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Effects of Tapioca Obtained From Cassava (*Manihot utilissima*) on the Disintegration and Dissolution Rates of Paracetamol Tablets

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Abstract—The properties of tapioca obtained from cassava (*Manihot utilissima*) have been evaluated. Its binding effect in tablets of paracetamol on the disintegration and dissolution rates was compared with tablets prepared with polyvinylpyrrolidone and gelatin. The nature and amount of the binders were found to alter the disintegration and dissolution rates of the tablets by reducing their wettability as measured by the adhesion tension of water. A linear relationship has been found to exist between the adhesion of water on the tablets and their disintegration and dissolution rates.

It is essential that the binding forces imparted by binders in tablet formulations should undergo fundamental modification in the presence of digestive fluids in the body so that the tablets can break down and release their active principle. Previous reports (Esezobo & Pilpel 1976; Kurup & Pilpel 1979; Itiola & Pilpel 1986) have shown that binders play a significant role in the disintegration and dissolution rates of tablets; the effect being dependent on the nature and quantity of the binder.

Preliminary work has recently been reported (Zubair et al 1988) on the use of tapioca (which is the dried fibrous remnant material obtained by the removal of a large percentage of starch from cassava (*Manihot utilissima*)) as a possible tablet excipient. The results showed tapioca to function as a weak binding agent in the formulation of paracetamol tablets.

The present report concerns an estimate of the wettability of paracetamol tablets (made with tapioca and two other binders—polyvinylpyrrolidone and gelatin) by measuring the contact angle, θ, of water on the surfaces of the tablets and hence their adhesion tension. The wettability of tablet surfaces has been shown to influence the disintegration and dissolution and subsequent release of the active ingredient (Fell & Efentakis 1978; Jones 1981; Igwilo & Pilpel 1983; Itiola & Pilpel 1986). It has recently been suggested (Itiola & Pilpel 1986) that measurements of the adhesion tension of water on tablet surfaces can be employed to monitor the effects that different binding agents will have on the drug release characteristics of particular tablets.

It was therefore thought worthwhile to see whether any correlation existed between the disintegration/dissolution characteristics of formulated paracetamol tablets and the adhesion tension of water on them. The equation of Kitazawa et al (1975) has also been used to analyse the dissolution process of tablets produced.

Materials and Methods

Unless otherwise stated, the materials and methods used in the preparation of the granules, determination of the tensile strength, disintegration and dissolution times of the tablets were identical to those described in Zubair et al (1988).

Measurement of contact angles and adhesion tensions

The contact angles of water (saturated with the basic formulation excluding the binder) on the tablets were determined by a method similar to that described by Kossen & Heertjes (1965) and Lerk et al (1976). The method consisted essentially of measuring the maximum height, h, of a drop of liquid on the tablets using a manually operated

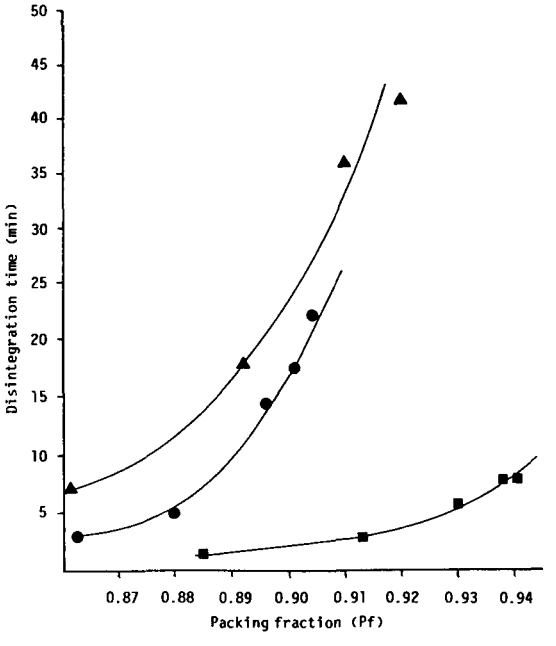

FIG. 1. Disintegration time (min) vs packing fraction (P_f) for paracetamol tablets containing 5% w/w binder. ▲——▲ gelatin, ●——● PVP, ■——■ Tapioca.

