J. Pharm. Pharmacol. 1982: 34: 9–13
Received July 24, 1981

0022–3573/82/010009–05 $02.50/0

Multiple compression of powders in a tablet press

N. A. ARMSTRONG*, N. M. A. H. ABOURIDA AND L. KRIJGSMAN†

Welsh School of Pharmacy, U.W.I.S.T., Cardiff and †Department of Pharmaceutical Technology, Rijksuniversiteit Leiden, Netherlands

Lactose, magnesium carbonate, phenacetin, microcrystalline cellulose and directly compressible starch compacts were repeatedly compressed in a tablet press, the tablets not being ejected from the die between compressions. When the interval between compressions was 1·3 s, all substances showed a decrease in the maximum force exerted by the tablet press, this being attributed to the formation of a structure of lower porosity. As the intervals between compressions is increased, the decrease in force is reduced, and in the case of microcrystalline cellulose and directly compressible starch, the force exerted at the second compression is greater than that exerted by the first.

Whilst powder compression is a widely studied area of research, few reports are available of the effects of compressing the same tablet more than once. Yet multiple compression is the basis of the well-known 'slugging' or precompression process for tablet manufacture. De Blaey & Polderman (1971) have extensively used a double compression technique in an attempt to evaluate the degree of elastic deformation in a powder system, and have related the work expended to tablet properties such as strength, dissolution and incidence of lamination. Dual compression has also been used by Armstrong & Morton (1977) to calculate the increase in plasticity brought about by the process of granulation. If the work used by the second compression of a tablet is indeed that required to overcome elasticity, it follows that if the tablet is compressed more than twice, work on subsequent compressions (i.e. third, fourth and so on), should be equal to that of the second. As a preliminary to such an investigation, the maximum force exerted by a tablet press, using constant punch settings, was measured for repeated compressions, since if the maximum force changes, a change in work output will be an unavoidable consequence.

MATERIALS AND METHODS

The solids used were lactose, microcrystalline cellulose (Avicel), directly compressible starch (Starex 1500), phenacetin, and magnesium carbonate. Powders were used as received.

Method of compaction. The punches of a Manesty E2 tablet press were fitted with strain gauges and a displacement transducer measured their relative positions. Signals from the transducers were conditioned and amplified and fed via an analog-digital converter (Burr Brown model MP 7216) into a microcomputer (Motorola 6800). The signals were stored and reproduced on demand via a teletype. Full details of the data recording and processing apparatus and its calibration are given elsewhere (Abourida 1980; Armstrong & Abourida 1980). The press was modified so that the tablets were not ejected from the die after compression.

The required weight of solid, correct to 1 mg, was transferred into the die of the press (12·5 mm diameter) and compressed repeatedly. Force levels were not controlled by adjusting the settings of the machine but by altering the weight of the powder taken. The interval between compressions was a minimum of 1·3 s with the tablet press running continuously at 46 strokes min^{-1}. For longer intervals between compressions the press was stopped. By examining the data from the displacement transducer, it was ascertained that on restarting the press, speed was gained sufficiently quickly so that the punch was always travelling at the same speed when it entered the die.

The maximum force exerted by the press for each compaction was recorded, and the punch settings were not altered during a series of compressions.

RESULTS AND DISCUSSION

By selection of an appropriate weight of solid, a range of compaction forces could be achieved without altering the minimum distance between the punches, the conventional means of altering the applied force in a tablet press. Each tablet was compressed thirteen times without ejecting it from the die, the number of compressions being limited by the memory capacity of the microcomputer. In the case of lactose, the maximum force registered decreased progressively with compression number. The

*Correspondence.

forces are expressed in terms of the parameter F_{rel}, which is defined as:

$$F_{rel} = \frac{\text{force exerted at the nth compression}}{\text{force exerted at the first compression}}$$

Fig. 1 shows the relationship between F_{rel} and compression number for lactose, using three different starting forces. The tablet press was run continuously at a rate of 46 strokes min, so the time interval between successive compressions was 1·3 s.

It is noteworthy that the decrease in F_{rel} with compression number is a function of the initial applied force, and at the highest forces, the curve is virtually parallel to the horizontal axis after about 10 compressions, whilst the curve for lower forces is still decreasing markedly.

