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Effect Of Sieve Size For Wet And Dry Screening On The Physical Properties Of Lactose Granules And Their Corresponding Tablets

By

S.Y. Osewa and R.N. Nasipuri
Department of Pharmaceutics,
Faculty of Pharmacy
University of Ife
Ile-Ife
Nigeria.

Summary

Various batches of lactose granules were prepared by wet granulation process using acacia, cassava starch and polyvinylpyrrolidone separately as binders by inter-changing sieves for wet and dry screening. The effects of wet and dry screen aperture sizes together with the effects of the binders used on the physical properties of such granules and the corresponding tablets were investigated. The bulk volume of granules was found to be increased as the aperture size of sieves for dry screening increased while keeping a particular

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sieve constant for wet screening. No significant difference was observed with regards to the effect of sieve size upon the flow rate.

It was also observed that keeping the sieve size for wet screening constant, the mean tablet weight increased while the tablet weight variation decreased as the sieve size for dry screening decreased. There found to be an observable relationship between the sieve sizes used for dry and wet screening, average granule size and hardness of tablets. When a particular sieve was kept constant for wet screening, an increase in the sieve aperture size for dry screening resulted in an increase in average granule size and a decrease in tablet hardness. This may be due to increase in void space, decrease in die fill and less bonding between the granules. The disintegration time of the tablets was found to be significantly influenced by the sieve size combination used for wet and dry screening. When sieves for wet screening were kept constant, an increase in the sieve size for dry screening generally produced tablets of lower disintegration time.

INTRODUCTION

Effects of sieve size and commonly used binders on the size distribution of lactose granules prepared by massing and force screening has been presented earlier by Nasipuri, Irono and Opakunle (1).

Various workers have reported the effects of changing granule size on the physical properties of the resultant tablets (2-8). Recently Nasipuri and Kuforiji (9) also studied the effect of granule size of starch as a direct compression carrier on the physical properties of chlorpheniramine tablets. Although different mesh size of sieves were used by the above workers to study the effect of granule sizes, no systematic study appears to have been made on the effects of sieve size for both wet and dry screening on the physical properties of granules and the resultant tablets. We have therefore, extended the earlier work of Nasipuri and others (1) and assessed to what possible effect the combination of wet and dry screen sizes in the conventional method of massing and screening may have on the physical properties of granules and the resultant tablets.

Materials

Lactose (Whey Products, U.K.) was used as supplied. Acacia and polyvinylpyrrolidone (PVP) were obtained from B.D.H., Poole, U.K. and were used at concentrations of 10% w/w solutions whereas cassava starch was prepared in the laboratory from the tubers of Mannihot utillisima and was used as a 10% w/w paste. Magnesium stearate was of B.P. grade.

Methods

Method of preparation of granules using various combinations of sieves of different aperture sizes by massing and force screening method have been reported earlier (1). Three different binders namely, PVP, acacia and cassava starch, were used to prepare the granules. Various batches of granules thus prepared were then used to determine the following granule properties:

Specific Bulk Volume And Bulk Density:

The specific bulk volume of the granulation was calculated by dividing the volume by the weight of the sample. 50g of granules from each batch was used for the purpose. The procedure was repeated three times for each individual group of granules. The reciprocal of the specific bulk volume gave the bulk density of the granulations.

Flow Rate Of Granules:

Flow rate of granules was determined using the granule flow tester, type GDT (Erweka) by timing the passage of 50g of granulation from each batch.

Compression of Granules:

Magnesium stearate, in a concentration of 0.50% w/w, was added to each batch of granules as a lubricant. The granules were then compressed on a single punch tabletting machine (Diaf A/S, Denmark) fitted with 6mm flat punch at a predetermined compression pressure. Machine adjustments and the volume of the die fill were kept constant during the investigation.

Tablet Weight Variation:

Twenty tablets from each batch were weighed individually on an analytical balance and the mean weight, standard deviation and coefficient of variation calculated.

