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EVALUATION OF BINDER ACTIVITIES ON THE PHYSICAL PROPERTIES AND COMPRESSION CHARACTERISTICS OF GRANULES PREPARED BY TWO DIFFERENT MODES

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ABSTRACT

The effects of various binders and binder concentrations in production of granules by two different granulation modes were first investigated on the basis of the granule size distribution. Increasing the amount of binder produced larger and less friable granules associated with a decrease in flow rate and an increase in angle of repose. The strength of granules prepared by either the wet conventional or the fluidized bed was a function of its mean particle diameter and of binder-content with the later factor being more predominant. The inclusion of paracetamol into the placebo formula decreased the granule crushing strength. The effect was more pronounced with smaller granules and decreased with increasing granule size.

The rank order of the paracetamol-PVP granules crushing strength was reversed for the tensile strength of their corresponding tablets, viz., the paracetamol-PVP tablets prepared from fluidized granulation exhibited a higher tensile strength than that compressed from wet granules. A new parameter index " θ_b index " which combines tablet characteristics is presented. The index proposed allowed an overall simpler quantitative evaluation of a binder activity. Incorporated into this index are four tablet parameters, viz., tensile strength, percent porosity, median dissolution time, and percent friability. A higher " θ_b index " infers better physical properties of tablets. Binders used in this study are then classified according to this index : PVP > gelatin > PEG 6000.

INTRODUCTION

The critical role of binders in the granulation process and the subsequent compression of granules has been well recognised. The physical properties of the drug-binder combinations actually determine the compression characteristics of the resulted tablets, and can be used to solve many production difficulties such as capping. The problem of capping occured during compression of paracetamol has been the subject of many studies (1-3). The effect of moisture on paracetamol compacts was investigated by Armstrong and Griffiths (4), who reported that compacts prepared from both moist and dry granules showed an increase in hardness to a maximum value and a subsequent decrease. A relation between the strength of the compacts, as affected by the nature of the binder, to the compression characteristics of the granules was presented (2).

The fate of the granule in the tablet compressed from a pharmaceutical material have been investigated (5-8). A scanning electron microscopy of the surface produced by tablet, fractured in the diametral compression test was used

to visualize the effect of compressional force, on the deformation of granules within a compact (9). An important conclusion was drawn out of this study that the compressional force and the concentration of the binder contribute more than granule strength to tablet tensile strength (9).

An interesting investigation comparing the mechanical properties of granules, the crushing force of tablets and their compression behaviour was reported (10). However, due to the large scatter of the data related to the asymmetry of the granules prepared in a conventional way, no definite conclusion could be attained. The strength of granules would also be expected to vary because of shape irregularities factor and the presence of localized powder or binder voids (11). In addition, the flow rate of rounded granules was considerably higher than of irregular ones.

Successful granulation in a fluidized bed resulted from a balance between material input and output (12), which is governed by operational factors such as the rate of binder addition, type and concentration of binders, and fluidizing air temperature. In a previous investigation (13), photographs of the granules dried by fluidization showed more symmetry and better flowability than the ones dried by a conventional method.

The intent of this study was to demonstrate the influence of the granules symmetry on their mechanical properties as well as on the compression behaviour of the corresponding tablets. The effects of povidone, gelatin, and polyethylene glycol 6000 added at different concentration levels, as binder solutions to obtain wet and fluidized granules will be discussed.

EXPERIMENTAL

MATERIALS

The drug paracetamol was obtained from (El-Kahira Pharmaceutical Inc., Cairo, Egypt); Lactose B.P. was obtained from (El-Nasr Pharmaceutical Inc., Cairo, Egypt); Magnesium

stearate from (E. Merk, Darmstadt, Federal Republic of Germany); Talc (BDH, Poole, England); Polyethylene glycol, PEG 6000 (BDH, Poole, England); Gelatin (B.P., Evans Medical, U.K.); Polyvinylpyrrolidone, PVP (B.A.S.F., A.G., Germany).

APPARATUS

STREA-Aeromatic AG, Muttenz, Switzerland. The following machine settings were maintained throughout the study: inlet air temperature at 50^{o}, fan capacity at position 8, constant fluidization with an average air volume of 50 m^3/h, and the pressure of compressed air was 0.6 bar; Tray Drying Oven, Despatch Oven Co., Minneapolis, M.N., USA; Erweka Oscillating Granulator, Heusenstamm, Federal Republic of Germany; O'HAUS Moisture Determination Balance, Model 6010, USA; A locally made apparatus for determining the crushing strength of granules; Carver Laboratory Press, Fred S. Carver, USA; Erweka hardness tester, Erweka-Apparatechau, Frankfurt, Federal Republic of Germany; Roche Friabilator, Voss Instrument Ltd., England; Erweka disintegration apparatus, G.m.b.h., Heusenstamm Kr. Offenbach, Main, Federal Republic of Germany; Erweka dissolution Apparatus, Erweka-Apparatechau, Frankfurt, Federal Republic of Germany; U.V. Spectrophotometer, Unicam SP 1800; Standard Sieve Series, V.E.B. Mettalweberei, Neustadt, Orla, DDR.

METHODS

The following formulation was used for all batch granulation operations:

	W(g)	W/W(%)
Hydrous lactose B.P.	160-145	32-29
Paracetamol	300	60
Avicel	20	4
Magnesium stearate:talc(1:9)	15	3
Dry binder	5- 20	1- 4
Distilled water	Q.S.	Q.S.

For placebo formula, paracetamol was substituted by lactose.

Wet Granulation:

A premix of paracetamol, lactose, and avicel was made in a Turbula mixer for ten minutes. This premix was then granulated with a pre-determined quantity of the granulating solution, at three different concentrations (1,3, and 4%W/W) of binder aqueous solution. The wet masses were forced into an oscillating granulator. The granulations were then dried on trays in an air oven for 12 hrs at 50°. Magnesium stearate and talc, in the ratio of 1:9, were then blended with the granulation.

Fluidized Bed Granulation:

The powders in the product container were mixed by fluidization for 1 min before adding the binder solution (14). The binder solution was then pumped in an atomized form using a calibrated metering pump and the spray nozzle. The nozzle was centered in the expansion chamber 39.5 cm above the distribution grid; An air pressure to the nozzle head of 0.6 bar was maintained for atomization of the binder solution. The total weight of water in each binder solution was kept constant and that of the solid binder was allowed to vary. Therefore, the degree of wetting imparted to the fluidized powders was a function of the addition rate of water. Three different addition rates of 10 ml/min, 15 ml/min, and 20 ml/min were used in this investigation. After the granulation process was completed, the drying cycle was initiated for drying the wet granules formed at the fluidizing air temperature for at least 20-25 min. The end of granulation was controlled by measuring the outlet wet bulb temperature of the fluidizing air.