Lactose is known to undergo fragmentation on compression (Hersey & Rees 1970) and these results can be explained on this basis. Higher forces cause fragmentation, and so the compact attains its ultimate porosity relatively quickly (i.e. after about 10 compressions). Lower forces bring about a smaller degree of fragmentation for each application of that force, and so a greater number of force applications are needed to bring the compact into a condition of minimal porosity.

Qualitatively similar data were reported by Bessho et al (1969), who compressed ascorbic acid, calcium citrate and microcrystalline cellulose repeatedly at a high and low force. They found that the applied force decreased with repeated compression, and attributed this to decreased porosity, though they did not suggest how the decreased porosity was achieved.

Similar experiments were carried out using magnesium carbonate, phenacetin, microcrystalline cellulose and directly compressible starch, the tablet press running continuously in each case (Figs 2, 3, 4A and 4B respectively). Close examination of some of the data obtained, especially at low forces, shows not a smooth curve but a series of plateaux. This is an artifact of the system, the sensitivity of which is such that one computer unit (or bit) is equivalent to a force of 70N. Thus the plateaux are derived by the computer rounding up or down to the nearest bit, and therefore drawing a smooth curve through the points is a justifiable procedure.

In each case, the same overall pattern is noted, in that the greater the force, the smaller the change

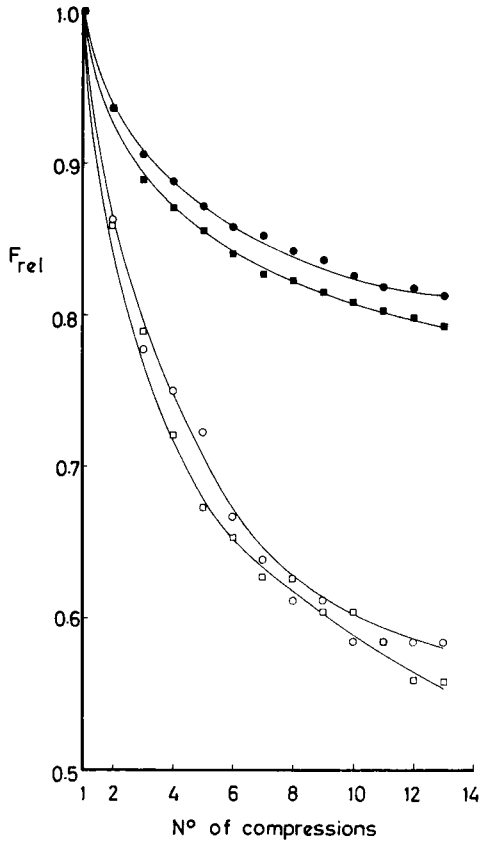

FIG. 1. The effect on F_{rel} of the multiple compression of lactose compacts. ● Initial force 12·3 kN. ■ Initial force 11·8 kN. □ Initial force 3·4 kN. ○ Initial force 2·9 kN.

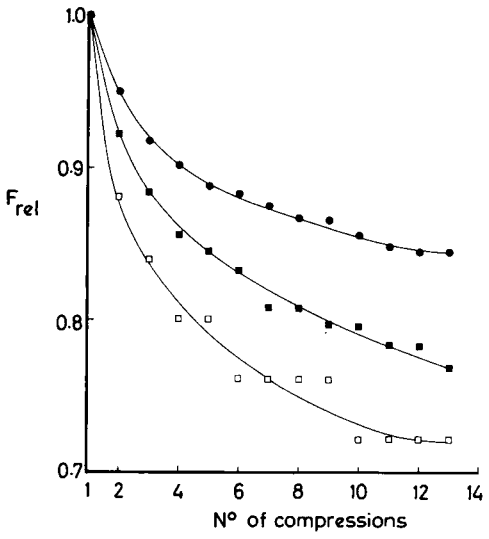

FIG. 2. The effect on F_{rel} of the multiple compression of magnesium carbonate compacts. ● Initial force 13·4 kN. ■ Initial force 5·9 kN. □ Initial force 2·1 kN.