Tablet Crushing Strength:

Hardness of tablets were determined using a Pfizer Hardness Tester (Chemical Division, Pfizer Inc., U.S.A.) which indicates the resistance to crushing in both pounds and kilogrammes. Mean crushing strength of ten tablets was determined from each batch.

Tablet Friability:

Friability value was determined by subjecting 20 tablets of known weight to a controlled series of falling shocks in a Roche Friabilator (Erweka), the drum of which was made to rotate for 4 minutes at 25r.p.m. The percentage loss due to abration was then calculated.

Disintegration Time:

Disintegration time of tablets was determined by the B.P. method using Manesty Tablet Disintegration Test Unit (Manesty Machines Ltd., U.K.). Five tablets were used at a time for each test. Distilled water at 36 - 38°C was used as the medium.

RESULTS AND DISCUSSION

Lactose was used in this study because this substance is considered as one of the most popular diluents in the production of compressed tablets and is used extensively for this purpose. Therefore study of factors affecting the physical standards of lactose tablets from granules prepared by inter-changing sieves for wet and dry screening may be considered important from the practical development point of view.

The specific bulk volume of the granulations indicates the volume per unit weight of the solid, the volume of the intra-particular pores and the volume of the inter-particle spaces. Effects of various sieve combinations for wet and dry screening on the average granule size, specific bulk volume and bulk density

Table I.

Effect of inter-changing sieves for wet and dry screening on the average granule size, specific bulk volume and bulk density of lactose granules

Binders:- A = 10%w/v PVP solution;
B = 10%w/v Acacia solution;
C = 10%w/v Cassava starch paste

a = Average granule size;
b = Specific bulk volume and
c = Bulk density.

Sieve Combination	Sieve aperture size (mm)		Binder A			Binder B			Binder C		
	Wet Screen	Dry Screen	a	b	c	a	b	c	a	b	c
A	0.833	0.833	800	1.81	0.62	850	1.61	0.62	910	1.86	0.54
B	0.833	1.00	970	1.99	0.50	1050	1.91	0.52	960	2.01	0.50
C	0.833	1.40	940	2.06	0.49	1035	1.84	0.54	1020	2.02	0.50
D	0.833	1.67	1020	2.17	0.46	1100	2.13	0.47	1060	2.14	0.47
E	0.833	2.00	1040	2.51	0.39	1085	2.30	0.43	1100	2.51	0.40
F	1.00	0.833	530	1.61	0.62	530	1.58	0.63	680	1.56	0.64
G	1.00	1.00	750	1.80	0.56	960	1.86	0.54	875	1.49	0.67
H	1.00	1.40	1015	1.93	0.52	1250	1.95	0.51	1255	1.81	0.55
I	1.00	1.67	1150	2.03	0.49	1255	1.94	0.52	1420	2.11	0.48
J	1.00	2.00	1270	2.23	0.45	1285	2.31	0.43	1360	2.15	0.47
K	1.40	0.833	500	1.73	0.58	510	1.60	0.63	650	1.60	0.63
L	1.40	1.00	630	1.87	0.54	660	2.01	0.50	720	1.79	0.56
M	1.40	1.40	950	2.03	0.49	1050	2.00	0.50	1130	1.80	0.56
N	1.40	1.67	970	2.08	0.48	1060	2.00	0.50	1130	1.90	0.53
O	1.40	2.00	1050	2.10	0.47	1150	2.10	0.47	1350	2.32	0.43
P	1.67	0.833	450	1.80	0.56	485	1.74	0.57	580	1.87	0.53
Q	1.67	1.00	500	1.85	0.54	630	1.79	0.56	685	1.82	0.55
R	1.67	1.40	700	1.98	0.51	760	1.89	0.53	830	1.83	0.55
S	1.67	1.67	910	1.99	0.50	940	1.99	0.50	1000	1.98	0.51
T	1.67	2.00	850	2.32	0.43	1070	2.10	0.48	1130	1.97	0.51
U	2.00	0.833	470	1.79	0.56	440	1.68	0.59	555	1.76	0.57
V	2.00	1.00	570	1.89	0.53	590	1.77	0.57	650	1.77	0.56
W	2.00	1.40	650	1.89	0.53	740	1.78	0.56	770	1.83	0.55
X	2.00	1.67	800	1.97	0.51	745	1.90	0.53	810	1.82	0.55
Y	2.00	2.00	750	2.22	0.45	800	2.16	0.46	900	2.10	0.47

using three different binders are presented in Table 1. Results show that the bulk volume increases as the aperture size of sieves for dry screening increases while keeping a particular sieve constant for wet screening. This observation holds good for all the binders used in this study.

