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THE COMPRESSIONAL PROPERTIES OF DEXTROSE MONOHYDRATE AND ANHYDROUS DEXTROSE OF VARYING WATER CONTENTS.

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ABSTRACT

The effect of moisture on the compressional properties of anhydrous dextrose and dextrose monohydrate was examined. Relationships between moisture content and both tablet tensile strength and tablet toughness were evaluated. An increase in the moisture content of anhydrous dextrose produced a corresponding increase in both strength parameters up to the 8.9% moisture level, possibly due to a recrystallising effect. However any further increase in moisture content beyond this point produced a marked reduction in both tablet tensile strength and tablet toughness. For dextrose monohydrate, any increase in moisture content obtained by exposure to elevated humidities led to a reduction in both tensile strength and toughness.

The consolidation of both anhydrous dextrose and dextrose monohydrate was improved with increasing moisture content, presumably due to a lubrication effect. The yield forces and percentage porosity obtained under compression for anhydrous dextrose were observed to decrease with increasing moisture content up to a level of 9.20%.

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INTRODUCTION

It is often stated that to obtain optimal tablet properties, the water content of a powder or granular system must be controlled to a reasonable degree of accuracy. The reasons for this have never been unambiguously established, though a variety of effects caused by the moisture content have been reported. It has been suggested, for example, that water may exert its effect by reducing resistance to particle deformation and reducing interparticulate friction [1], by reducing the strength of interparticulate bonds and hence reducing tablet strength [2], and by reducing the amount of fragmentation occurring on compression [3]. The effect of crystal bridge formation by dissolution and subsequent recrystallisation of the solid in water must also be considered.

Recent advances in tablet machine instrumentation and data manipulation, and the introduction of more elaborate parameters to describe compressional behaviour may afford the means of properly evaluating moisture-mediated effects, and possibly establishing whether such critical control of moisture content is necessary.

MATERIALS

α-D anhydrous dextrose, α-D dextrose monohydrate and materials used to generate environments of known relative humidity were all GPR grade reagents (B.D.H. Ltd, U. K.). Dextrose monohydrate as supplied was found to contain 7.80% water.

METHODS

The 180-250um fraction of anhydrous dextrose and dextrose monohydrate was isolated using a Pascall 'Inclyno' sieve shaker, and this fraction was used for all subsequent work.

Moisture was introduced by exposing the powders to a range of relative humidities brought about by saturated salt solutions in closed glass tanks maintained at 20-23°. Powder samples were spread in thin layers approximately 2mm deep on aluminium foil trays. On each tray was also placed a petri dish containing a layer of powder of the same thickness. The dish was weighed at regular time intervals until it achieved constant weight, when it was assumed that all powder on that tray had reached equilibrium with its surroundings. The following humidities and saturated electrolyte solutions were used:- 93%, potassium nitrate; 87%, potassium chloride: 75%, sodium chloride; 71%, lithium acetate; 68%, cupric chloride; 58%, sodium bromide; 5%, silica gel [4]. The water content was measured using Karl Fischer reagent and a dead-stop end point technique (Radiometer, Copenhagen, Denmark), and is expressed as percentage wet weight.

The powders were compressed on a F3 excentric press (Manesty Machines, Liverpool, U.K.), fitted with 12.5 mm die and flat-faced punches. The upper punch was equipped with four 350 ohm strain gauges forming a full Wheatstone bridge. A linear variable displacement transducer (Sangamo-Weston, Type 13284, Bognor Regis, U.K.), was fitted to the lower punch holder and actuated by means of the moving upper punch. In this way, punch separation and hence tablet thickness during compression could be measured. Signals from the force and displacement transducers were amplified and fed, via an analog-digital converter, into an Acorn computer. Data were stored on magnetic disc, and compressional parameters were derived from them.

A suspension of 5%w/v magnesium stearate in acetone was applied to the die wall and punch faces, and the liquid was allowed to evaporate. The powder was weighed in a controlled environment and then introduced rapidly into the die cavity. The powder was then compressed, the flywheel of the press impeded by a manually applied brake and the tablet ejected from the die.

After compression, the tablets were exposed for 24 hours to the same environment that the original powder had been exposed to. Tablet weight and dimensions were recorded, and the crushing strength then measured using a CT40 strength tester (Engineering Systems, Nottingham, U.K.). The applied force and cross-head movement of the CT40 were continously monitored during strength measurements, From these data, tablet tensile strength [5] and tablet toughness [6] were calculated, the latter being expressed as the area under the curve of applied force plotted against cross-head displacement.

