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THE INFLUENCE OF THE RATE OF PRODUCTION OF TABLETS AT CONSTANT PRESSURE UPON THEIR PHYSICAL PROPERTIES

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ABSTRACT

Spray dried and granulated lactose was subjected to sieve analysis, and flow rate together with angle of repose also determined. Tablets of lactose were prepared, at pressures of 50 and 120 MN/m^2 at production rates from 1 to 80 per minute, using an instrumented single punch tablet machine.

The physical properties of the tablets determined were hardness, thickness, uniformity of weight, friability and disintegration time. They were found to conform to United States Pharmacopoeal standards for uniformity of weight and thickness, friability decreased with tablet hardness.

Examination of tablet surfaces, using a scanning electronmicroscope, revealed differences in structure related to speed of production with smoother more compact surfaces produced as tabletting rate was increased. This was most pronounced at the highest punch pressure and probably is the result of faster consolidation of particles and their surface fusion. A result of this was that disintegration time for tablets, produced at a given pressure, increased in direct proportion to the speed of production. Repose angles in the range of 24 - 30° had no significant effect on

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physical properties of tablets and whatever the rate of production die fill and consequently tablet weight did not vary.

Rate of tablet production can, as shown here, influence their physical properties with those produced at higher rates having increased disintegration times and probably less satisfactory dissolution characteristics.

INTRODUCTION

Flow rates and angle of repose are of paramount importance and pre-requisite for good tablet weight uniformity and associated physical properties of tablets. Many reports in the past two decades have been published dealing with flow rates and angle of repose[1,2,3,4,5,6,7], yet no clear correlation between the flow properties and uniformity of tablet weights has been established.

Knoechel et al.[8], reported that as the speed of tableting increased, the die fill and consequently tablet weight decreased. However, they did not measure the flow rate and angle of repose. Gunsel and Lachman[9], as well as Tan et al.[10], studied flow properties and tablet weight uniformity. They found large intertablet weight variation as machine speed increased.

In the work reported here the influence of the rate of production of tablets upon their physical properties, as well as possible mechanisms involved in compact formation have been investigated.

MATERIALS AND EQUIPMENT

Spray dried Lactose and Lactose powder,(obtained from Courin and Warner Ltd.), Acacia, Potato starch and Magnesium stearate all B.P. quality were used. An instrumented single punch machine(Manesty Type F3) fitted with 12.5mm flat punches was used. The punches were instrumented as described by Shotton and Ganderton[11]. A calibration curve was produced as described previously[12]. A scanning electron microscope(Cambridge Instrument 150SEM) was used to determine the structure of surfaces of tablets. Crushing strength of the tablets was determined using a Pfizer hardness tester and a Roch friabilator was used to determine friability values. Manesty tablet disintegration unit, equipped with thermostat($\pm$ 1^{o}C) was used. Endecott test sieve shaker was used for particle size analysis using U.S. standard sieves.

METHOD

Granules were prepared as described previously[13]. Particle size analysis was performed on granulate and spray dried lactose using U.S.standard sieves in series 20,40,60,80 and 100. A 100Gm sample was analysed in the shaker for 5 minutes, then 5% W/W potato starch and 0.5%W/W Magnesium stearate were added and mixed in a glass tumble mixer and stored in screw capped jars.

DETERMINATION OF ANGLE OF REPOSE AND FLOW RATE

Flow rates, expressed in Gm./Sec., were determined as described[14], and were found to be 25Gm/Sec & 20Gm/Sec. for spray dried and granulated lactose respectively. Five measurements were made, the average standard deviation was approximately 0.55Gm/Sec.

Repose angles were measured by the fixed funnel(1cm diameter orifice) and free standing cone procedure described by Train[15]. The height and contour of the base of the powder was measured and tangent of the repose angle was found to be 26^{o} and 29^{o} for spray dried and granulated lactose respectively. The reported repose angles represent the average of five determinations with the average standard deviation of approx. 0.67^{o}. Moisture content of the samples during determination was less than 2%.

TABLET COMPRESSION

Five batches of tablets were prepared from each of granulated and spray dried lactose at two constant pressures of 50 and 120MN/m^{2}. The first batch was made manually by rotating the flywheel at approx. 1 rpm. The other four batches were made as usual using various setting speeds(40,55,65 and 80 tablets/min.). Mean tablet weights were obtained by weighting 20 tablets on torsion balance.

Tablet hardness was determined by using a Pfizer hardness tester (ten tablets were analysed for each batch). Friability values are the per cent weight loss determined after 20 tablets were rotated in the Roche friabilator for 4 minutes(25 rpm). Thickness measurements were obtained either by measuring the total length of a column of 10 to 20 tablets or by measuring individual tablets with a dial micrometer and averaging the values obtained. For disintegration test, tablets were subjected to the U.S.P. disintegration test, the fluid used was 750ml of deionized water at $37^{o}\pm 1$.