Moisture Determination:

The granulation moisture content was determined using O'HAUS moisture balance. An amount of 10 g of wet granules

were exposed for 15 min to an IR lamp set at 1.5 inch mark with an intensity of 6 watt. The weight of the granules was then read on a scale, and the percentage of moisture content was calculated as explained in a previous study (13).

Granules Evaluation:

The dried granules prepared were stored in a well closed containers and were evaluated for the following criteria:

I. Sieve Analysis

Particle size analysis was performed on all granulations by sieving through a nest of U.S. standard sieves ranging from 63um to 2.5mm mesh sizes on a sieve shaker. Approximately 100 g of granules were subjected to the sieve shaker for 5 min. The weight of the granules retained on each sieve was determined and the particle size distribution was then established.

II. Friability

The granule friability was determined using a Roche friabilator set at 20 rpm. Friability was expressed in percent after 4 min.

III. Flowability and Angle of Repose

The flow rate was measured using a glass funnel 7 cm stem length and 1.4 cm internal stem diameter. The angle of repose was determined by the fixed funnel and free standing cone method (15).

IV. Measurement of Granule Crushing Strength

The technique followed to determine the crushing strength of a granule was similar to the ones used before (9,16). However, some modifications were introduced. Instead of the hypodermic syringes, a hollow glass tube of 28 cm in length was used. The lower end of this tube is wider than the upper one with a window of 2x3 cm cut into it, to facilitate the placement of the granule on the glass plate. An internal glass tube with close ends and 1/3 of the external one in length,

was introduced into the hollow external tube from its wider part. A polished glass plate of 3 cm in diameter was attached to the internal tube end by means of epoxy resin. A third glass tube with one open end, served as a load cell to which mercury could be introduced, was positioned vertically on the internal tube. The instrument was installed in a vertical position on a glass plate which rests on two wooden supporters.
One granule of different sizes (2.5, 2, 1.6 and 1.25 mm) was placed in the center between the glass and the polished glass plates. The granule can be examined by using a magnifying mirror beneath the glass plate.
Mercury was added, by means of a glass dropper, into the glass tube opening at a constant rate of 50 g/min (17) until the single granule failed. The total weight of the two internal tubes and the mercury required to fracture a granule was considered as the crushing strength.
Ten measurements of randomly chosen granules were tested, and the average load in grams was taken as the crushing strength.

Characterization of Compressed Granules:

A carver press was used to produce tablets. A quantity of 500 mg of 20/30 mesh granules were introduced into a circular die 1.2 cm in diameter and compressed between flat-faced punches. All tableting was conducted at a compaction pressure of 90 $MN.m^{-2}$. The compacts were immediately removed from the die and weighed. A micrometer was used to measure their diameter and thickness. The prepared tablets were subjected to the diametral-compression test to determine their tensile strength. A modified Erweka hardness tester was used, and a close procedure to that described in previous publications was followed (18,19).

Uniformity of weight was determined by the B.P. method using 20 tablets from each batch. Friability value was

expressed as percentage using Roche friabilator. For each batch of tablets, the disintegration time was determined according to the B.P. method using Erweka disintegration apparatus. An average of 10 determinations was used at a time for each test. Tablet porosity was calculated from the true and apparent densities as prescribed (3).

An Erweka dissolution rate apparatus was used to monitor the drug release rate for the different batches. A quantity of 900 ml of 0.1N HCL at 37 $\pm$ 0.5° was used as the dissolution medium. The shaft of the basket, where the tablet was placed, was stirred at 60 rpm by means of an electric motor. Samples of 5 ml were withdrawn at appropriate intervals, and the volume taken was substituted by an equal volume of pre-warmed test solution. After suitable dilution with 0.1N HCL, the concentration of paracetamol in each sample was then determined spectrophotometrically by measuring the absorbance at 245 nm. The content uniformity was determined according to the U.S.P. method. Each tablet was triturated individually to fine powder and well shaken with 100 ml of 0.1N HCL and then assayed spectrophotometrically.

RESULTS AND DISCUSSION

Granulation is the process by which fine powders are converted to granules with the desired properties to ensure good tablets production. The role of binders in the granulation operation, as well as the granulation mode employed are considerably critical. Figure 1 depicts the relationship between the cumulative % under size and the granule size for paracetamol granules prepared by wet granulation method, for three different PVP concentrations, i.e., 1,3, and 4%W/W. An increase in the binder concentration yielded larger granules. The size corresponding to 50% on the cumulative percentage axis was taken as the average granule size. The values obtained are

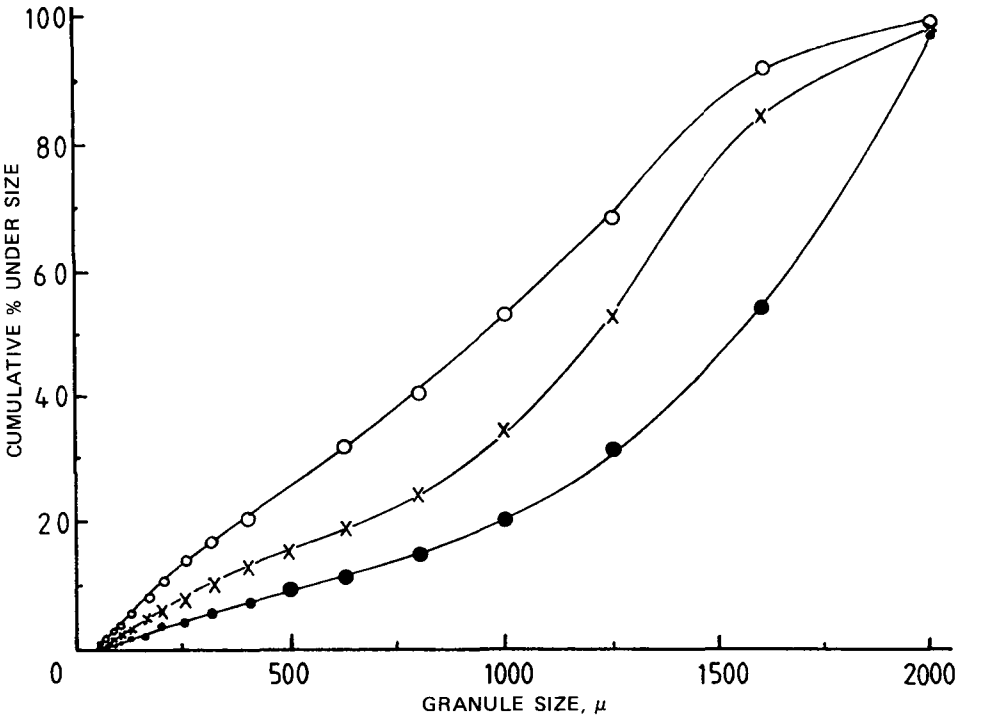

FIGURE 1

Effect of PVP-concentration on the cumulative % under size as a function of granule size for paracetamol granules prepared by wet granulation method. Key: O ,1% PVP; X ,3% PVP; ● ,4% PVP.