Theoretically, the void space should increase as the granule size is increased, thereby increasing bulk volume. Marks and Sciarra (5) have pointed out that the true effect of granule size upon bulk volume may be disguised by certain contributing factors like granule shape, rate and direction of flow etc. But Nasipuri et. al. (1) have shown that for any particular wet screen aperture size, the average granule size increases as the dry screen aperture size is increased; therefore, the increase in the specific bulk volume in the present investigation appears to follow the theoretical pattern i.e. the bulk volume increases as the granule size is increased. But as the analysis of variance on the result shows that at the 95% probability level, the treatment effect is not statistically very significant, the true effect of the sieve size upon specific volume, therefore, may have been modified by factors like positioning of the granules in relation to each other, while the granule size range may not have been sufficiently different from each other to show a significant difference in the results.

Flowability of granules was found to be affected, though not significantly, by interchanging sieves for wet and dry screening (Fig. 1) Except in certain cases, where there was found to be an interrupted trend, generally decreased flow rate was observed as the dry screen aperture size was increased while keeping the aperture size for wet screen constant. While studying the effect of sieve size and commonly used binders on the size distribution of lactose granules, Nasipuri and others (1) showed earlier that an overall increase in average granule size was obtained as the dry screen size was increased (values of average granule size are included in Table 1). It may therefore, be probable that the increased flow rate of granules in the present investigation is due to the decreased average granule size that has been formed by various sieve combinations. The analysis of variance showed that the treatment effect is not very significant at the 95% level of confidence and this may be due to the presence of varying amount

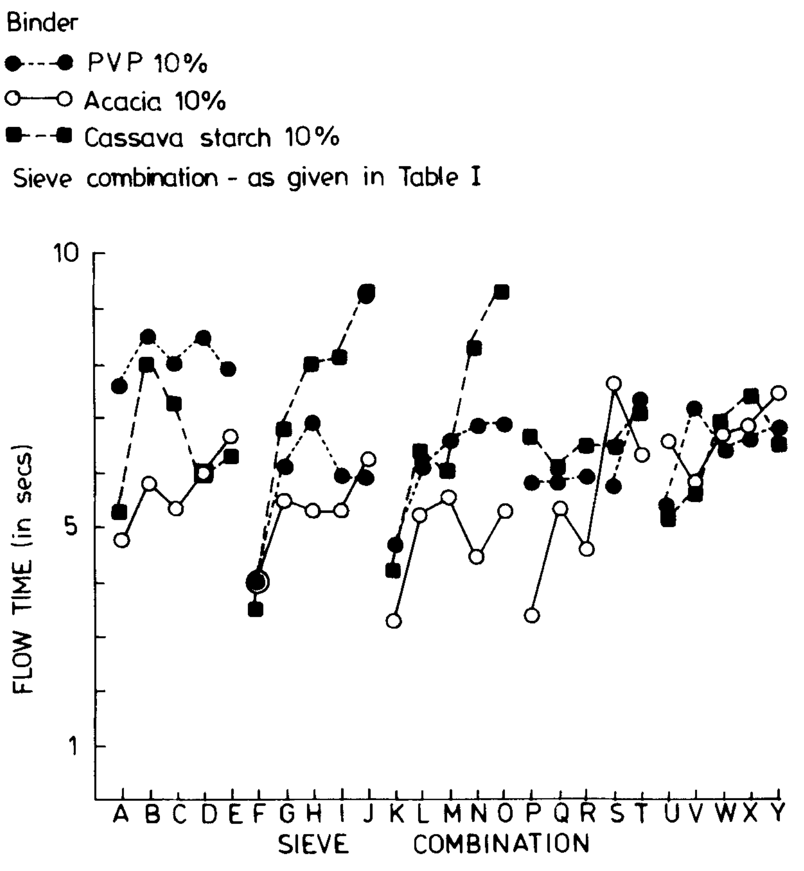

Fig. 1. Effect of sieve size for wet and dry screening on the flowablility of lactose granules

