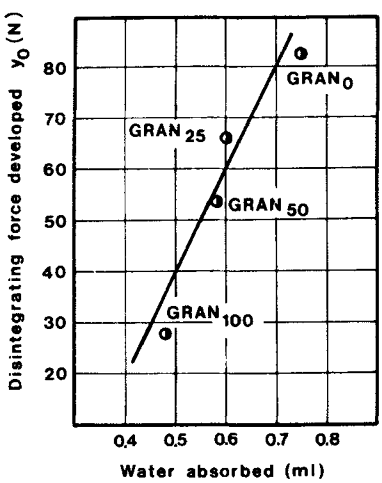


Fig. 3— Relationship between y_0 and water absorption.

The maximum force developed (y_0) depends on the qua lity and quantity of the disintegrating agent and seems to be related to the amount of water absorbed by the tablet: this is particularly evident in GRAN series where the amount of water absorbed decreases together with the disintegrating force developed (Figure 3),

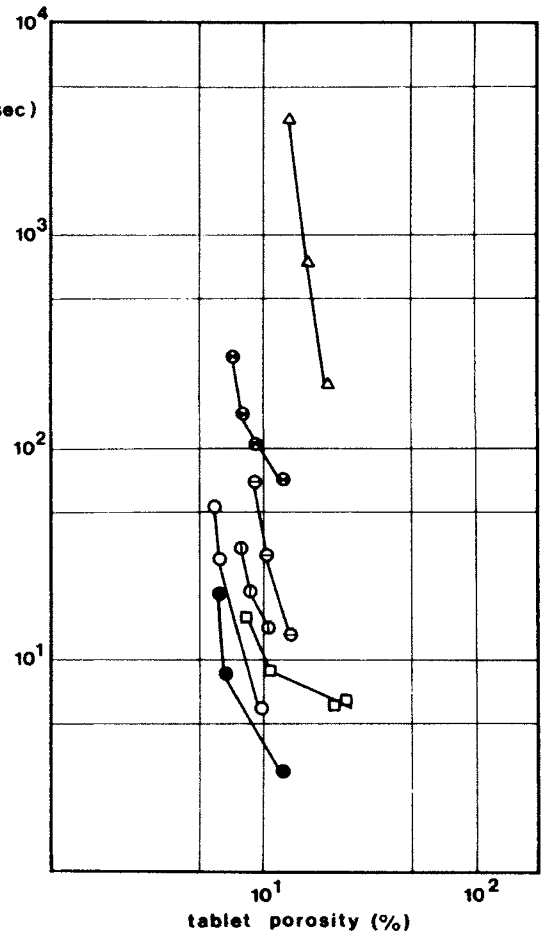


Fig. 4 - Relationship between tablet porosity and b value.

ASA_5 ○ ; ASA_{10} ● ; ASA_c Avicel ⊖ ; ASA_c Elcema ⦶ ;

ASA_c Sta-Rx ⊖ ; STZ △ ; GRAN □ .

following the decrease of intragranular starch percentage from $GRAN_0$ to $GRAN_{100}$ tablets.

The time of the half force development (b) is related to the water penetration rate (1) and increases on decreasing tablet porosity (Figure 4).

TABLE 3

Characteristics of Tablets Containing Starch or its Derivatives

	Force level hN	Hardness N	Porosity %	y_o N	b sec	USP XIX D.T. sec
ASA_5	56	30	9.7	15.3	5"86	12"
	159	65	6.2	39	30"05	18"
	310	79	6.0	46.5	53"77	32"
ASA_{10}	46	12	12.7	18.3	3"08	6"
	165	65	6.9	46.2	8"51	8"
	273	72	6.4	66.6	22"33	12"
ASA_c 3%	79	30	-	20.8	127"	112"
	148	86	-	34.3	269"	210"
	245	168	-	54.9	1049"	600"
ASA_c	95	26.4	10.7	64.7	14"	13"
Elcema	181	45.6	8.6	71.6	21"	19"
	282	53	8.0	74.5	34"	24"
ASA_c	93	22.7	13.5	15.8	13"	23"
Sta-RX	191	54.7	10.3	14.7	31"	105"
	285	66.3	9.3	14.5	70"	187"