listed in Table 1. The greater binder effectiveness with higher concentrations may be attributed to the corresponding increase in binder's adhesiveness. In addition to the geometric mean diameter enlargement, an increase in the percentage of PVP in the formula augmented its binding properties and a less friable granulations resulted (Table 1). These results were in accordance with a previously reported study on lactose granulations with different concentrations of the same binder (20). When evaluating the flow rate of a granulation, the principal factors affecting the granules friability must be considered

TABLE 1

Physical Properties of Paracetamol Granules Prepared by Wet Granulation Method Using Povidone as a binder

Physical Properties of Granules	Formula Weight of PVP (% W/W)		
	1.0	3.0	4.0
Average granule size, u	950	1230	1540
Friability, %	15.50	10.68	5.80
Angle of repose	28.09°	29.67°	30.14°
Flow rate, g/sec	4.87	3.76	3.21
Crushing strength:			
a) Slope, n	2.00	1.90	1.80
a) Intercept, k	-4.19	-3.78	-3.39

a) According to Eq. 2.

since one factor may offset the effect of another. All granulations exhibited a decrease in flow rate and an increase in angle of repose with increasing percentages of PVP in the formulation as illustrated in Table 1.

Granule strength is an important factor as it affects changes in particle size distribution of granules, as well as their compressibility into cohesive tablets (9).
Its usefulness lies as a quality control parameter for manufacturing of reproducible granulations. For a certain PVP concentration the granule strength is a function of its mean particle diameter. It has been reported that (9):

$$C_g = k D^n \qquad \text{Eq. 1}$$

where C_g is the granule crushing strength, D is the granule diameter and k and n are constants for a given formulation. The logarithmic form of Eq.1 is then represented by:

$$\log C_g = k + n \log D \qquad \text{Eq. 2}$$

Log crushing strength of paracetamol granules, C_g , were plotted versus log granule diameter, D, and illustrated in figure 2. The constants k and n were evaluated by linear regression of the plots obtained using different binder concentrations and presented in Table 1. As the binder concentration increased, a decrease of the slope is resulted implying that the amount of the binder in the formula influences the granule resistance to crushing to a greater extent than the particle size (9,21).

Granulation in a fluidized bed is essentially controlled by technical conditions, viz., the rate of binder addition, fluidizing air temperature, and type and concentration of binder used. An investigation on placebo formulation, prior to drug addition, was carried out in order to establish the effects of different variables on the physical properties of the final

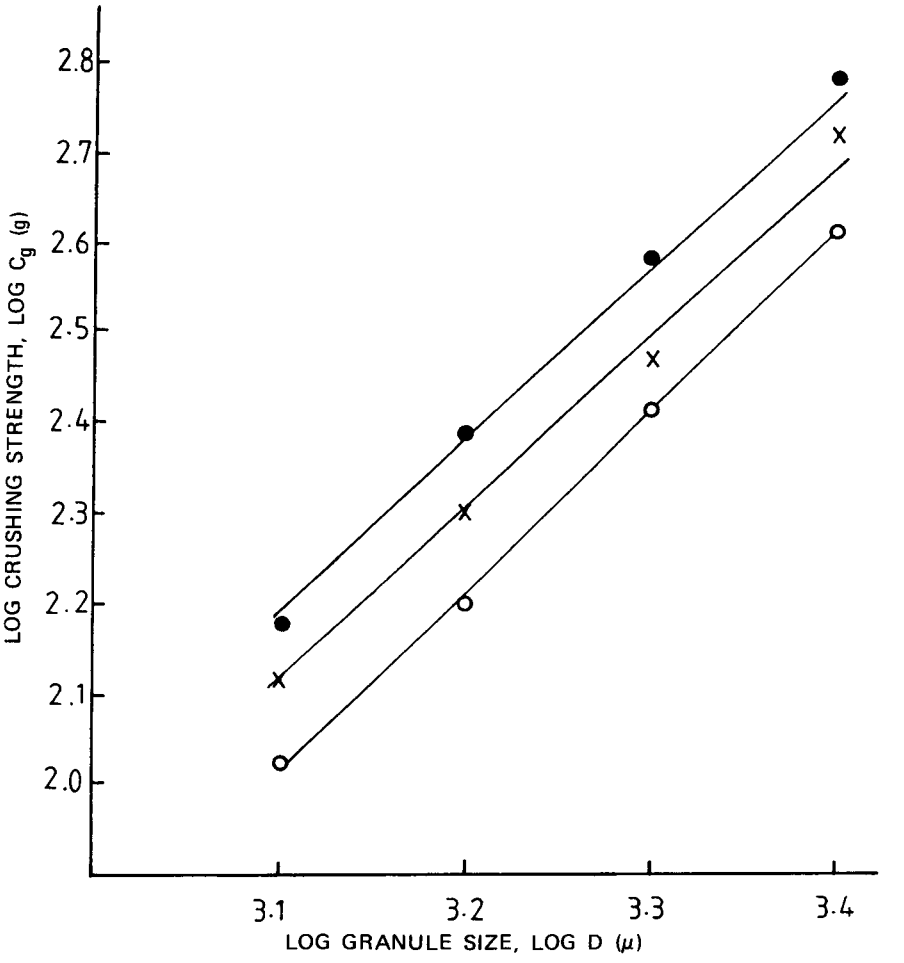

FIGURE 2

Relationship of paracetamol granules size prepared using PVP solution as a binder, to granules crushing strength. Key: O, 1%W/W PVP; X, 3%W/W PVP; ●, 4%W/W PVP.