of 'fines' in the different batches of granules that may have modified the flow rate results. Rubinstein and Blane (8) observed a relationship between flow properties and the size of lactose and calcium phosphate granules containing bendrofluazide. Using a specially designed apparatus, Marks and Sciarra (5) also found the flowability of granules to be affected by the size of the granules. They observed greater flow rate of the granules through an orifice as the size was decreased.

It has been found that the sieve combinations for wet and dry screening have effect on the properties of granules. It would therefore, be expected that the sieves used for the wet and dry screening of granules

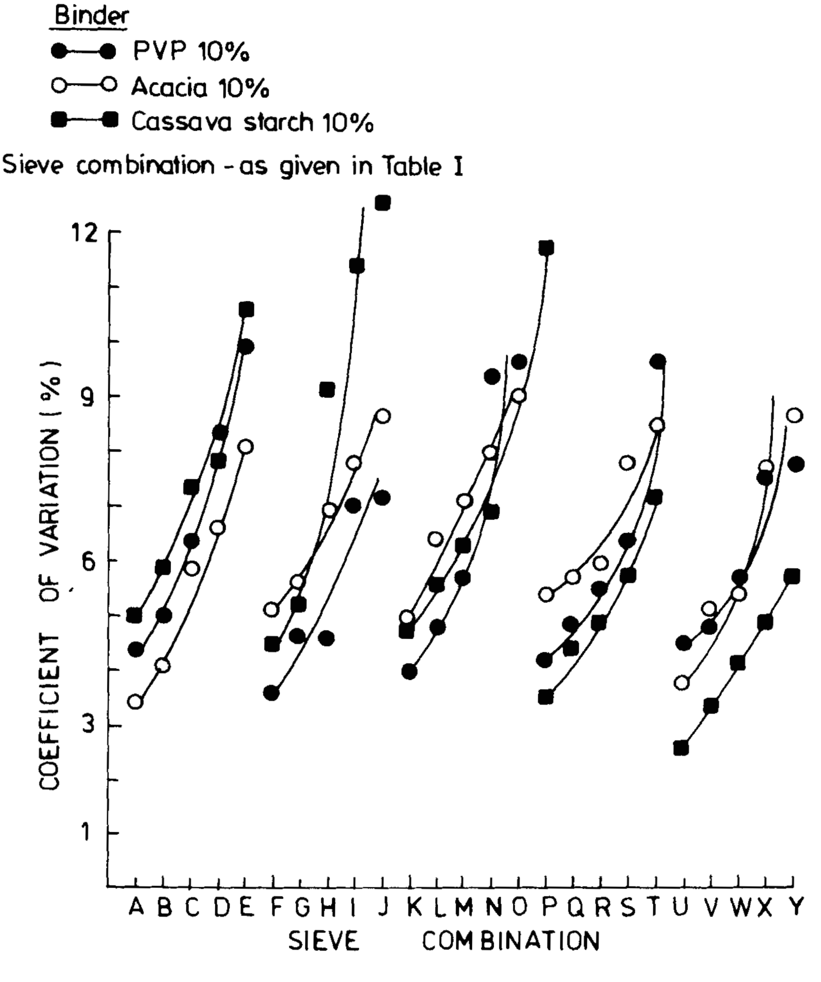

Fig. 2. Effect of interchanging sieves for wet and dry screening on the weight variation of lactose tablets

may also have effect on the properties of tablets prepared from such granules. Effects of interchanging sieves for wet and dry screening on the weight variation of lactose tablets are given in Fig. 2. It can be seen from the results that keeping wet screen size constant, as the dry screen size increased there is an increase in weight variation as evidenced from the higher values of the coefficient of variation. Statistical analysis also shows that the sieve size effect for wet and dry screening is significant at the 99% level of confidence (Table 2). Comparing the result with the sizes of granules that are produced by various sieve combinations, it can be seen that the weight variation reduces as the granule size becomes smaller. This is expected since smaller granules would exhibit more regular packing resulting in more uniform die fills during compression than larger granules. Although Marks and Sciarra (5) reported an interrupted trend in weight variation due to granule size, Rubinstein and Blane (8) and Kassem et. al. (6) observed that reducing granule size decreases the tablet weight variation.

