The relation between compression force and dissolution time of tablets

SIR,— From the work of Levy, Antkowiak & others (1963) and of Ganderton, Hadgraft & others (1967) it is clear that processing variables may greatly influence the disintegration time of tablets or the dissolution rate of active ingredients. Levy & others demonstrated that the dissolution rate of salicylic acid decreases with increasing force of compression; Ganderton & others found that by increasing compression force the rate of disintegration of phenindione tablets progressively decreases, whereas the dissolution time follows a more complicated pattern. Morrison & Campbell (1965) and Wood (1967) have clearly shown that measuring the dissolution time is the method of choice since the disintegration time is less indicative of the physiological activity of tablets.

Several authors, including Lewis & Train (1965) and Lewis & Shotton (1965), have shown that at increasing compression forces the relative density of tablets becomes greater until a maximum is reached. The force at which the maximal relative density is obtained depends on the composition of the tablet concerned.

We have compared the dependence of both the dissolution time and the relative density on the force of compression. These studies were made on granulates generally used for the production of tablets containing small amounts of active ingredients, sodium chloride, 1·5%, being added to the powders before granulation so that the dissolution time could be measured conductometrically. In most experiments the granulate composition was: lactose 78·5, sodium chloride 1·5, potato starch 20%, mucilage of starch q.s. The granulate was passed through a Manesty oscillating granulator, dried in a fluidized bed dryer and passed through a 20 mesh sieve. Particles which were not retained on a 50 mesh sieve were discarded. After the addition of 3% of talc and 1% of magnesium stearate, flat tablets of 9 mm diameter were made on a single punch tabletting machine (HOKO) both punches of which are instrumented with strain gauges. The compression force was recorded on an oscilloscript (Philips PT 2104).

The dissolution time was determined by immersing the tablet in a stainless steel wire basket of 16 mesh in 75 ml of water at 25° or 37° which was circulated at a controlled speed of 8 ml/sec with the aid of a magnetic stirrer. The conductivity of the solution was measured with a Philips conductometer PR 9501 and the results were plotted against time. Recording the dissolution rate has

TABLE 1. RELATION BETWEEN COMPRESSION FORCE, RELATIVE DENSITY AND DISSOLUTION TIME

	Compression force (kg)	Relative density	Dissolution time (sec)	C.V.
1	220	0·81	1400	14·0
2	260	0·82	955	11·2
3	290	0·83	680	15·0
4	318	0·85	440	16·3
5	430	0·89	135	16·0
6	500	0·90	110	14·2
7	520	0·91	110	12·4
8	650	0·94	129	11·4
9	900	0·96	250	10·5
10	1140	0·97	380	5·0
11	1350	0·97	425	2·9
12	1640	0·97	440	3·4
13	1800	0·97	440	2·1
14	2000	0·97	440	3·6

Note: C.V. (the coefficient of variation) is only given for the dissolution time and not for the relative density since this is always less than 0·5%.

the additional advantage that comparisons can be made between the pattern of dissolution, e.g. by calculating the time required for the dissolution of 25, 50 and 90% of the sodium chloride. We chose as the criterion the time required for the dissolution of 90% of the salt.

The relative density, defined according to Lewis & Train (1965), is the ratio of compact density to density of the solid material. We always listed 10 tablets compressed at the same force for dissolution time. In Table 1 the average values for the 90% dissolution times and the relative densities at 14 different compression forces are listed. The dissolution time becomes constant at practically the same compression force at which the relative density becomes constant: the difference in dissolution time between tablets compressed at forces of 1350 and 1640 kg is still significant at the 0·95 level, whereas the difference in relative density of these tablets is no longer significant.

This correlation was confirmed for tablets of different compositions, although the first part of the graph was often different. In the present instance the dissolution time showed a minimum value, whereas with other tablets an initial decrease was not found: e.g. the dissolution time of tablets made from the same powder mixture but using a 10% gelatin or gum acacia solution as the granulating solution did not show the minimum. A steady increase in dissolution time was found with increasing compression force until a maximal value was reached, again at the compression force at which the relative density because constant.

Since tablets usually are compressed at a pressure lower than the critical one described, a comparison of their dissolution times seems only completely reliable if the relation with the compression force is known.

J. POLDERMAN
D. R. BRAAKMAN

Pharmaceutical Laboratory of the State University of Leiden,
Department for Pharmaceutical Technology,
Hugo de Grootstraat 32, Leiden, the Netherlands.

February 17, 1968

References

Ganderton, D., Hadgraft, J. W., Rispin, W. T. & Thompson, A. G. (1967). *Pharm. Acta Helv.*, **42**, 152–163.
Levy, G., Antkowiak, J. M., Procknal, J. A. & White, D. C. (1963). *J. pharm. Sci.* **52**, 1047–1051.
Lewis, C. J. & Train, D. (1965). *J. Pharm. Pharmac.*, **17**, 33–41.
Lewis, C. J. & Shotton, E. (1965). *Ibid.*, **17**, *Suppl.* 71 S–81 S.
Morrison, A. B. & Campbell, J. A. (1965). *J. pharm. Sci.*, **54**, 1–8.
Wood, J. H. (1967). *Pharm. Acta Helv.*, **42**, 129–152.