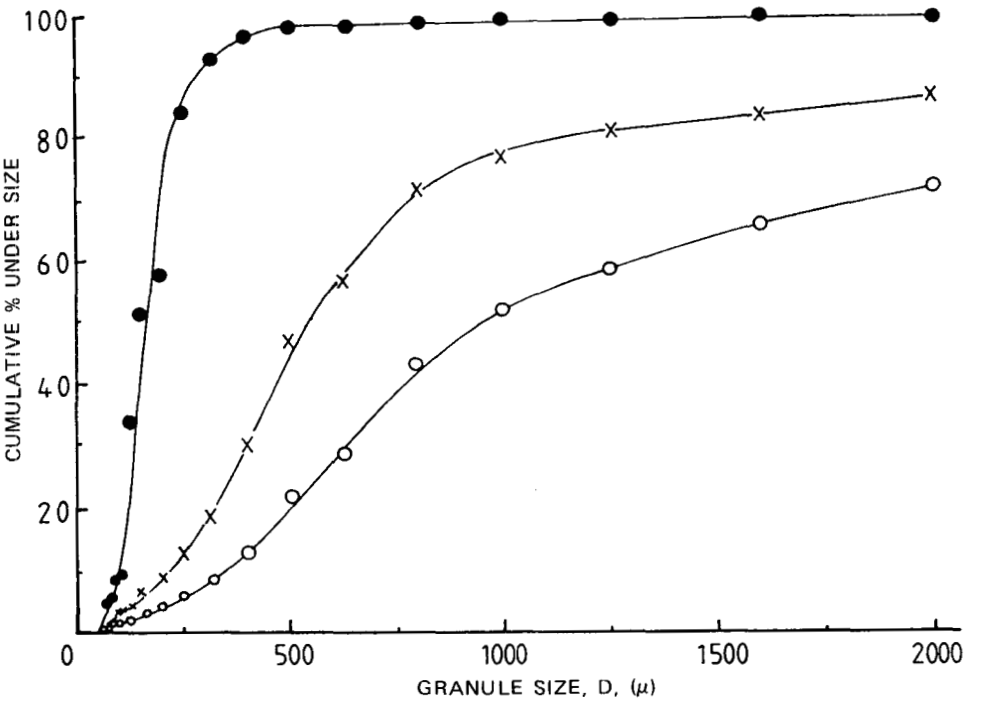

FIGURE 3

Effect of the rate of addition of 4%W/W PVP on the cumulative % under size as a function of granule size for granules prepared in fluidized bed. Key: ● , 10ml/min; X , 15ml/min; 0 , 20ml/min.

granulation. The effect of the rate of adding two different binders to the fluidized materials, on the particle size of the resulted placebo granulation were shown in Figures 3 and 4. Plots of cumulative percentage under size versus granule size, at three different rate of addition of 4%W/W povidone solution to the placebo formula were illustrated in Figure 3. An average granule size of 160 μ was obtained with a 10 ml/min binder addition rate. By increasing the rate of adding the povidone solution to 15 ml/min, an enlargement in the average granule size was observed, viz., 540 μ. This increase in the mean

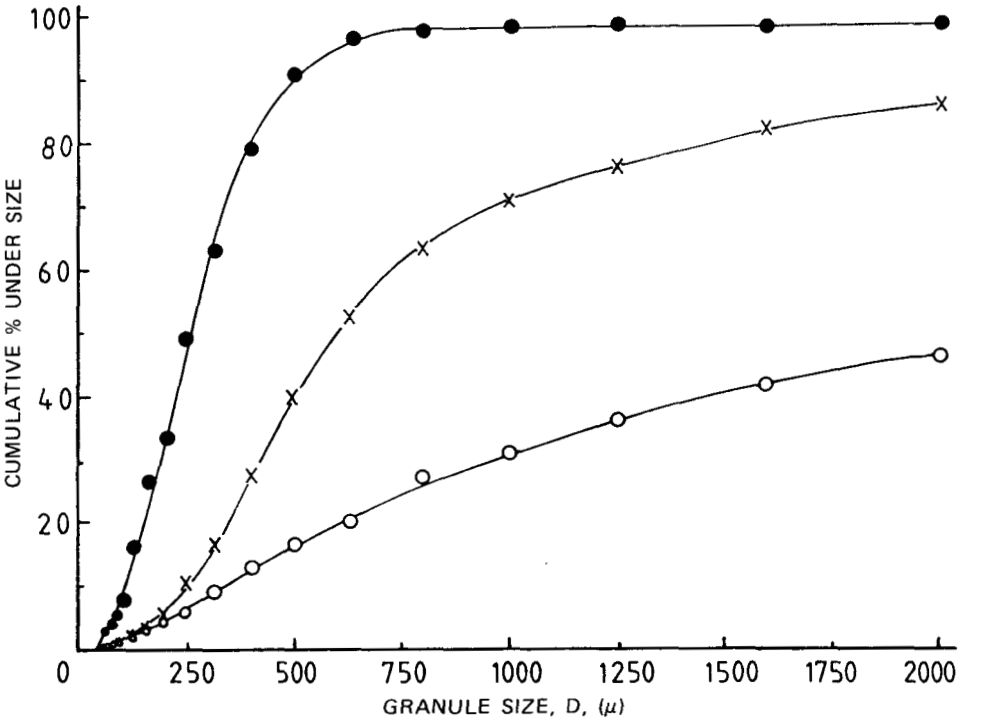

FIGURE 4

Effect of the rate of addition of 4%W/W gelatin on the cumulative % under size as a function of granule size for granules prepared in fluidized bed. Key: ● , 10ml/min; X , 15ml/min; O ,20ml/min.

granule size may be due to the higher penetration and wetting capabilities by the aqueous binder solution, resulted from the increased liquid flow through the atomizing nozzle (14). In turn, this led to an overall slower rate of evaporation of the solvent by the drying medium. Further increase in the binder addition rate to 20 ml/min increased the granule size, and an average granule size of 980 μ is derived.