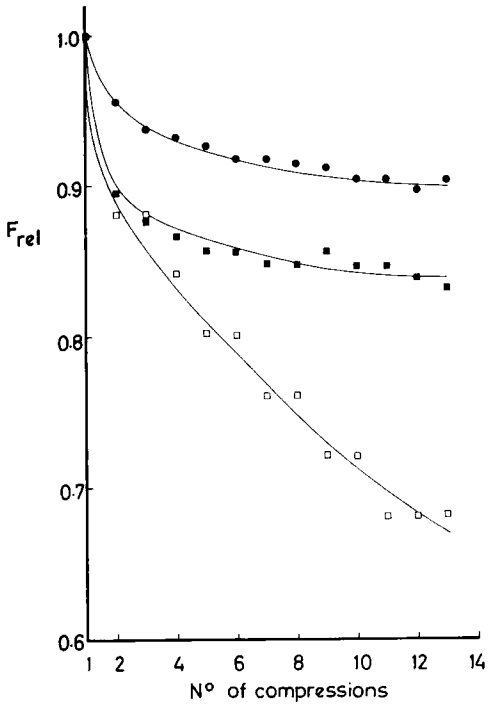

FIG. 3. The effect on F_{rel} of the multiple compression of phenacetin compacts. ● Initial force 10·4 kN. ■ Initial force 7·7 kN. □ Initial force 2·1 kN.

in force with successive applications. However, the substances show qualitative differences. The behaviour of magnesium carbonate is similar to that of lactose. Phenacetin, however, whilst showing a continual decrease in F_{rel} when low forces are applied, reaches a plateau after 4 or 5 applications of a force of about 10kN. Thus phenacetin readily reaches its state of minimum porosity, indicative either of a weak particulate structure, which fragments easily, or a more readily deformable structure. Whether such deformation is permanent or reversible cannot be determined from these data.

Results from microcrystalline cellulose and directly compressible starch are of particular interest in that both substances show only a small decrease in F_{rel} with compression number. Furthermore though a force dependency can be detected, it is by no means as marked as in the case of the other substances. Thus if it is accepted that the hypothesis that the decline in F_{rel} is due to the formation of a progressively denser compact, both microcrystalline cellulose and directly compressible starch rapidly achieve their minimum porosity and only a comparatively small force is needed for this purpose. Their usefulness as directly compressible excipients would presumably follow from this.

All results reported thus far were obtained with the tablet press running continuously, i.e. recompressions were taking place at intervals of 1·3 s. Assuming a typical compression force of 12 kN, integration of the area under the force-displacement curve (De Blaey & Polderman 1970), gives a work input of about 5 J for the first compression and about 1 J for the second and subsequent compressions. Whilst a fraction of this work is utilized by the generation of new surfaces and the formation of interparticulate bonds, it is believed that most work expended on compressing a solid is converted to heat. Hanus & King (1968) for example found that the increase in temperature of a tablet after compression was directly proportional to the force and rate of compaction, whilst Travers & Merriman (1970)

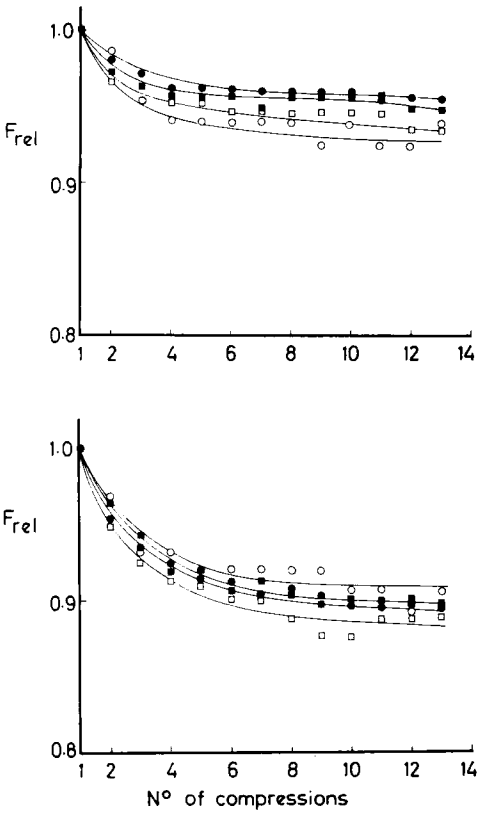

FIG. 4A. The effect on F_{rel} of the multiple compression of microcrystalline cellulose compacts. ● Initial force 14·6 kN. ■ Initial force 10·1 kN. □ Initial force 7·0 kN. ○ Initial force 5·1 kN. B. The effect on F_{rel} of the multiple compression of compacts of directly compressible starch. ● Initial force 12·5 kN. ■ Initial force 10·1kN. □ Initial force 6·1 kN. ○ Initial force 4·8 kN.

found that temperature increases depended on the substance being compressed.