The same relationship between y_o, b values and disintegration times holds true also for the other series of tablets, where the compression force level represents the only variable. All the tablets examined, containing starch or its derivatives (Table 3) as disintegrating agents, show an increase in y_o and b values on increasing of compression force (except for y_o values of tablets containing Sta-RX). The increase of y_o values on increasing of compression force is in agreement with the reports of certain authors (8)(9), according to whom the starch grains swelling is more effective at reduced porosity values. According to some others (12), this is in agreement with the observation that in certain formulations the smaller pore diameter, the greater the capillary pressure developed is. For tablets containing Avicel as a disintegrating agent (Table 4), on increasing compression force, b value but not y_o value increases. This indicates that Avicel, a non swelling agent, is capable of developing a disintegrating force (10).

TABLE 4

Characteristics of ASA_c Avicel Tablets

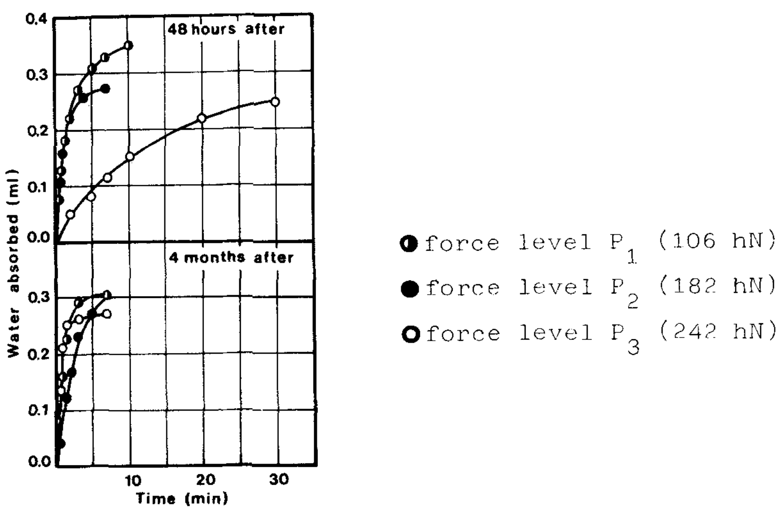
Force level	Hardness N	Porosity %	y_o N	b sec	USP XIX D.T. sec
70	25	12.3	42.2	72"	80"
110	36	9.1	43.1	105"	97"
185	41	7.9	42.2	146"	160"
290	45	7.3	43.1	275"	235"

The possible changes caused in tablets properties by storage may deeply influence the disintegrating force parameters. STZ tablets (Table 5) represent an example of that: y_0 and b values as well as penetration rate and disintegration time, deeply change after 4 months storage at room conditions.

TABLE 5

Characteristics of STZ Tablets (48 Hours/4 months storage)

force level hN	Hardness N	Porosity %	y_0 N	b sec	USP XIX D.T. sec
106	88/66	20.6/22.1	17/5.5	21"/4"	255"/31"
182	167/156	16.2/18.2	17/4	76"/5"	2160"/70"
242	206/172	13.4/17.6	22/1.5	384"/10"	5570"/328"



CONCLUSIONS

The joint consideration of y_0 and b values allows to evaluate the characteristics of the studied formulations and of obtained compacts.

To consider simultaneously the two parameters $y_0/2b$ ratios were calculated. This value depends on compression force and generally decreases on increasing compression level (Figure 5).