Figure 4 shows the effect of the rate of addition of 4%W/W gelatin, to the placebo formula, on the average granule size resulted. A value of 600 μ granule size was noted at 15 ml/min

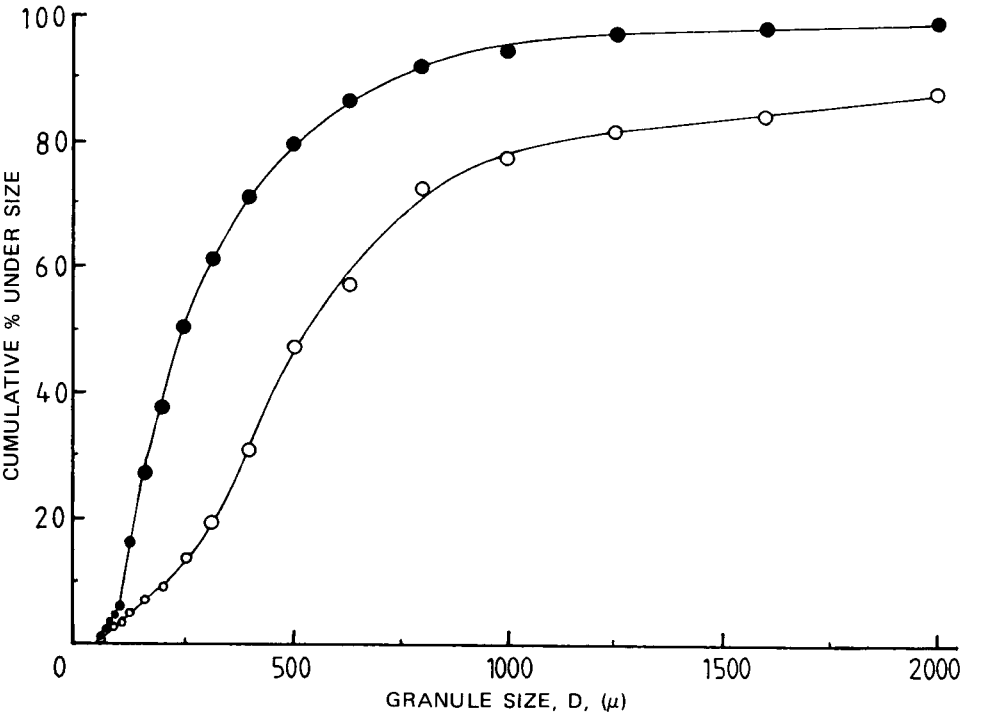

FIGURE 5

Effect of adding paracetamol to the placebo formulation granulated with 4%W/W PVP on the cumulative % under size as a function of granule size for granules prepared in fluidized bed. Key: ● , paracetamol-containing formulation; O , placebo formulation.

binder addition rate, whereas at the rate of 20 ml/min, a perceptible agglomeration occured. In comparing these results with the ones obtained with povidone (Figure 3), a larger average granule size resulted when gelatin solution was used. Accordingly, a rate of 15 ml/min was chosen for the granulation in fluidized bed since a moderate particle size granules were formed and to avoid any attrition effect on the large agglomerates (22). A single set of other operational variables such as the air temperature, and velocity was selected and maintained for all batch granulations.

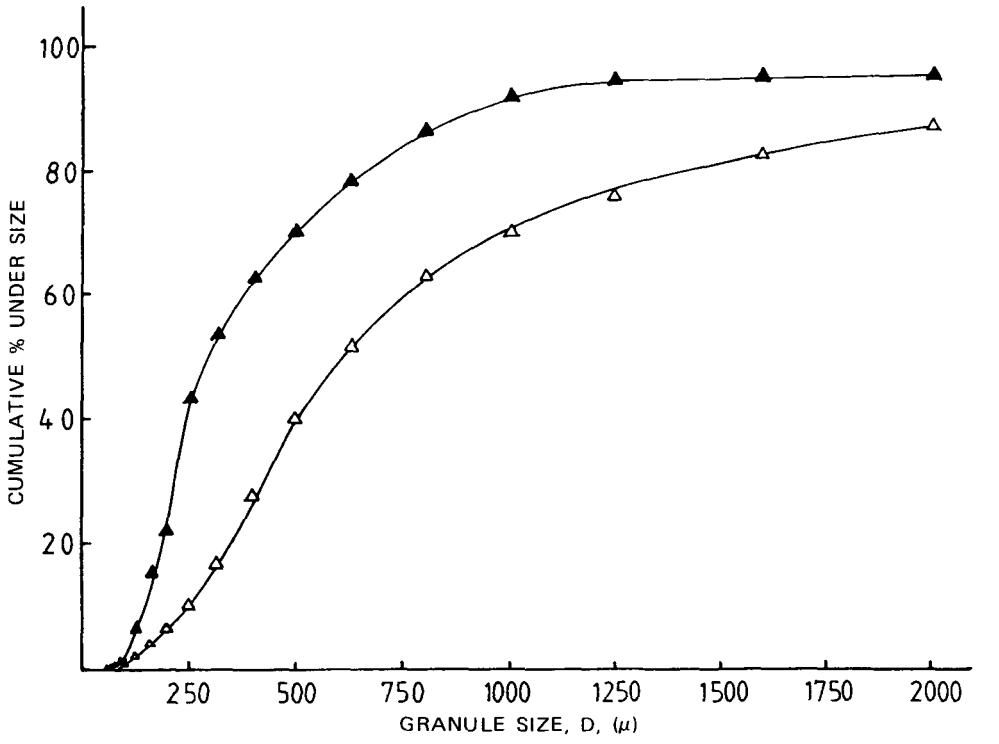

FIGURE 6

Effect of adding paracetamol to the placebo formulation granulated with 4%W/W gelatin on the cumulative % under size as a function of granule size for granules prepared in fluidized bed. Key: ▲, paracetamol-containing formulation; Δ, placebo formulation.

The inclusion of the micronised paracetamol in the granulations prepared by using either 4%W/W PVP or gelatin, led to a decrease in the average granule size in both cases as demonstrated in Figures 5 and 6. The effects of different binders on the average granule size for paracetamol granulations prepared by fluidization was illustrated in Figure 7. Using 4%W/W gelatin as a binder solution produced larger granules than with povidone or polyethylene glycol, this later gave the smallest average granule size. An investigation of