There is thus the possibility that the differences in compressive behaviour described above were due to differences in the heat content of the tablets, i.e. a function of their specific heat and thermal conductivity. If the latter is low, then the heat generated by one compression will not have dissipated before the next compression generates more heat, and thus the tablet will get hotter at a rate depending on its specific heat. As a consequence, other temperature related properties, e.g. particle rheology, will change.

Accordingly each substance was repeatedly compressed using a range of forces as before. However, the interval between compressions was extended to 1, 5 and 20 min, the assumption being that after 20 min, heat generated in the tablet by compression would have been transferred to the tablet press, the latter acting as a heat sink, and thus changes in compressive behaviour brought about by a rise in temperature would be expected to be absent.

Fig. 5 shows the change in F_{rel} with compression number for lactose, compressed at about 12kN and the intervals between compressions being 1·3 s, 1 min and 5 min. For the sake of clarity, compression data derived at only one force are presented in the figure though more complete data are given in Table 1. Also data derived after an interval of 20 min between compressions is omitted, since for all substances, it proved identical to that obtained after 5 min intervals.

Since F_{rel} decreases more swiftly as the time interval is increased, it must be surmised that at longer time intervals, the punch encounters a structure more liable to deformation and/or fragmentation, or a structure which offers less resistance to the punch. It is considered that the latter mechanism is more probable. As the heat within the compact is lost, contraction of the individual particles within the tablet will occur. This will be reflected in an overall diminution of the external dimensions of the tablet, but will also result in an increased porosity as the particles separate slightly from one another. This will give an overall weakening of the tablet structure. This change is not so marked with phenacetin. Compacts of the latter, which is a more elastic substance (Armstrong & Haines-Nutt

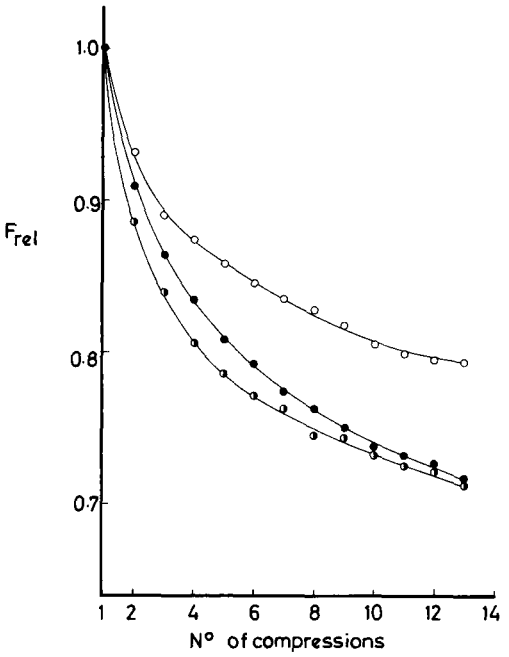

FIG. 5. The effect of change of interval between compressions on F_{rel} of lactose compacts. ○ Time interval 1·3 s, Initial force 12·6 kN. ● Time interval 1 min, Initial force 12·2 kN. ◑ Time interval 5 min, Initial force 12·7 kN.

Table 1. Force changes between the first and thirteenth compressions.