Calculation of consolidation parameters

The relationship between applied force and compact density was calculated according to the Heckel equation [7] , both with the compact under load by manipulation of the force and displacement data, and after ejection from the die by determining the weight and dimensions of the tablet. Linear regression analysis was carried out over a force range of 5kN to 15kN, and the reciprocal of the slope, which is equivalent to the yield force calculated.

The work of elastic recovery [8] was evaluated for all moisture contents and compression forces for both anhydrous dextrose and dextrose monohydrate. Linear regression analysis was applied to the decompression work and compression force data. The data were then normalised by dividing the elastic decompression work by the maximum applied force, and the result plotted against moisture content.

RESULTS AND DISCUSSION

The relationship between tablet tensile strength and applied force over a range of moisture contents is shown in Figure 1, and by erecting verticals from the abscissa, the tablet strength obtained by application of three representative forces of 14, 19 and 25kN can be estimated. The relationships between these and water content are shown in Figure 2. As the water content of anhydrous dextrose is increased, tablet tensile strength rises until a maximum is reached at around 8.9% water at all three forces examined . At higher water contents than this, tablet strength falls sharply until at 9.66%, very weak tablets were produced.

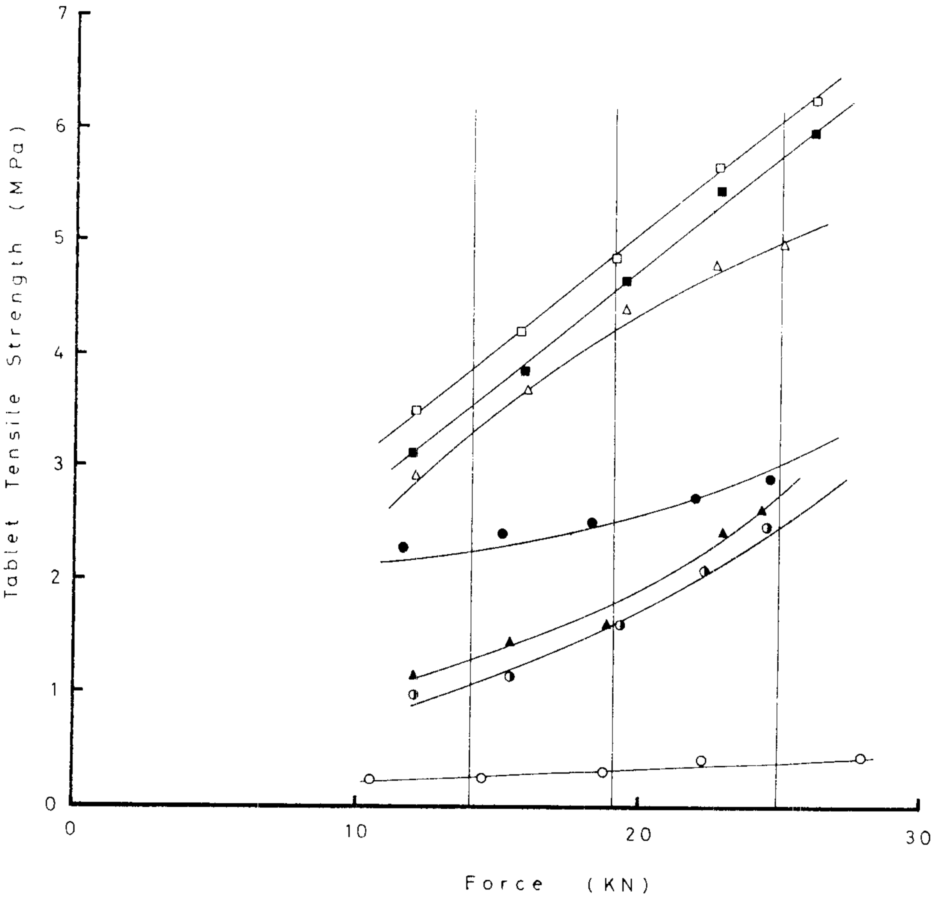

FIGURE 1.