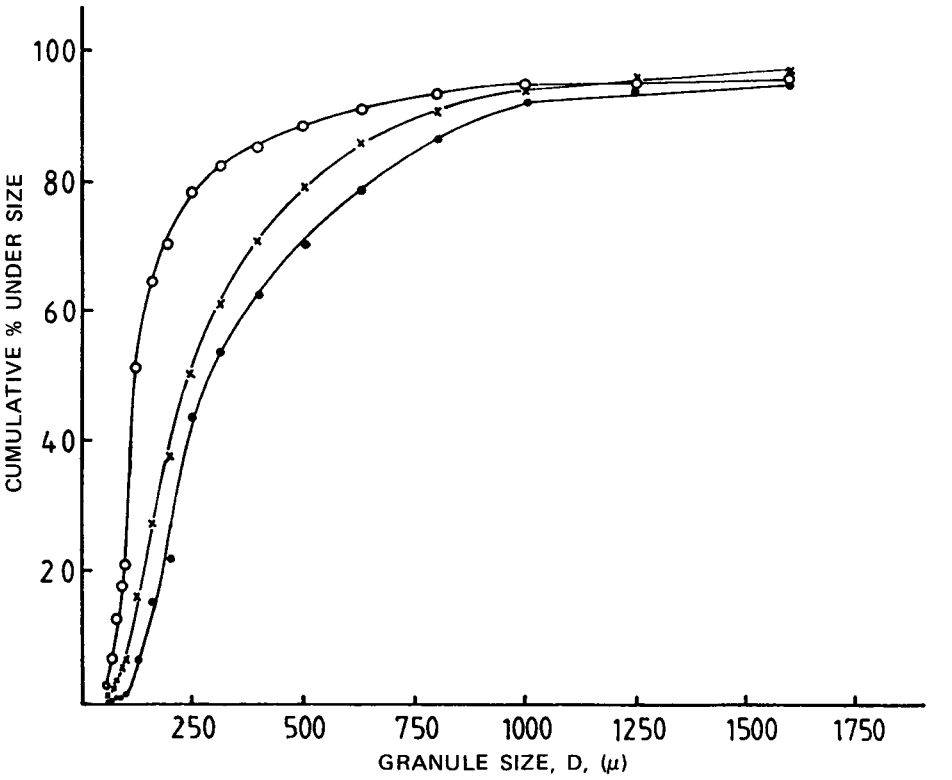

FIGURE 7

Effect of different binders (4%W/W) on the cumulative % under size as a function of granule size for granules prepared in fluidized bed. Key: O , PEG 6000; X , PVP; ● , gelatin.

the individual physical properties of each granulation, prepared using different binder solution, was illustrated in Table 2. The degree of friability was inversely proportional to the granule diameter, which is consistent with a previous finding (23). All granulations showed a decrease in flow rate and higher angle of repose with increasing average granule size. In addition, the flow rate of granules obtained by fluidization using 4%W/W PVP as a binder (Table 2) was

TABLE 2

Effect of Different Binders, at 4%W/W Concentrations, on the Properties of Paracetamol Granulations Prepared in Fluidized Bed

Physical Properties of Granules	PVP	Gelatin	PEG 6000
Average granule size, μ	250	280	125
Friability, %	4.00	3.00	9.70
Angle of repose	27.48°	28.07°	25.65°
Flow rate, g/sec	7.31	6.64	10.22
Crushing strength:			
[a] Slope, n	1.33	1.55	1.05
[a] Intercept, k	-2.82	-2.05	-2.20

[a] According to Eq. 2.

considerably higher than the corresponding ones prepared by the wet conventional method (Table 1).

For a given binder the granule strength is a function of its size. The effect of 4%W/W povidone, gelatin, and polyethylene glycol on the log granule crushing strength, C_g, for granulations prepared in fluidized bed is shown in Figure 8. Increasing the granule size gave stronger granules, and the higher crushing strength values were obtained when gelatin solution was used as a binder. The lines were regressed and the constants k and n, according to Eq.2, were evaluated and presented in Table 2. The higher slope was derived with 4%W/W povidone.

The relationship between the granule size and its crushing strength, for placebo formula and in presence of paracetamol, when 4%W/W PVP or gelatin were used is illustrated in Figure 9. It was noticed that the inclusion of paracetamol in the formula decreased the crushing strength of the granules. However, the effect was more pronounced with smaller granules and decreased with increasing the size until identical strengths were obtained when granule size is larger than 2.5×10^{-2} cm for both binders. Figure 10 illustrates the relationship between the crushing strength and the granule size using 4%W/W PVP as a binder. As can be seen in this figure, the granules obtained by conventional wet method exhibited a greater mechanical strength than the ones prepared by fluidization. Determination of the percentage moisture content for granules prepared from both methods, revealed a higher value for granules prepared by wet granulation method than that obtained by fluidization in fluidized bed. viz., 2.85% and 1.4% respectively.

The effect of moisture on the strength of bulk solids was the target of many investigations (24,25). The greater mechanical strength exhibited by wet granules may be due to their higher moisture content than the granules prepared in fluidized bed. Upon exposure to ambient room conditions after preparation, the

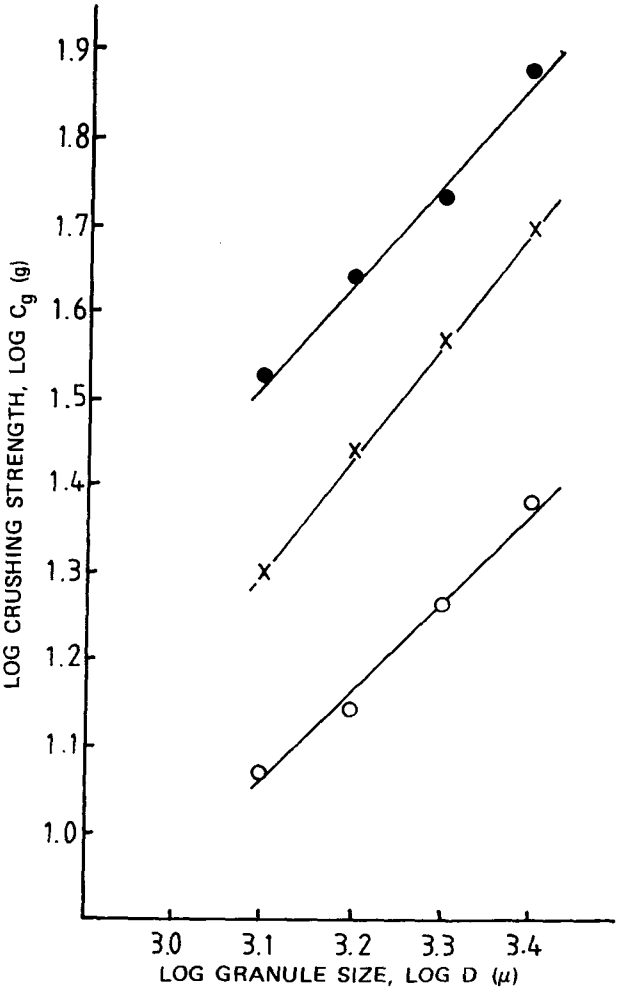

FIGURE 8

Effect of different binders (4%W/W) on the log paracetamol granule crushing strength as a function of log granule size for granulation prepared in fluidized bed. Key: ● , gelatin; X , PVP; O , PEG.