MICROSCOPIC OBSERVATION OF REPLICATED SURFACES OF COMPACT

Five standard replicates from each batch of tablets were prepared and examined by scanning electron microscope.

RESULTS AND DISCUSSION

A good flow property can manifest itself in direct compression tableting. This criterion is a function of particle size, shape factor etc. To evaluate this property materials used were subjected to sieve analysis and range of particle size together with flow rate and angle of repose were determined (table 1). Although Gole et al.[5] found no correlation between flow rate (W) and angle of repose(θ), there is evidence that :

$$W=g(d)^{*}$$

and $$\theta=h(d)^{*}$$

therefore, $$W=g[h^{-1}(\theta)]$$

as a result , $$W=f(\theta)$$

* Where g and h denote "function of"

This function has a maximum at a particular diameter. Assuming log-normal particle size distribution, results obtained indicate that when angle of repose was kept in the lower working range 25-30° the flow rate was adequate to fill the die cavity regardless of production rate. Inter-tablet weight variation did not exceed the U.S.P. weight variation tolerance (FIGURE 1).

TABLE 1 : The Influence of the Rate of Production of Tablets upon their Physical properties. (Batches A and a are prepared from Spray Dried Lactose at 50 and 120MN/m^2 respectively - Batches B and b are prepared from Granulated Lactose at 50 and 120MN/m^2 respectively).

Batch No.	Tablets per min.	Disint.time min.sec.)*	Breaking load(Kg)*	Friability (%W.loss)+	Tablets W(mg) +	%C.V.for weight	Thickness (cm) +	Particle size range
A1	1	4.30	0.85	0.41	523	0.62	0.325	50% retained
A2	40	4.20	1.00	0.61	530	0.41	0.320	on mesh 60
A3	55	4.30	1.30	0.52	546	0.36	0.315	6% passed
A4	65	5.20	1.50	0.38	545	0.78	0.312	mesh 100
A5	80	5.80	1.60	0.35	545	0.90	0.310	mesh 60 =
a1	1	8.30	5.00	0.36	527	0.40	0.310	250 μm and
a2	40	8.10	5.50	0.40	535	0.34	0.310	mesh 100 =
a3	55	8.40	5.60	0.33	542	0.82	0.305	149 μm.
a4	65	10.40	5.70	0.19	546	0.50	0.308	
a5	80	11.45	6.20	0.14	544	0.52	0.300	
B1	1	5.10	1.30	0.58	465	0.42	0.310	60% retained
B2	40	5.15	1.30	0.59	475	0.61	0.300	on mesh 40
B3	55	5.10	1.40	0.51	465	0.34	0.300	and 2% passed
B4	65	5.30	1.65	0.48	460	0.71	0.300	mesh 100.
B5	80	7.30	1.70	0.42	470	0.55	0.310	mesh 40 =
b1	1	9.20	6.20	0.32	470	0.35	0.315	420 μm and
b2	40	9.40	6.20	0.30	460	0.37	0.310	mesh 100 =
b3	55	9.30	6.50	0.29	475	0.50	0.300	149 μm.
b4	65	10.10	7.00	0.25	465	0.85	0.300	
b5	80	12.10	7.20	0.24	470	0.52	0.300	

* Each figure is mean of 10 tablets.

+ For each test 20 tablets were analysed.

Note : Repose angle and flow rate were found to be 26^{o} , 25Gm/Sec. and 29^{o}, 20Gm/Sec. for spray dried and granulated lactose respectively.

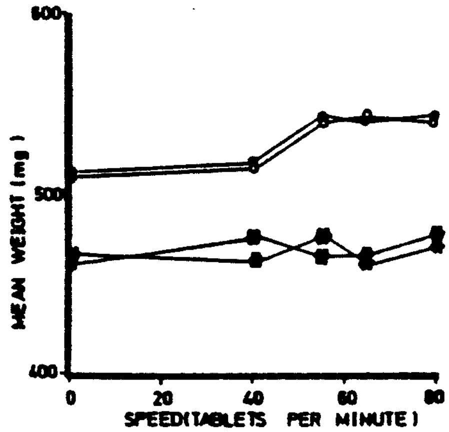

FIGURE 1 : The influence of rate of production of tablets upon their weight(●, o , spray dried lactose and ★, ☆ granulated lactose).

It is known that a shorter duration of maximum compression results in decreased mechanical strength of tablets(due to lack of plastic flow[16]). However, tablets prepared by rotating the fly wheel the press manually gave tablets of lower hardness as compared to thos prepared at higher speed settings(table 1).