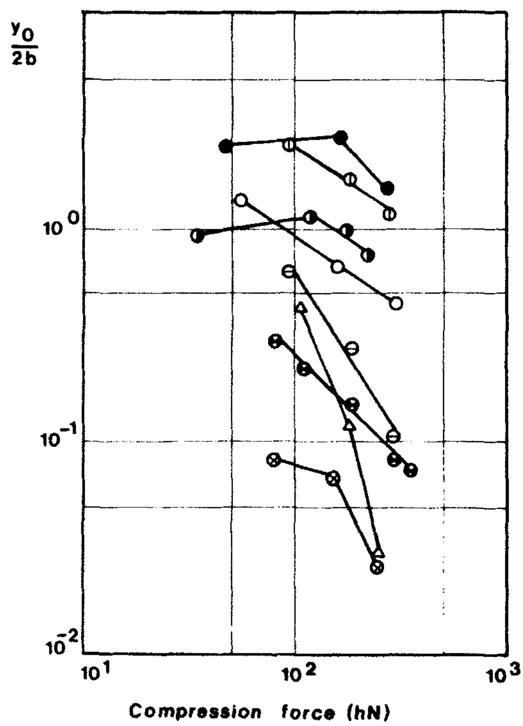


Fig. 5 – Relationship between $\frac{y_0}{2b}$ and compression force level.
ASA_5 ○ ; ASA_{10} ● ; ASA_c 3% ⊗ ; ASA_c 15% ◑ ; ASA_c Avicel ⊕ ; ASA_c Elcema ⦶ ; ASA_c Sta-Rx ⊖ ; STZ △.

For some formulations containing high percentages of starch, it starts decreasing when a certain force level is reached. The disintegration time of tablets depends on $y_0/2b$ values: as shown in figure 6, the points relative to different tablets are grouped beside a straight line (correlation coefficient 0.968).

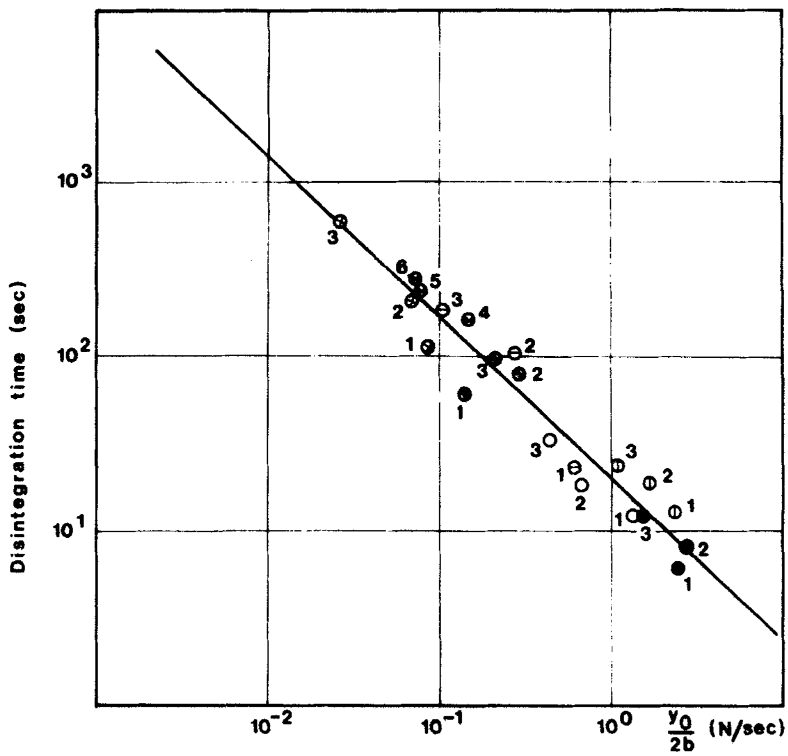


Fig. 6 – Relationship between $\frac{y_0}{2b}$ and disintegration time. ASA_5 ○ ; ASA_{10} ● ; ASA_c 3% ⊗ ; ASA_c Avicel ⊖ ; ASA_c Elcema ⦶ ; ASA_c Sta–Rx ⊖. The numbers indicate the compression force levels.

The decrease of $y_0/2b$ values on increasing of tablets hardness (Figure 7) may indicate that the disintegrating force measurement, as well the hardness measurement, involve the separation of the bonds between particles.

Therefore a new evaluation of a compact disintegration characteristics may be obtained through the determination of $y_0/2b$ value.