The change in tablet tensile strength with force at a number of water contents.(○, 9.66%; ●, 9.20%; □, 8.90%; ■, 8.60%; △, 6.20%; ▲, 0.90%; ◑, 0.34%)

Qualitatively similar behaviour was noted with dextrose monohydrate, but tablets formed by the latter were weaker than those formed from anhydrous dextrose of the same water content. Thus it is unlikely that the alteration of tabletting properties of anhydrous dextrose with increasing water content is due to a progressive change of anhydrous dextrose to dextrose monohydrate.

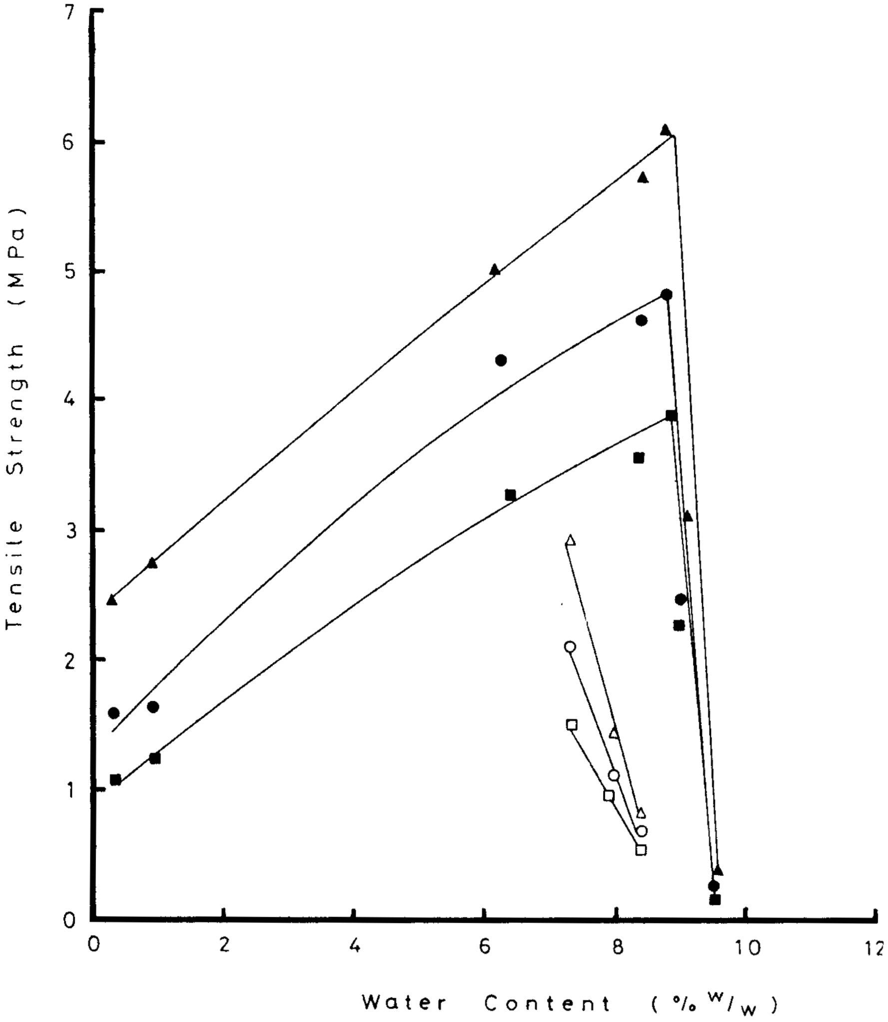

FIGURE 2.

The relationship between the tensile strength of tablets compressed at 14 (■,□), 19 (●,○) and 25 (▲,△)kN and their water content. (closed symbols, anhydrous dextrose; open symbols, dextrose monohydrate.)

The marked increase in tensile strength of anhydrous dextrose tablets with increasing moisture content is believed to be due to two main effects:-

(i). increased lubrication, both interparticular and at the die wall upon compression, resulting in improved force transmission from the upper to the lower punch, and hence greater consolidation is brought about by application of a given force.

(ii). recrystallisation from a saturated solution during compression. It is possible that a saturated solution is formed when the anhydrous dextrose is compressed in the presence of moisture. The aqueous solubility of solids is known to increase substantially when pressure is applied. Thus a solution may form readily under pressure which, when pressure is removed, will be saturated and from which recrystallisation will occur.

Movement of this solution may now occur due to surface tension forces towards regions of high specific area within the compact, which correspond to the flaws within the dextrose particles or the particle contact points. Recrystallisation in those areas of weakness would result in an increase in tensile strength. The extent of recrystallisation will, up to a limiting moisture content, presumably depend upon the quantity of saturated solution formed.

