A method of characterizing tablet formation

Previously Newton, Rowley & others (1971) reported that the tensile strength of tablets prepared from three weight ranges of lactose, form a common linear relation with the mean compaction pressure used in forming the tablet. For a lower weight range, however, a separate linear relation existed. It was postulated that this difference was due to differences in stress distribution within the small weight tablets. When the compression of different quantities of powder by a single punch tablet machine is considered, an alternative explanation appears possible. When powder is compressed by the upper punch, the force applied increases as the distance moved by the punch increases, until the maximum for the given punch setting is obtained, after which the force decreases as the punch is withdrawn. The force-time plot obtained for a small quantity of powder is shown in Fig. 1a. If a larger mass of powder is compressed at the same upper punch setting, the upper punch will travel the same distance, but because the bottom punch is lower and there is a larger quantity of material which can yield, there is less resistance to movement of the upper punch and the force applied is smaller (Fig. 1b). In the latter case, to obtain the same applied force as that in Fig. 1a, the upper punch must move a greater distance, resulting in a larger dwell time and a different rate of loading (Fig. 1c). Hence, for the same applied force (which for constant diameter punches is directly proportional to the applied pressure), the two powder masses have been subjected to different compaction conditions. When the

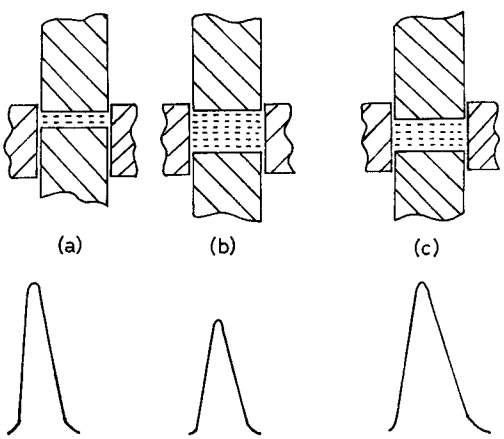

FIG. 1. Representation of compression cycle. The upper diagrams indicate the die fill and punch travel. The lower curves give the corresponding u.v. recorder traces. (a) Small powder sample. (b) Large powder sample with same upper punch travel as (a). (c) Large powder sample with increased upper punch travel to provide corresponding force as that produced in (a).

u.v. recorder charts of the previous work of Newton & others (1971) were examined, these results were readily observed. The traces, run at a speed of 100 mm/s, approximated to equilateral triangles for both upper and lower punches. The characteristics of compaction were, therefore, identified by measuring the area of these triangles and averaging the upper and lower punch results, to give a mean force-time result, A. The regression analysis relating mean area A and tensile strength σ_x provided the following equations with the correlation coefficient given in brackets:—

0·4 g	$\sigma_x = 0{\cdot}1197A$	−0·76	(0·98)
0·6 g	$\sigma_x = 0{\cdot}115A$	−0·46	(0·99)
0·8 g	$\sigma_x = 0{\cdot}113A$	−0·31	(0·94)
1·0 g	$\sigma_x = 0{\cdot}112A$	−0·519	(0·984)

Comparison of these regression lines, in pairs, by the method of Newton & others (1971), proved that the lines did not differ significantly from each other. A common regression equation: $\sigma_x = 0{\cdot}114A - 0{\cdot}517$ (0·981) fitted the data.

These results suggest that compaction force or pressure does not completely characterise the formation of a tablet. Varsano & Lachman (1966), de Blaey & Polderman (1970) and Fell & Newton (1971) have reported the measurement of work done in making the tablet. Without the consideration of the time factor involved, work done may also be inadequate. For instrumented tablet machines without systems for accurate determination of punch travel, the present concept of force-time measurement offers a possible solution.

Lilly Research Centre Ltd.,
Erl Wood Manor,
Windlesham,
Surrey, U.K.

J. M. NEWTON
G. ROWLEY

October 20, 1971

REFERENCES

DE BLAEY, C. J. & POLDERMAN, J. (1970). *Pharn. Weekblad.*, **105**, 241–250.

FELL, J. T. & NEWTON, J. M. (1971). *J. pharm. Sci.*, **60**, 1428–1429.

NEWTON, J. M., ROWLEY, G., FELL, J. T., PEACOCK, D. & RIDGWAY, K. (1971). *J. Pharm. Pharmac.*, **23**, *Suppl.*, 195S–201S.

VARSANO, J. & LACHMAN, L. (1966). *J. pharm. Sci.*, **55**, 1128–1133.

Aggregation of (+)-propoxyphene hydrochloride in aqueous solution: circular dichroism measurements

Highly water-soluble derivatives of insoluble or sparingly soluble drugs often associate in aqueous solution in much the same way as do surface-active agents (Florence, 1968). An understanding of the mechanism of such self-association is important since this property can influence the chemical stability of the drug itself as well as its tendency to interact with other drugs. We have shown, using nuclear magnetic resonance spectroscopy, that the non-narcotic analgesic (+)-propoxyphene HCl (I) associates in aqueous solution (Thakkar, Wilham & Demarco, 1970). The association is hydrophobic, involving primarily an overlap or stacking of the aromatic rings.

We now report some unusual findings in the circular dichroism (CD) spectra of aqueous (+)-propoxyphene HCl. Our observations are novel in that although changes in the CD spectra of some surface-active agents have been seen upon association (Bonkoski & Perrin, 1968, 1969; Mukerjee, Perrin & Witzke, 1970; Perrin & Witzke, 1971), the appearance of new bands upon association in a single solvent has not been reported before for such small molecules. Several chlorophyll and protochlorophyll pigments, which are monomeric in diethyl ether, have been shown to dimerize in carbon tetrachloride with the production of new CD peaks by the exciton splitting phenomenon (Houssier & Sauer, 1970). Resonance interaction between excited states of identical chromophores can cause exciton splitting with the resultant production of closely spaced CD curves of equal magnitude and opposite sign (Warshaw, Bush &