When a particular sieve size was kept constant for wet screening and the sieve aperture size for dry screening

Table 2

Analysis of variance* for the weight variation of lactose tablets

SV	DF	SS	MS	F. Test
Between treatments	2	8909.208	4454.604	8.69
Within treatments	22	11277.179	512.599	
Total	24	20186.387		

*At the 99% probability level, the tabulated F (2,22) = 5.72 and the calculated F equals to 8.69. Therefore, the treatment effect is significant.

was increased, there was a corresponding decrease in the crushing strength of tablets (Fig. 3). This is probably due to the change in the granules from smaller to larger size as has been shown earlier (1), the die fill weight and also the increase in the void space. Marks and Sciarra (5) have shown that as the granule size is reduced, the die fill weight is increased. Kassem and others (6) also reported that a decrease in

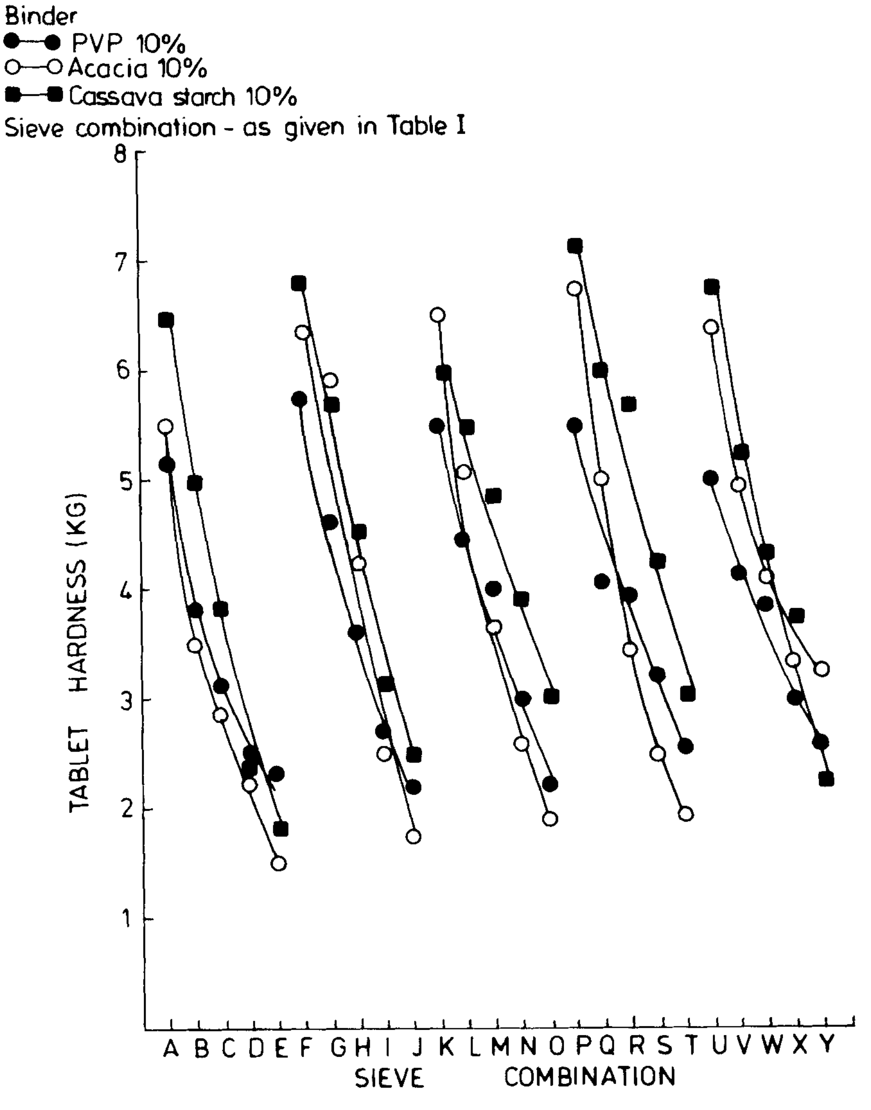

Fig. 3. Effect of sieve size for wet and dry screening on the hardness of lactose tablets

granule size resulted in an increase in hardness thought to be due to an increased area of contact because of a decrease in void space. On the other hand, Rubinstein and Blane (8) did not find any relationship and indicated that granule size cannot be considered as a primary variable influencing tablet crushing strength.

The crushing strength results in the present study were verified by numerous readings and a statistical analysis of variance. The sieve size effect on this parameter was found to be highly significant at the 99% level of confidence (Table 3).

Table 3

Analysis of variance* for crushing strength of lactose tablets

SV	DF	SS	MS	F. Test
Between treatments	2	43.8679	21.9339	28.6815
Within treatments	22	16.8243	0.7647	
Total	24	60.6922		

*At the 99% probability level, the tabulated F (2,22) equals to 5.72 and the calculated F equals to 28.6815. The treatment effect, therefore, is highly significant.

Tablet friability is the measure of the strength of tablets and their ability to withstand abuse during normal handling and transportation. Figure 4 shows the effect of interchanging sieve size for wet and dry screening on the friability value of lactose tablets. There is an observable relationship between the sieve size combination, the size of the granules and the friability value of the resultant tablets. When a particular sieve was kept constant for wet screening and increasing the sieve size for dry screening (which corresponds to an increase in granule size), there was an increase in the friability value of tablets. It was further derived statistically that the sieve size effect is highly significant at the 99% probability level (Table 4).

The trend in the results appears to be definite and reproducible in the case of acacia and cassava starch binders. In the case of PVP binder however, there found to be somewhat interrupted trend in the friability values. The rise in the friability values of the tablets with PVP as binder when compared to those of cassava starch and acacia as binders may be due to a binder dependent effect. Weak granules tend to behave