The large differences in tablet tensile strength between dextrose monohydrate and anhydrous dextrose of the same moisture content can be attributed to the different manner in which water is held within the two species, as well as differences in the mobility of the water. In the monohydrate form, the water of crystallisation is locked into the crystal structure, and is therefore not available to encourage bond formation. In the anhydrous form, the moisture exists in a relatively free mobile form, and hence is available for lubrication and dissolution and subsequent recrystallisation of the solid on compression.

It is also apparent from Figure 1 that addition of water to dextrose monohydrate led to an even greater reduction in tensile strength. This is believed to be due to the presence of a water film on the particle surfaces which acts as a physical barrier and prevents interparticulate bonding. Hydrodynamic resistance may also play a part in reducing tablet strength, especially at higher compression forces.

Figure 3 is a representation of the variation of tablet toughness with moisture content at three representative compression forces. It is apparent that the relationship between tablet toughness and moisture content is qualitatively similar to the relationship between tensile strength and moisture. Therefore it would seem that toughness plots do not provide additional information, but this is not so.

The inset to Figure 4 represents two hypothetical toughness curves. A represents the co-ordinates of the point of failure i.e. the force and cross-head position at which the tablet fractures, and thus the area of the right-angled triangle OAB can be readily calculated. Thus the ratio of the areas of surface OPAB to OAB is greater than unity whereas that of OQAB to OAB is less than one. The former has been claimed to be indicative of plastic behaviour and the latter is typical of substances which consolidate by brittle fracture[9].

This ratio was calculated for each batch of tablets at a given moisture content of anhydrous dextrose. It was observed that the value remained independent of the compression force within a batch of tablets. Figure 4 shows how the ratio changes with added water. At moisture contents less than about 6%, the value is less than one, but it progressively increases and at higher moisture contents, exceeds unity, indicative of the effect of water in increasing the plasticity of the system. This result is particularly interesting in view of the fact that dextrose fragments upon compression.

If the densities of the tablets after ejection from the die are measured, density at any given applied force is seen to rise with water content up to about 9% water. This supports the theory that water acts as a lubricant, and greater consolidation is achieved for a

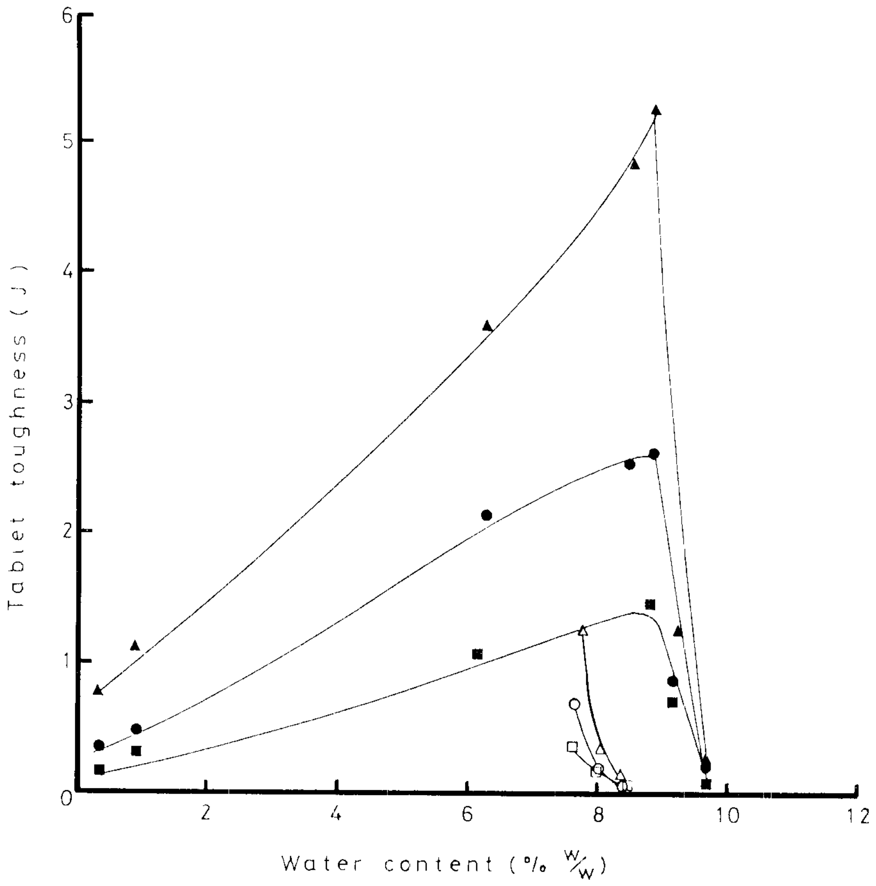

FIGURE 3.

