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POWDER CONSOLIDATION DURING PHARMACEUTICAL TABLETTING*

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ABSTRACT

The consolidation of powders during compaction can be relatively easily measured and indicates both the mechanism of consolidation and mechanical properties of the drug. Knowledge of whether a particular powder consolidates by fracture or by plastic deformation can be invaluable in a preformulation study. The development pharmacist may have to overcome bioavailability or stability problems arising during processing as a result of consolidation mechanisms.

INTRODUCTION

During the tabletting of pharmaceuticals, powders or granules are compacted to form an adherent mass. This operation of consolidating the powder may offer the

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development pharmacist useful information on the properties of the drug or excipient being compacted. Such information may be useful in the subsequent evaluation of stability or bioavailability data as well as giving a useful measure of the mechanical properties of the substance.

Empirical treatment of consolidation data may be traced back to the work of Walker (1), who obtained a relation between the relative volume, Vr, of a compact and the forming pressure, P.

$$Vr = C - k \ln P \qquad (1)$$

where the relative volume is defined as the ratio of the bulk volume at pressure P to the volume at infinite pressure and C and k are constants. Similar equations have since been put forward by many workers in the fields of geology, ceramics and powder technology. However, these equations can only be considered as curve fitting exercises - to fit the available data. Moreover, the constants contained in equations of this type have doubtful physical significance and cannot be assigned to a particular parameter of the powder being compacted or to the geometry of the system.

A more meaningful, if still empirical, approach was taken by Heckel (2), who considered that the consolidation or decrease in porosity with increased pressure

could be likened to a first order chemical reaction. From this approach, he obtained a relation between apparent density, D, and forming pressure, P.

$$\ln \left(\frac{1}{1-D}\right) = KP + A \qquad (2)$$

where K and A are constants. In this case, however, the constants were shown to have some relationship to the system, since K was found to be equal to the reciprocal of the mean yield pressure and A was a function of the original compact volume. In fact, A is not always constant, but depends upon the degree of packing to which the powder has been subjected and also on the geometry of the system. It tends to a constant value for large diameter compacts in which the powder is well packed.

Using a model derived from statistical mechanics, Bockstiegel (3) similary evolved an equation for powder considation, which may be simplified to the form of equation (2).

Use of equation (2) is capable of distinguishing between the mechanism of consolidation. For example, sodium chloride consolidates mainly by plastic deformation (4). Taking different particle size fractions gives rise to different bulk volumes or initial values of A (i.e. when P = 0). During compaction, the initial particle size influences the consolidation of

the material giving a type A curve (fig.1). Consolidation of lactose (4) and sucrose (5) proceeds mainly by fragmentation of the particles. The initial particle size having little effect on the consolidation curve as can be seen from the type B curve (fig.2) (6). Potassium chloride behaves similarly to sodium chloride whereas potassium citrate behaves similarly to lactose and sucrose (7).

More recently, a third type of behaviour (type C) has been reported for fatty acid powders (fig.1) (8). Where a binary mixture of lactose and a fatty acid powder was used, there was a general shift from type B to type C consolidation as the percentage of fatty acid powder in the mixture was increased.

APPLICATION

If during the processing of a pharmaceutical product there are changes in the particle size of the drug,

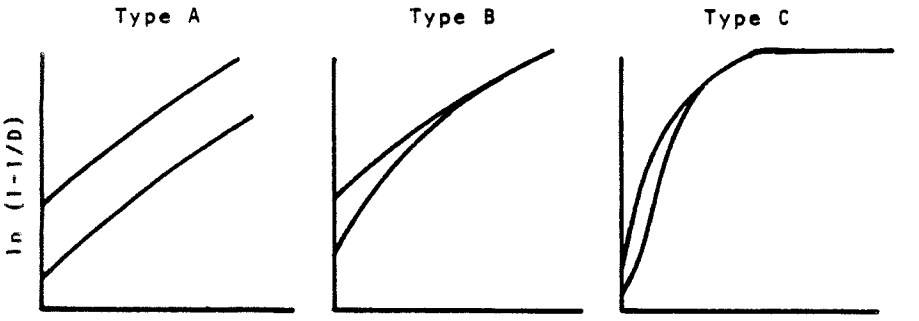

FIGURE I

those changes may have an influence on both the stability and availability of that drug, due to the increase in surface area. For example, aspirin has been shown to fracture during tabletting and then, on further increase in pressure to rebond. This maximum in the surface area graph has been shown to coincide with the maximum dissolution rate for aspirin tablets prepared over a range of different pressures (9).

Clearly, it would be an advantage for the formulator to know how his drug will behave on compression. Measurement of changes in surface area are relatively complex (10,11). It is much more simple to measure the compact dimensions at different forming pressures and plot equation (2) (12).

However, there are problems in the interpretation of equation (2). These have not been quantified in this context to any extent. The geometry of the system will be important, since it will affect the packing of the powder. The depth of fill will influence the actual pressure at any point in the compact due to the logarithmic pressure loss down the compact length due to friction. The method of measurement of the compact, whether *in situ* in the die or after ejection, allowing for elastic recovery to take place. The presence of trace contaminants, including moisture or lubricants. The particle size effect *per se* as

indicated by the work of Griffith (13). The significance of the above parameters must be ascertained before reliance can be put on the interpretation of the results (14). In view of our current knowledge, it is probably better to use relatively thin fills of clean dry powder in a clean die of relatively large diameter.

Further work in this area, such as the elucidation of elastic recovery by the compression of starch grains (15) and the additional evidence offered by measuring stress ratios during consolidation (16), will enable the development pharmacist to gain a considerable knowledge of the drug from relatively simple experiments during preformulation.

REFERENCES

1. E.E.Walker, Trans. Faraday Soc., 19, 73, 83 (1923).
2. R.W.Heckel, Trans. Metall. Soc., A.I.M.E., 221, 671, 1001 (1961).
3. G.Bockstiegel, "Proc. 1st. Internat. Conf. Compaction and Consolidation of Particulate Matter", ed. A.S.Goldberg, London : Powder Advisory Centre.
4. J.A.Hersey and J.E.Rees, "Particle Size Analysis, 1970", eds. M.J.Groves and J.L.Wyatt-Sargent, London : Society for Analytical Chemistry.
5. J.S.Hardman and B.A.Lilly, Nature, 228, 353 (1970).

6. J.A.Hersey and J.E.Rees, Nature, 230, 96 (1971).

7. J.A.Hersey, E.T.Cole and J.E.Rees, "Proc. 1st. Internat. Conf. Compaction and Consolidation of Particulate Matter", ed. A.S.Goldberg, London : Powder Advisory Centre.

8. P.York and N.Pilpel, J. Pharm. Pharmac., 25, Suppl. 1P (1973).

9. E.Cid and Fr.Jaminet, Pharm. Acta Helv., 46, 167 (1971).

10. T.Higuchi, A.N.Rao, L.W.Busse and J.V.Swintosky, J. Amer. Pharm. Ass. (Sci.Ed.), 42, 194 (1953).

11. N.A.Armstrong and R.V.Griffiths, Pharm. Acta Helv., 45, 583 (1970).

12. J.A.Hersey, Austral. J. Pharm. Sci., NS2, 47 (1973).

13. A.A.Griffith, Phil. Trans. Roy. Soc. London, Ser.A., 221, 163 (1920).

14. J.A.Hersey, J.E.Rees and E.T.Cole, J. Pharm. Sci., 62, 2060 (1973).

15. H.Hess, F.I.P. Abstracts, Stockholm 1973, 31.

16. J.E.Carless and S.Leigh, J. Pharm. Pharmac., 26, 289 (1974).