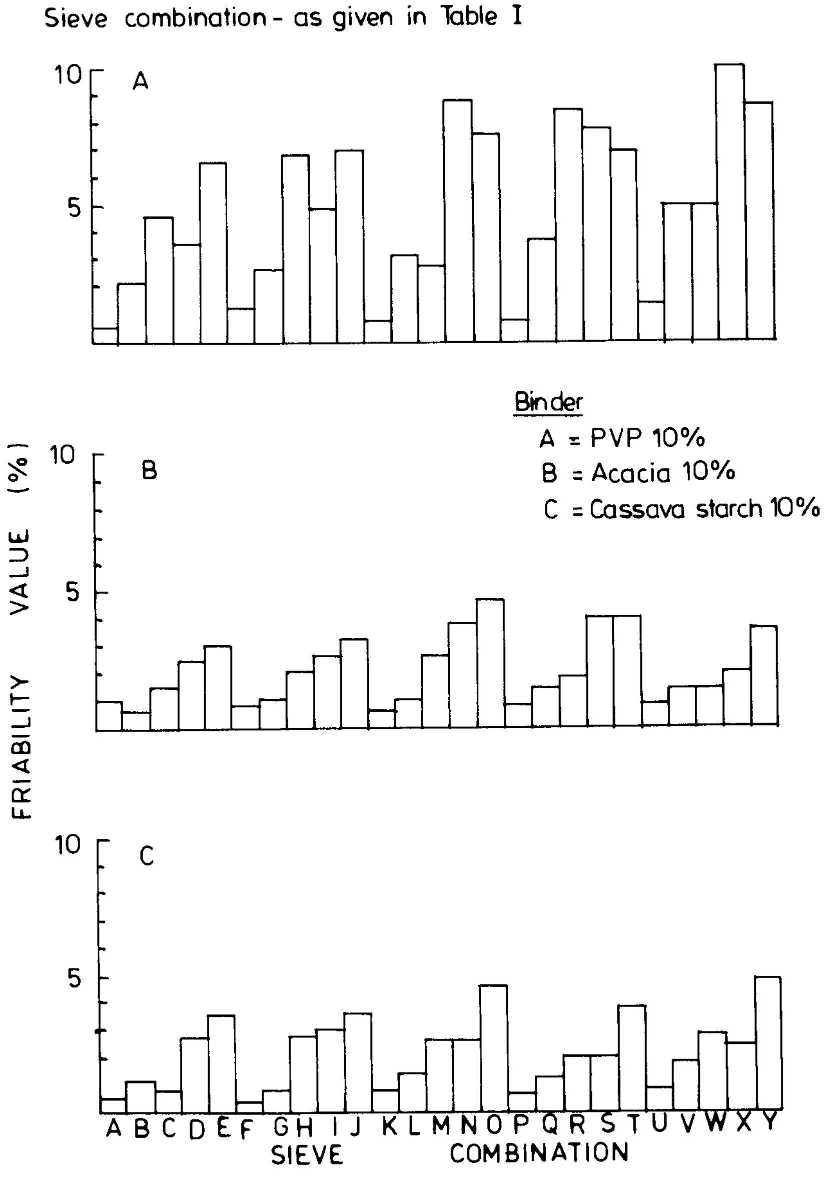

Fig. 4. Effect of interchanging sieves for wet and dry screening on the friability value of lactose tablets

Table 4

Analysis of variance* for friability value of tablets

SV	DF	SS	MS	F. Test
Between treatments	2	154.867	77.433	14.814
Within treatments	22	114.994	5.227	
Total	24	269.861		

*At the 99% probability level, the tabulated $F\ (2,22) = 5.72$ and the calculated F equals 14.814. The treatment effect, therefore, is quite significant.

unpredictively since they may break up to a greater or lesser extent depending on the size of the sieves for wet and dry screening.

Figure 5 represents the effects of sieve size on the disintegration time of lactose tablets. Results show that keeping a particular sieve size constant for wet screening, if the sieve size for dry screening is