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travelling microscope. The contact angles were then calculated from the equations:

$$\cos\theta = 1-\left(\frac{Bh^2}{3(1-\varepsilon)\,(1-Bh^2/2)}\right)^{\frac{1}{2}} \quad (1)$$

(for $0<\theta<90°$), where h is the height of the liquid drop in cm, ε is the volume porosity of the tablet (which is 1-packing fraction), θ is the contact angle; B is $Pg/2\gamma$ and P is the liquid density in gcm^{-3}, g is 981 cms^{-2} and γ is the surface tension of the liquid in mNm^{-1}, which was measured with a torsion balance (White Electrical Instruments Co Ltd, Worcs, UK). To ensure that the reproducibility of the contact angles was within $\pm 2{\cdot}0\%$, drops were delivered from an Agla syringe positioned 0·8 cm above the surface of the tablet and the test assembly was covered with a perspex lid. Measurements were made in sextuplate on individual tablets. The adhesion tensions, AT, were calculated from the cosine of the contact angle using the equation:

$$AT=\gamma\cos\theta \quad (2)$$

Results

The results of the tensile tests on the paracetamol tablets were found to fit the general equation:

$$\text{Log } T=A\,P_f+B \quad (3)$$

with a correlation coefficient of $>0{\cdot}97$. A and B were constants which depended on the nature and amount of binder present. P_f was the packing fraction.

The values of the disintegration times were plotted as a function of packing fraction and representative plots for tablets containing 5% w/w of the binders are illustrated in Fig. 1. Typical dissolution profiles for tablets containing 5% w/w tapioca binder compressed to different packing fractions are shown in Fig. 2. From these, the values of t_{50} (the time required for 50% of paracetamol to be released) were calculated.

The integrated form of the equation of Noyes & Whitney (1897) is given as

$$\text{Ln}\left(\frac{Cs}{Cs-C}\right)=kt \quad (4)$$

where Cs is the concentration of the solute at saturation, C is its concentration at time t, and k is a dissolution rate constant. Values of $\text{Ln}\left(\frac{Cs}{Cs-C}\right)$ were plotted versus t (Kitazawa et al 1975) as shown typically in Fig. 3 for tablets containing 2·5% w/w of the binders and compressed to a packing fraction of approximately 0·90. Depending on the nature and concentration of binder used, it is seen (Table 1, Fig. 3) that either a single straight line of slope k_1 or two straight lines of slopes k_1 and k_2 were obtained. The time at which the lines intersect is t_1.

The values of T, D, t_{50}, t_1, k_1 and k_2 for all the tablets at a packing fraction of 0·90 are presented in Table 1. It is seen that the values of D and t_{50} increased with binder concentration. The values of the cosine of contact angle (cos θ) and adhesion tension (AT) of water on the tablets at $P_f=0{\cdot}90$ are tabulated in Table 2. It is seen that the AT values decreased with binder concentration. Fig. 4 shows the plots of the linear relationships between t_{50} and wettability of the tablets as measured by adhesion tension.