The relationship between the toughness of tablets compressed at 14, 19 and 25kN and their water content. (Symbols as in Figure 2).

given applied force. However above 9.2%, consolidation is markedly reduced. It is of particular interest to note that at 9.66% water, the density does not change with an increase of applied force over about 15kN, implying that some limiting density value has been achieved (Figure 5).

Porosity data obtained after tablet ejection gives little indication of the porosity under an applied load, and although the two

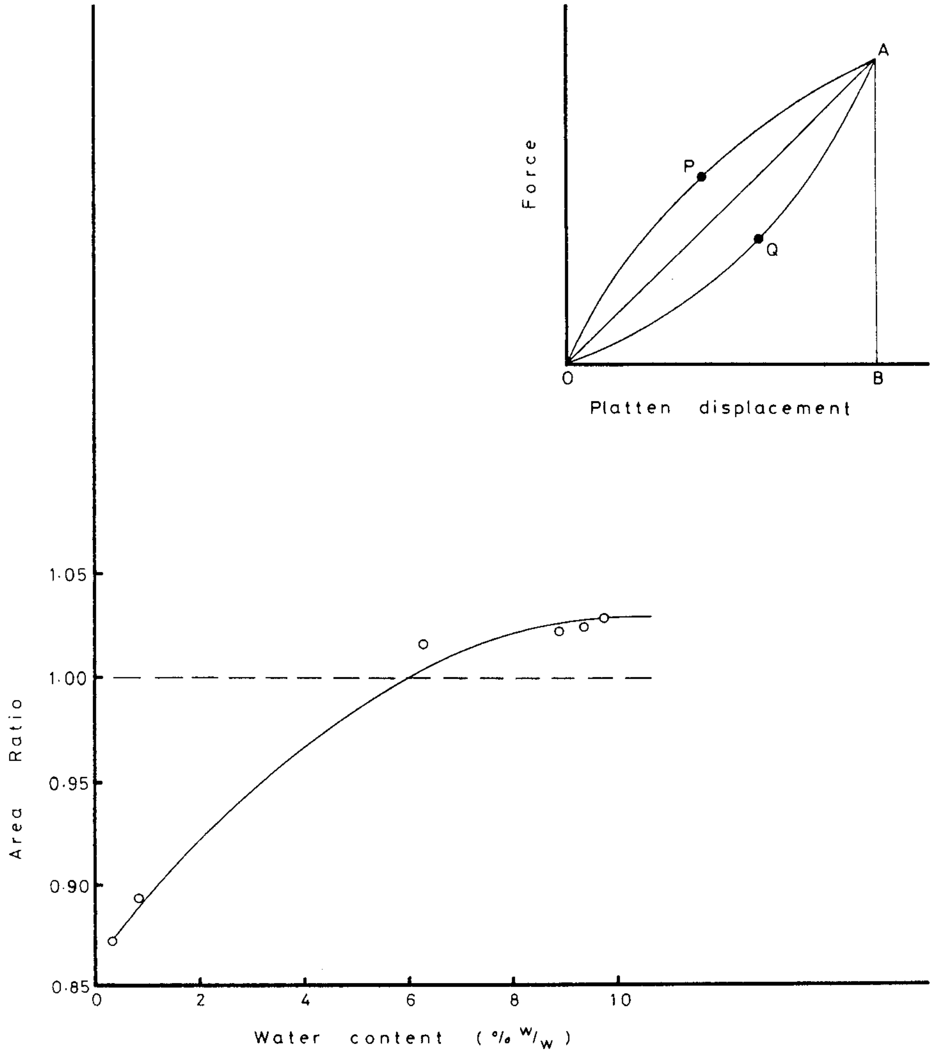

FIGURE 4.

The relationship between area ratio and water content. For the definition of area ratio, see text and the inset to Figure 4.