Time interval	Lactose		Magnesium carbonate		Phenacetin		Microcrystalline cellulose		Directly compressible starch	
	F_1	F_{rel}	F_1	F_{rel}	F_1	F_{rel}	F_1	F_{rel}	F_1	F_{rel}
1·3 s	12·6	0·793	12·5	0·843	11·3	0·909	4·5	0·932	11·5	0·898
	16·0	0·838	16·1	0·870	15·8	0·917	11·8	0·962	15·8	0·913
1 min	12·2	0·714	12·5	0·819	11·7	0·900	4·5	0·983	11·9	0·981
	15·6	0·792	15·6	0·847	15·6	0·925	12·4	1·000	15·8	0·981
5 min	12·7	0·715	12·2	0·775	11·6	0·893	4·6	1·033	11·9	1·000
	15·8	0·777	15·7	0·816	15·9	0·959	12·3	1·011	15·6	0·990

All forces are in kN.

$$F_{rel} = \frac{\text{Force exerted at 13th compression}}{\text{Force exerted at 1st compression } (F_1)}$$

1972) lose their strength by elastic recovery in a relatively short time. Hence any loss of strength due to thermal contraction is of minor significance.

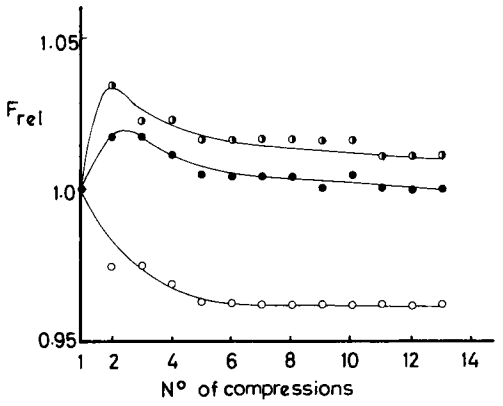

FIG. 6. The effect of change of interval between compressions on F_{rel} of microcrystalline cellulose compacts. ○ Time interval 1·3 s, Initial force 11·8 kN. ● Time interval 1 min, Initial force 12·4kN. ◑ Time interval 5 min, Initial force 12·3 kN.

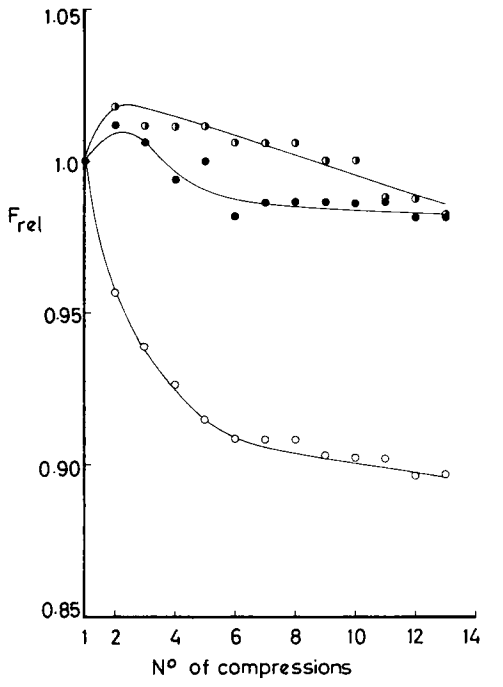

FIG. 7. The effect of change of time interval between compressions on F_{rel} of compacts of directly compressible starch. ○ Time interval 1·3 s, Initial force 12·0 kN. ● Time interval 1 min, Initial force 11·7 kN. ◑ Time interval 5 min, Initial force 11·7 kN.

The behaviour of microcrystalline cellulose and directly compressible starch is of particular interest (Figs 6, 7), since F_{rel} shows a smaller change as the time interval is increased, indicative that a structure which is more resistant to consolidation develops with time. Thermal contraction presumably is still present, and may cause an increase in porosity as described above, but this is outweighed by some factor which strengthens the tablet structure. It is particularly noteworthy that with both these substances, F_{rel} values greater than unity are obtained when the interval between compressions is one minute or greater. Thus when the punch compresses the substance on the second occasion, it encounters a structure which is more resistant to consolidation than the original powder. Though Bessho et al (1969) used microcrystalline cellulose in their studies, they did not encounter F_{rel} values greater than one because of the short time intervals between compressions which they used.

Tablets made from microcrystalline cellulose and directly compressible starch both show very low residual die-wall pressure and are readily ejected from the die of the tablet machine, though Sixsmith (1975) has refuted the claim that microcrystalline cellulose is itself a lubricant. The following mechanism is therefore suggested. As the compressing force is removed, radial contraction occurs, rapidly relieving die wall pressure. This may be associated with axial expansion. Subsequently a relatively slow change takes place in which interparticulate bonds form a structure which is more resistant to further consolidation.

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