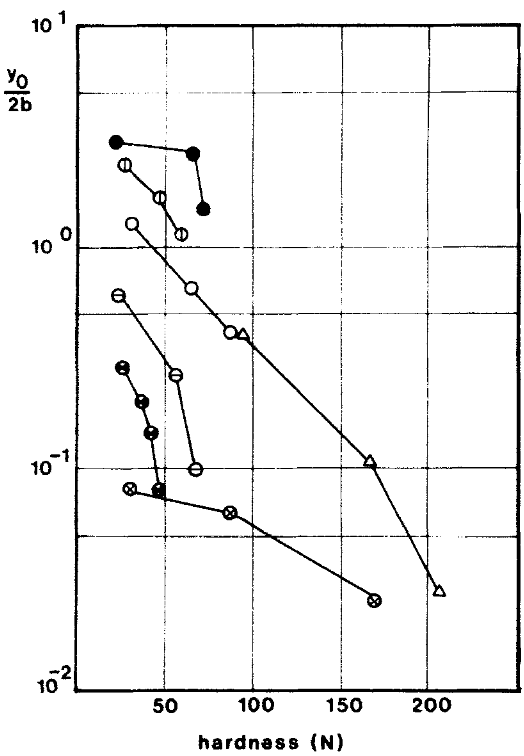


Fig.7 - Relationship between $\frac{y_0}{2b}$ and hardness.
ASA_5 ○ ; ASA_{10} ● ; ASA_C 3% ⊗ ; ASA_C Avicel ⊕ ; ASA_C Elcema ⦶ ; ASA_C Sta-Rx ⊖ ; STZ △ .

On the basis of the results obtained for the same formulation, the disintegration time of the tablet seems to depend on b value more than on y_0 value (Figure 8). This would confirm the Nogami hypothesis and the results reported in (7) according to which water penetration process rather than particles separation determine the rate of tablet disintegration (11).

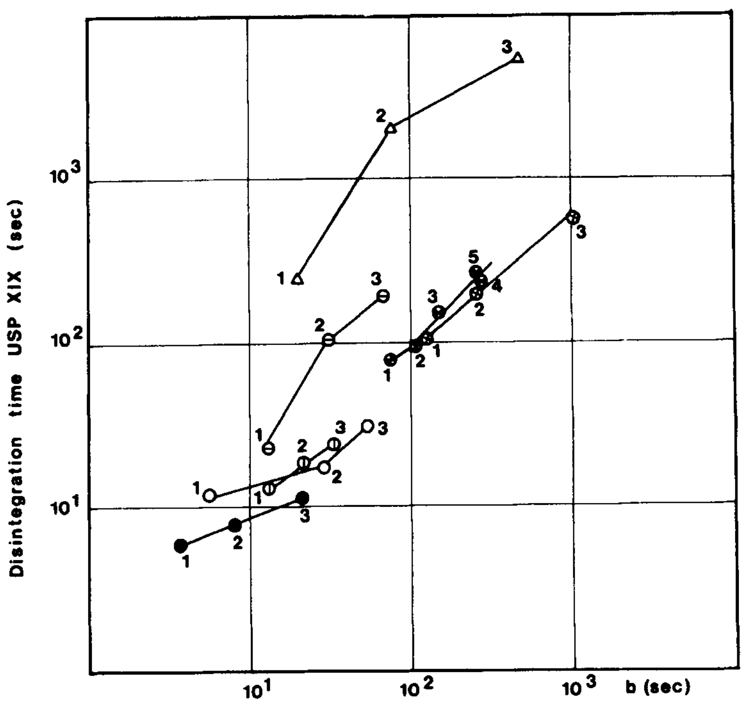


Fig. 8 - Relationship between disintegration time and b value. ASA_5 O; ASA_{10} ●; ASA_c 3% ⊗; ASA_c Avicel ⊖; STZ Δ; ASA_c Elcema ⦶; ASA_c Sta-Rx ⊖. The numbers indicate the compression force levels.

On the other hand, the maximum force (y_0) value seems to be related to the result of disintegration process, that is the dimensions of the particles generated. It was observed that tablets showing high y_0 values disintegrate into smaller fragments than those developing low force levels. It would be interesting to confirm this by investigating the relationships between y_0 and the size distribution of particles generated.

The disintegrating force curves may also indicate whether the compact behaves as an omogeneous structure with regard to water absorption. Compacts breaking up into small fragments show reproducible curves, (Figure 9), whereas for tablets showing lamination or formation of large fragments, a great variance in y_0 and b values (Figure 10) can be seen.