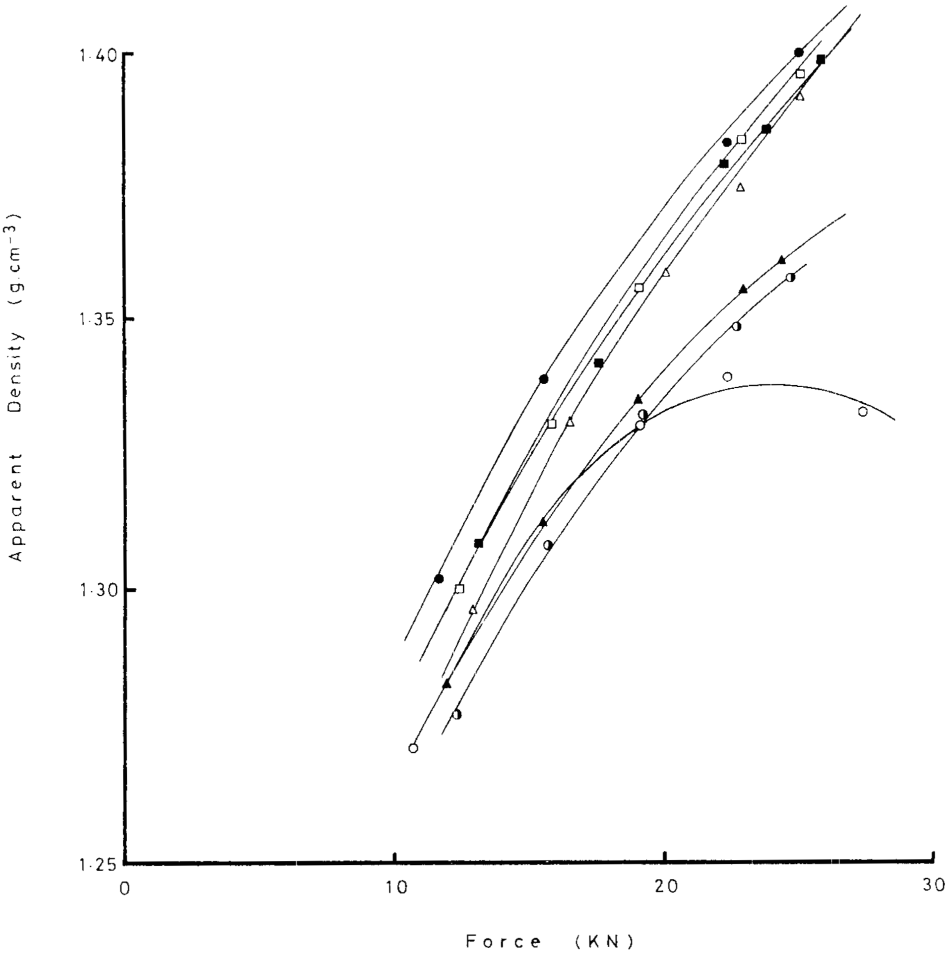

FIGURE 5.

The relationship between apparent tablet density and applied force for anhydrous dextrose. (Symbols as in Figure 1.)

porosities should be linearly related for a substance of constant elastic behaviour, this will not be so if water alters the elasticity of the system. Examination of force and displacement data obtained whilst the tablet is actually being compressed shows that under load, the porosity is much less than that of the ejected tablet. Calculation of the 'in-situ' porosity when the applied force reaches 20kN are

TABLE 1

Constants derived from force and displacement data of anhydrous dextrose and dextrose monohydrate manipulated according to the Heckel equation.

Material	Moisture (%w/w)	In-situ Porosity	In-situ Yield force (kN)	After ejection Yield force (kN)	After ejection Correlation Coefficient
Anhydrous dextrose	0.34	21.0	14.1	33.8	0.997
	0.90	17.0	13.5	31.1	0.959
	6.20	10.0	11.0	19.0	0.966
	8.60	8.2	10.5	16.0	0.979
	8.90	9.5	10.2	16.1	0.995
	9.20	9.1	10.1	15.6	0.997
	9.66	22.0	10.0	-	-
Dextrose monohydrate	7.80	3.9	11.0	35.3	0.999
	8.00	3.4	10.8	40.0	0.984
	8.70	3.2	10.5	48.8	0.992

shown in Table 1. Since these porosities are calculated with respect to the density of the solid component, it follows that if the calculated porosity is equal to or less than the water content, the tablet pores are totally filled with water. It is of interest to note that at the 9.2% moisture level, where maximum consolidation was observed after tablet ejection, a 9.1% in-situ porosity is obtained at 20kN compression force. This may suggest that maximum consolidation is achieved when the water present just fills the pores within the tablet.At 9.66% moisture content, water was observed to exude at the die walls on compression at 20 kN.