When friability values of tablets prepared at different rates were determined it was found that increased in speed of tabletting was associated with decrease in friability values(FIGURE 2) and consequently hardness increase. This increase in mechanical strength was most pronounced at the highest punch pressure which was probably due to faster consolidation of particles.

The speed of production also influenced the disintegration time of the tablets. Increase in the production rate caused an increase in the disintegration time (FIGURES 3&4), with sharper slope for tablets prepared at higher applied pressure.

Many tablet ingredients have an optimum speed of compression[17] Scanning electromicrograph of tablet surfaces produced at different

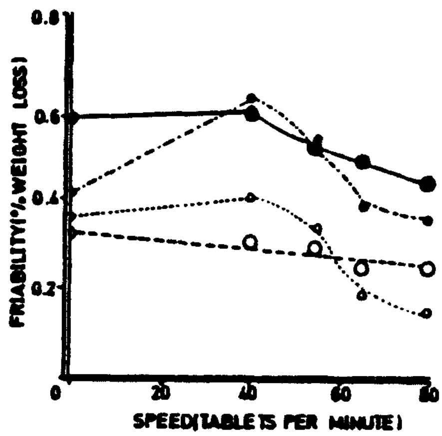

FIGURE 2: The influence of rate of production of tablets upon their friability values(• , ● spray dried and granulated lactose tablets prepared at 50MN/m^2 , o, O spray dried and granulated lactose tablets prepared at 120MN/m2).

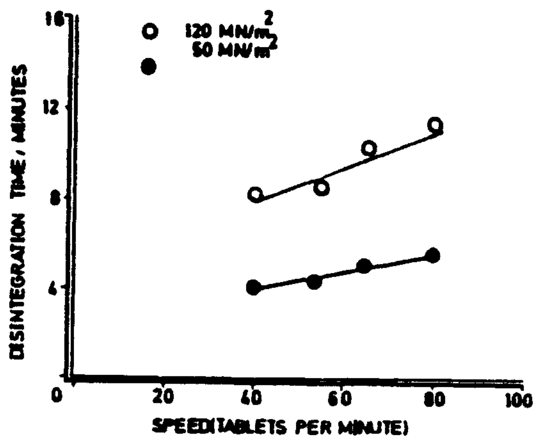

FIGURE 3 : The influence of rate of production of tablets upon their disintegration time. (Spray dried lactose tablets).

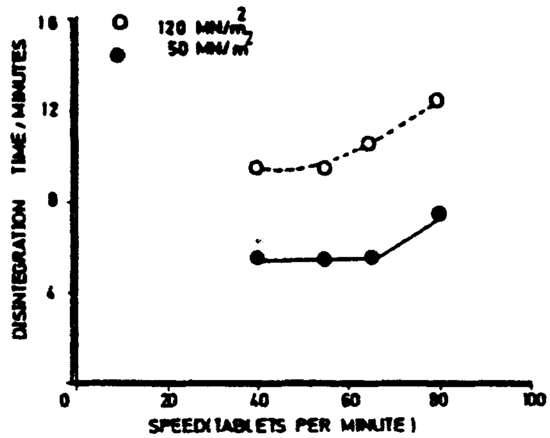

FIGURE 4 : The influence of rate of production of tablets upon their disintegration time. (Granulated lactose tablets).

production rates but constant pressure showed different surface structure which is due to a faster compaction of particles on the surface and probably surface fusion. These differences in geometry of solid surfaces can reduce rate of penetration of fluid into a tablet and disintegration time is prolonged[18]. In compaction, punch pressure is dissipated to the die wall, so that the further the material is from the punch face, the lower is the degree of compaction[19]. The same decay of pressure from the punch face also occurs when the production rate is high, as seen here by examining scanning electromicrographs of tablet surfaces.

In compaction, to eliminate void space, punch pressure would compress the die content into a compact form. Particle fracture occurs, when the stresses within the particles become large enough for a crack to propagate and produce melting of an asperity. The first law of thermodynamics requires that energy expended manifest itself as heat[20]. The possibility of formation of a liquid film at the particle surface is supported by thermodynamics analysis[21]. As a result of numerous simultaneous internal processes and friction with the surface of punch and die, and also evolution of heat a more homogenous compact is formed, which can influence all the physical properties of tablets.

Summing up the results, inter-tablet weight variation could be minimized by careful control of particle size, angle of repose and flow rate. Mechanical strength of tablets increased with production rate and this was most pronounced at higher pressures. Production rate generally increased the disintegration time and consequently resulted in tablets with longer dissolution time.

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