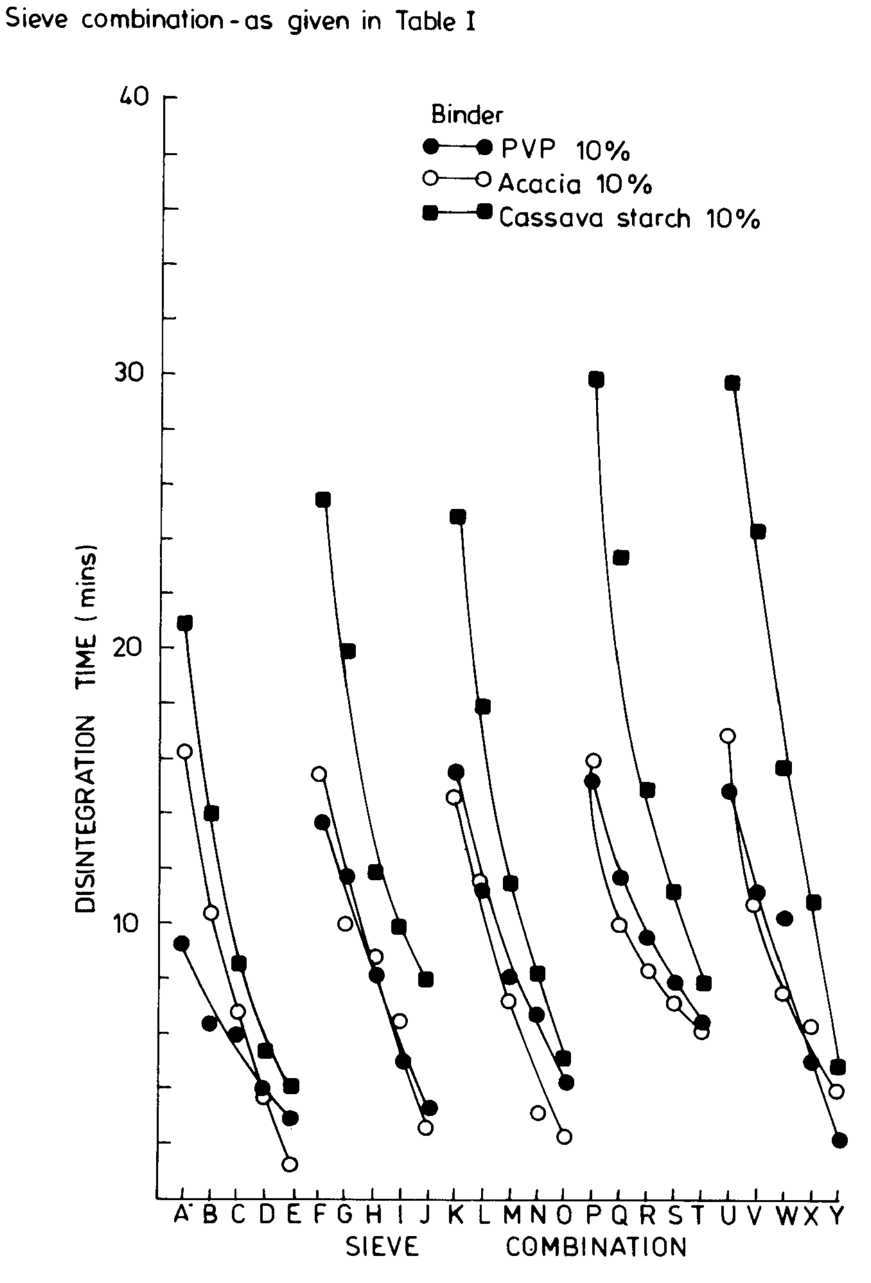

Fig. 5. Effect of sieve size for wet and dry screening on the disintegration time of lactose tablets

increased, there is a decrease in the disintegration time and this occured with all the three binders. This may be related to the granule size in that as the size of granules decreased, the disintegration time increased. This is probably due to the increase in die fill, as demonstrated by increase in tablet weight, with consequent increase in the degree of compaction, stronger binding between granules and thus increase in the hardness of tablets. Although this is in agreement with the findings by Kassem and others (6), it was reported by Rubinstein and Blane (8) that granule size per se does not significantly affect disintegration time. Marks and Sciarra (5) also did not obtain significant results which was thought to be due to the limitations of the disintegration apparatus as well as the fact that there are other factors which may have a greater effect upon the disintegration time. But in the present investigation, a definite and reproducible trend was observed in respect of the effect of granule size on disintegration time (Fig. 5) and the results were found to be highly significant statistically at the 99% level of confidence (Table 5).

Table 5

Analysis of variance* for the disintegration time of tablets

SV	DF	SS	MS	F. Test
Between treatments	2	318.7938	159.3969	51.1017
Within treatments	22	66.6144	3.11884	
Total	24	387.4083		

*At the 99% probability level, the tabulated F (2,22) equals to 5.72 but the calculated F equals to 51.1017. The treatment effect is therefore, highly significant.

From the results obtained on the tablet hardness and disintegration time it appears that cassava starch paste is a relatively stronger binder than both PVP and acacia solutions. This is so because granules prepared using 10% cassava starch paste as the binder and with almost all sieve combinations produced tablets of greater hardness and of higher disintegration time than granules prepared with either 10% acacia solution or 10% PVP solution (Figs. 3 & 5).

This study shows that the physical properties of granules and the resultant tablets often depends on the combination of sieves used for wet and dry screening in the preparation of granules. This not only regulates the average size of granules but also other granular and tablet properties. It is therefore, concluded that in the production of tablets by wet granulation method, the choice of sieves used for wet and dry screening of granules may not depend on the sound scientific bases alone it may often depend on experience.

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