If densification data are manipulated according to the Heckel equation, further information may be obtained. A small decrease in the value of the intercept on the ordinates, obtained under compression, was observed upon increasing the moisture content of anhydrous dextrose. This implies a reduction in the extent of densification by particle rearrangement during die filling. The observation may be explained on the grounds that interparticular moisture and liquid bridges hold the particles further apart as moisture content increases, leading to a more open structure.

Figure 6 illustrates the relationship between the yield force obtained 24 hours after ejection and the moisture content. An increase in the moisture content of anhydrous dextrose resulted in a decrease in the yield force obtained up to about 9.2% moisture. A further increase in moisture led to an increase in yield force. The difference between the minimum yield force of 15.55 kN and the maximum, 33.78kN is substantial. Good correlation coefficients were obtained at all moisture levels except 9.66%. A similar trend is seen if the yield force is calculated from porosity data obtained in-situ, i.e. before the tablet is ejected from the die. The absolute values are much smaller in magnitude, and no increase is seen at moisture levels in excess of 9.2%.

From Table 1, it is noticeable that the porosities under compression at 20kN of dextrose monohydrate tablets were extremely low. However the yield forces obtained after ejection are high, and this suggests a very strong elastic recovery for dextrose monohydrate.

By estimating the elastic work of recovery [8], and then normalising by dividing by the maximum applied force, the relationship between elastic work of recovery and moisture content is apparent (Figure 7). Elasticity gradually decreases as moisture content is increased to beyond 9.2%, when a marked increase in elasticity is obtained. Thus the reason for the reduced consolidation at a water content of 9.66% is, in part at least, because the system is more elastic, and tablet integrity is reduced by greater elastic recovery. The mirror image relationship of the tensile strength-force and elastic recovery-force curves is striking.

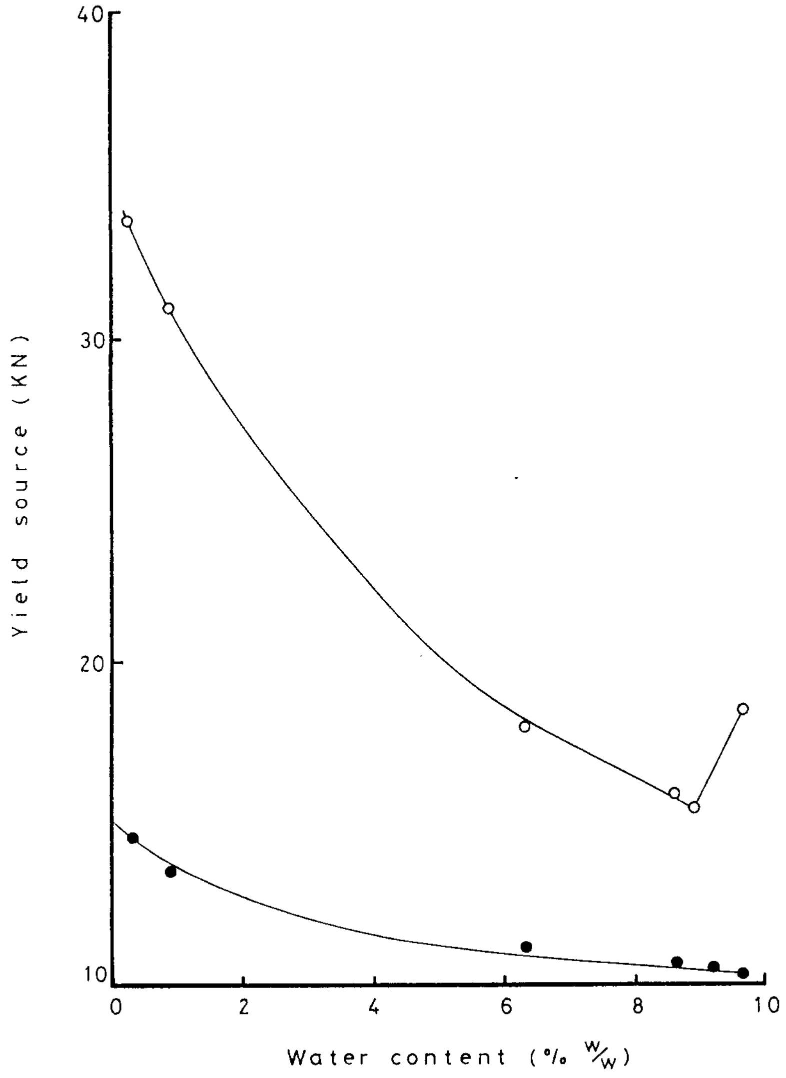

FIGURE 6.