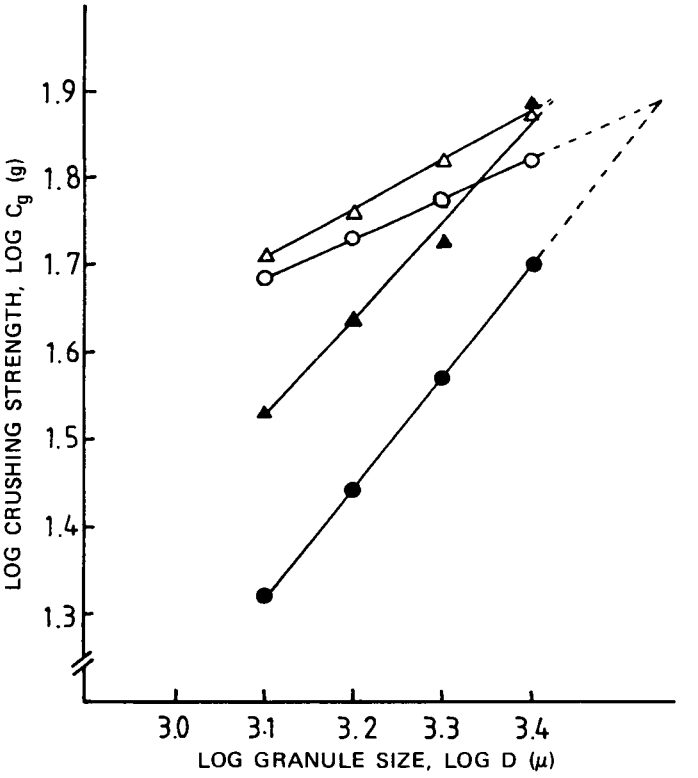

FIGURE 9

Relationship of granule size to granule crushing strength for granulation prepared in fluidized bed. Key: Open symbols for placebo formula; and close symbols for formula containing paracetamol; O , with 4%W/W PVP; Δ , with 4%W/W gelatin.

crushing strength of the granules obtained by wet technique increased as a result of partial moisture loss (25).

The ultimate evaluation of a tablet granulation lies in its tableting characteristics. Accordingly, tablets were compressed from granulations prepared by both techniques. The relationship of granule size to tensile strength of paracetamol tablets granulated with 4%W/W PVP, using wet and fluidized granulation modes, and compressed at 90 MNm^{-2} is

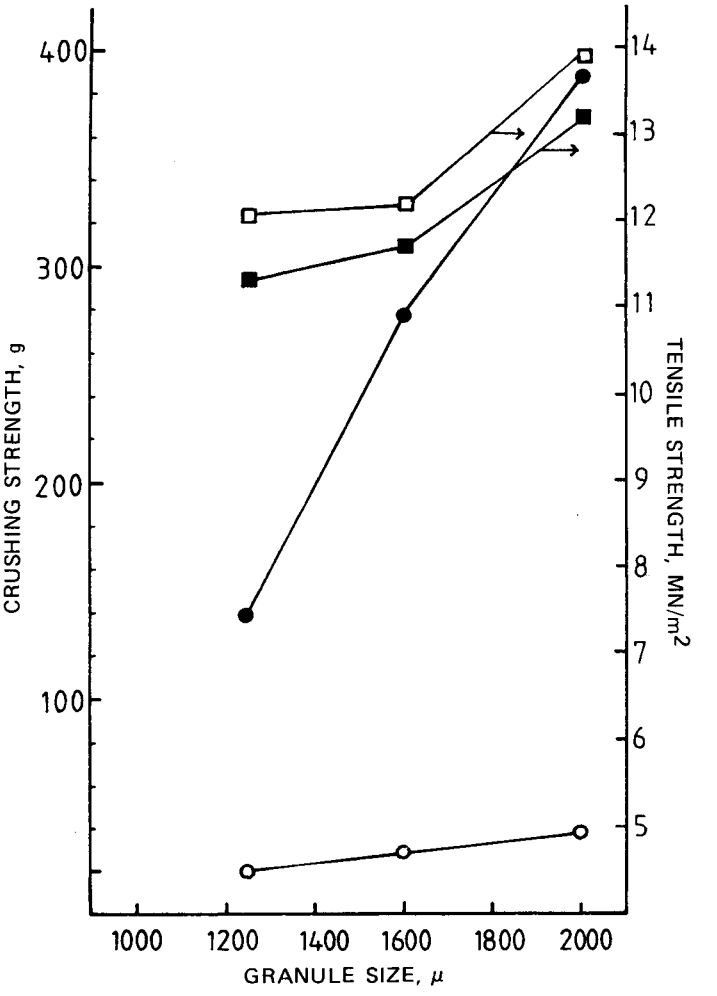

FIGURE 10

Relationship of granule size to granule crushing strength and tensile strength of paracetamol compressed tablets. Granulating solution used was 4%W/W PVP. Key: Open symbols for granulation prepared in fluidized bed; and close symbols for granules obtained by wet mode.

also demonstrated in Figure 10. As the granule size is enlarged, there is a corresponding increase in the granule strength as well as in the tensile strength of tablets compressed from these granules. The tablets produced from fluidized granulation showed a higher tensile strength than the wet ones. The weakest granules produced the strongest compacts, viz., the rank order of the granule crushing strength was reversed for the tensile strength of the resulted tablets. A similar finding was noted before (26) and justified as more plastic flow occured giving a greater axial to radial conversion of force. It has also been reported that the paracetamol-PVP granules undergo more plastic flow/crushing than paracetamol alone (10). On complete removal of axial pressure, a residual die wall pressure was exerted by both granules types but was much higher for paracetamol-PVP than for paracetamol. As the paracetamol tablet is ejected from the die, capping occured which could be related to the high elastic recovery leading to the breakage of interparticulate bonds. It was reported that a high stress ratio of 3.47 was obtained for paracetamol tablets implying a considerable elastic recovery has occured when the axial pressure is withdrawn (10). In contrast, the paracetamol-PVP tablets exhibited a low stress ratio, a reduced elastic recovery and no capping occured.