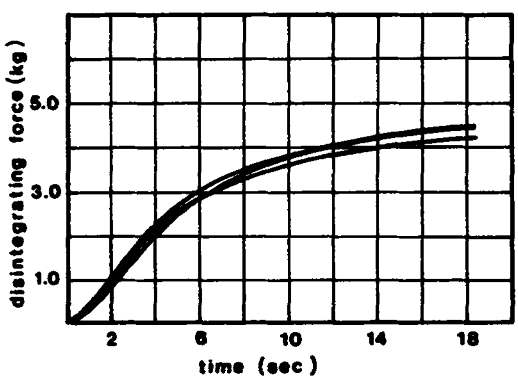


Fig. 9 – Disintegrating force patterns of three tablets $GRAN_{25}$.

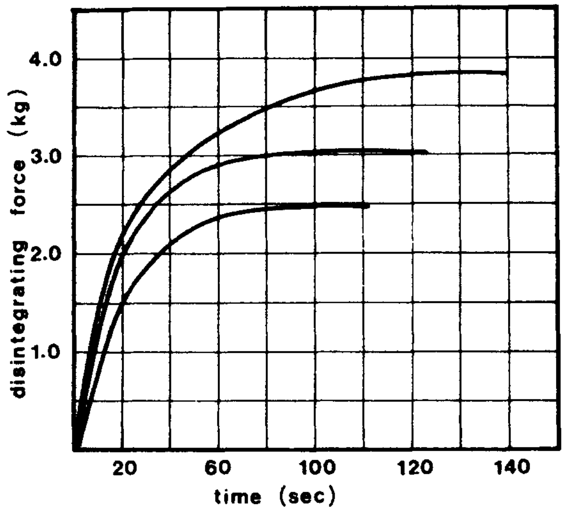


Fig. 10— Disintegrating force patterns for three tablets ASA_C 15% 236 hN.

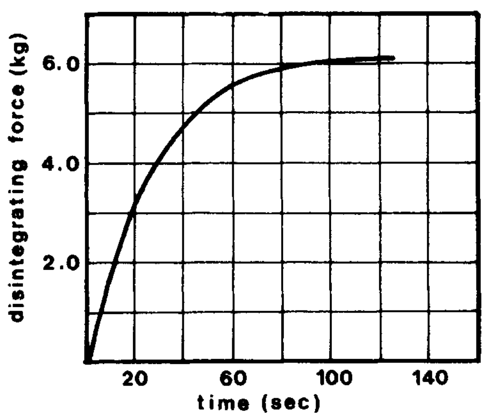


Fig. 11 - Disintegrating force pattern of an exploding tablet ASA_C Elcema

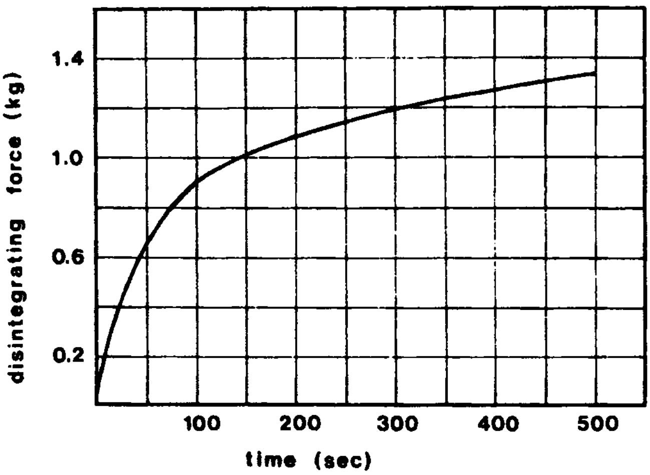


Fig. 12 — Disintegrating force pattern of a tablet undergoing erosion ASA_c Sta-Rx 285hN.

Moreover the shape of the curve is different depending on the type of disintegration process: tablets exploding in water give a rapidly saturated curve (Figure 11), while for tablets undergoing erosion, the force saturation is reached in much longer time (Figure 12). The measurement of v_a and b parameters will be very usefull to understand the disintegration mechanism.

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