The variation of the yield force, derived by manipulation of compression data according to the Heckel equation, with water content. (●, using tablet porosity before ejection; ○ , using tablet porosity after ejection).

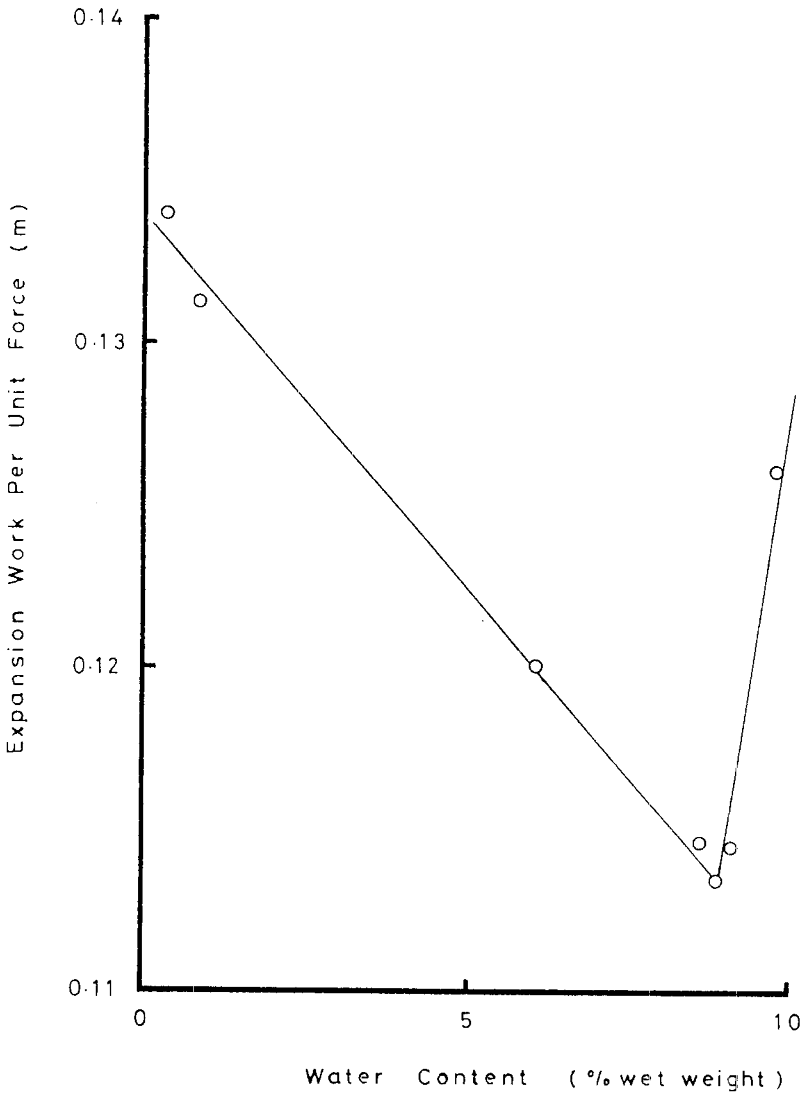

FIGURE 7.

The relationship between elastic expansion work per unit applied force and water content.

As stated earlier, the inflection of the tablet strength-moisture content curves (e.g. Figure 1) takes place at a water content of about 9%, and the in-situ porosity is of the same order, i.e. a hydrostatic resistance to consolidation will occur. However it is of interest to note that this critical moisture content occurs after exposure to a relative humidity of 87%. van Campen et al [10, 11] have shown that a water soluble substance exposed to a humid atmosphere will contain water as vapour unless the humidity exceeds a critical value, termed RH_0. The water will then be present as a liquid. It is of interest to note that van Campen quotes a value of RH_0 of 81.3% for both dextrose monohydrate and anhydrous dextrose, and thus dextrose exposed to 87% relative humidity should contain liquid water in its pores. If this hypothesis is valid, it follows that water vapour can promote dissolution and recrystallisation on compression by condensing on application of pressure, but that liquid water is needed for a hydrostatic effect to be observed.

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