Since dissolution is governed by the degree of fusion/adhesion between particles in a compact, therefore standardization of materials in terms of their compression characteristics may provide further insight into binders activities. Amount of paracetamol dissolved versus time profiles were generated for tablets compressed from granules prepared, with 4%W/W PVP, by the two granulation modes and presented in Figure 11. The dissolution rate profiles were not significantly different in both cases, which allowed a conclusion to be drawn that the more symmetrical granules obtained by fluidization mode (13), is not a major factor affecting the dissolution rate of

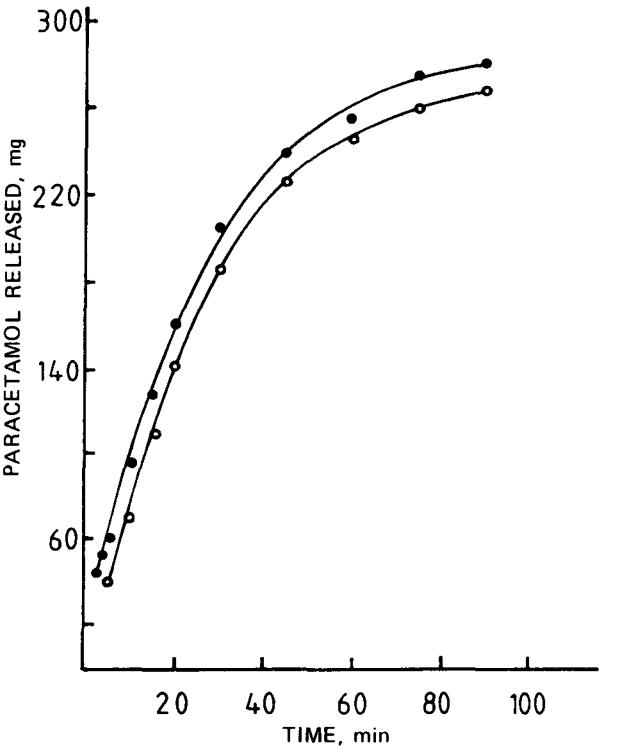

FIGURE 11

Dissolution rate profiles of paracetamol tablets containing 4%W/W PVP. Key: O , compressed from wet granules; ● , compressed from fluidized granules.

paracetamol-PVP tablets. The dissolution rate profiles for paracetamol-binder tablets compressed from fluidized granules using 4%W/W PVP, gelatin, or PEG are shown in Figure 12. The times required for 50, and 90% dissolution of the paracetamol from the tablets are demonstrated in Table 3. The PEG-containing granulation exhibited the faster dissolution rate profile, whereas the formulation containing gelatin had the slowest dissolution rate. As a water-soluble binder, PEG may enhance dissolution by increased wetting of the mass, with

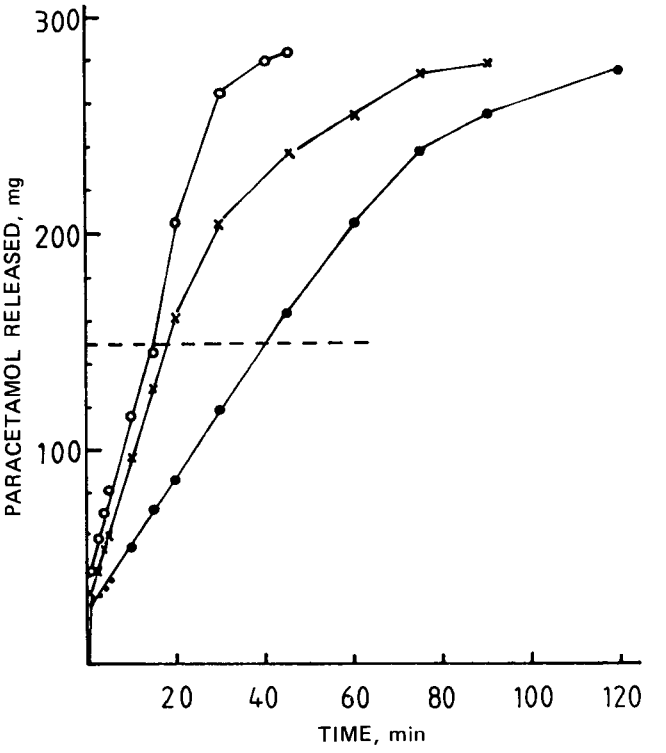

FIGURE 12

Dissolution rate profiles of paracetamol tablets prepared from fluidized granules. Key: ● , 4%W/W gelatin-containing tablet formulation; X , 4%W/W PVP-containing formulation; O , 4%W/W PEG-containing formulation.

good solvent penetration (27). Other factors which contribute to the dissolution rate of paracetamol-binder tablets are the tensile strength and the friability. The values obtained for the three binders under investigation are listed in Table 3. PEG showed a lower tensile strength with higher friability than the two other binders, followed by PVP then gelatin.

From Table 3, it is obvious that tablets compacted from granules containing a particular binder may exhibit some desirable properties, however these special qualities may be

TABLE 3

Effect of Different Binders on the Compression Characteristics of Tablets Compressed from 20/30 Mesh Size Granules Prepared in a Fluidized Bed

Tablets Properties	4%W/W Binder PVP	Gelatin	PEG 6000
Tensile strength, σ, MN/m^2	0.84	1.29	0.35
Disintegration time, min	2.32	3.10	1.20
Friability, %	1.28	1.15	7.52
Porosity, %	25.08	21.88	27.25
Drug release time:			
$T_{50\%}$, min	18.00	40.00	15.00
$T_{90\%}$, min	72.00	112.00	28.00
Drug content, %	94.00	92.00	93.50
[a] θ_b index, MN/m^2.min	0.914	0.614	0.085

a) According to Eq. 3.

encountered by other undesirable ones. In order to assess a single numerical value which could help in the evaluation of a specific binder activity, a binder index is proposed in which four tablet parameters are incorporated. Although the number of parameters which must be considered for a good tablet production is quite high, they are all correlated in a way. The " θ_b index " derived in this work, for an overall binder activity evaluation, is represented by:

$$\text{" } \theta_b \text{ index " } = \frac{\sigma \times \text{Porosity}}{T_{50\%} \times \text{Friability}} \qquad \text{Eq. 3}$$

where σ, is the tablet tensile strength in MN/m^2, the porosity is in percentage, $T_{50\%}$, is the median dissolution time in min, and the friability is in percentage. According to Eq 3, " θ_b index " has a unit of $MN/m^2.min$.

The values calculated using Eq.3 for the three binders used are presented in Table 3. PVP exhibited the highest index, i.e., 0.914 $MN/m^2.min$, followed by gelatin with a value of 0.614 $MN/m^2.min$, and finally PEG had the lowest " θ_b index " of 0.085 $MN/m^2.min$. The computed binder index for PVP is 11 times greater than that for PEG.

The proposed equation is based on the following criteria: (1) a high tensile strength value to withstand handling; (2) a high porosity for tablets produced; (3) a low median dissolution time; and (4) a low friability. A higher " θ_b index " infers better physical characteristics of the resulted tablets.

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