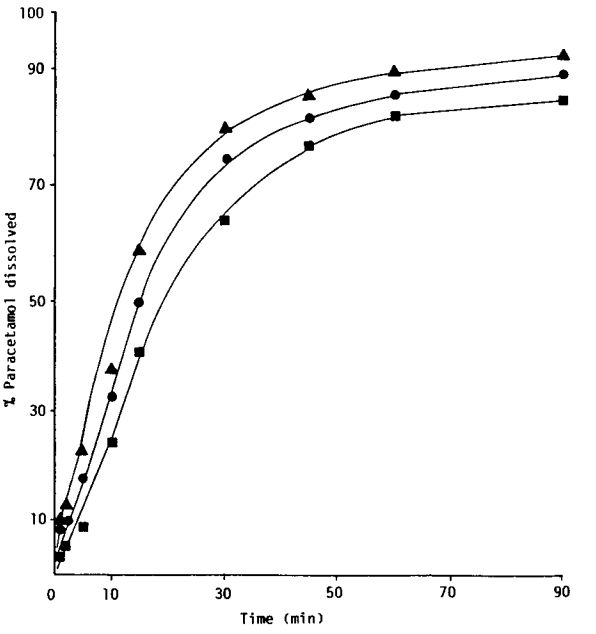

FIG. 2. Effect of packing fraction (P_f) on the dissolution profiles of tablets containing 5% w/w tapioca. P_f values: ■——■ 0·920, ●——● 0·880, ▲——▲ 0·857.

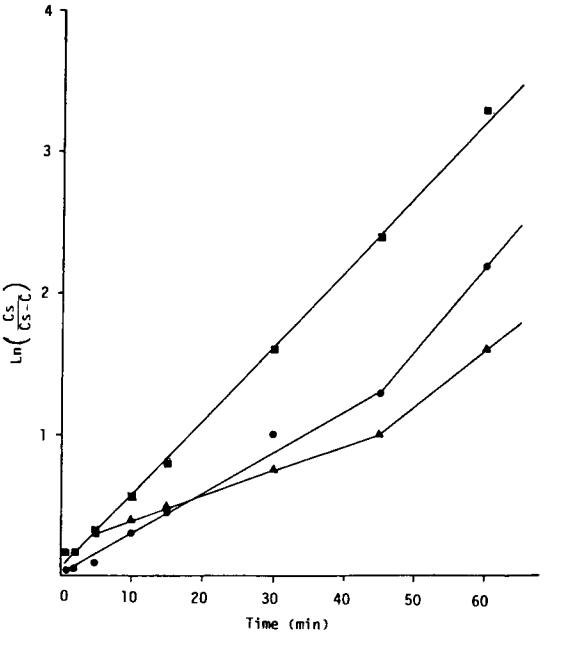

FIG. 3. Ln(Cs/Cs-C) versus time plot to determine dissolution rate constants for paracetamol tablets containing 2·5% w/w binder. P_f values: ▲——▲ gelatin 0·917, ●——● PVP 0·899, ■——■ Tapioca 0·907.

Table 1. Tensile strength, disintegration time and dissolution characteristics of paracetamol tablets at $P_f = 0.90$.

Binder	Concn of binder (% w/w)	T (MNm^{-2})	D (min)	t_{50} (min)	t_1 (min)	k_1	k_2
	0·00	2·82	1·25	17·00	30·0	0·043	0·060
PVP	2·50	3·40	4·50	29·50	45·0	0·029	0·058
	5·00	3·76	17·00	35·50	45·0	0·020	0·037
Gelatin	2·50	3·40	4·00	38·50	45·0	0·018	0·040
	5·00	3·85	23·50	44·00	45·0	0·012	0·027
Tapioca	2·50	2·57	0·75	16·00	a	0·053	a
	5·00	3·10	2·00	17·25	a	0·056	a
	10·00	3·63	4·75	28·00	30·0	0·030	0·058

a Indicates where a single straight line with slope k_1 was obtained.

Table 2. Values of cosine of contact angles and adhesion tension of water on paracetamol tablets.

		Water saturated with the basic formulation			
Binder	Concn of binder (% w/w)	Drop height, h (cm)	Porosity	Cos θ	AT (mNm^{-1})
	0·00	0·1031	0·111	0·8310	59·2
PVP	2·50	0·1409	0·103	0·7794	55·5
	5·00	0·1473	0·110	0·7455	53·1
Gelatin	2·50	0·1427	0·108	0·7626	54·3
	5·00	0·1640	0·112	0·7230	51·5
Tapioca	2·50	0·1295	0·099	0·7870	56·0
	5·00	0·1455	0·100	0·7570	54·0
	10·00	0·1530	0·105	0·7445	53·0

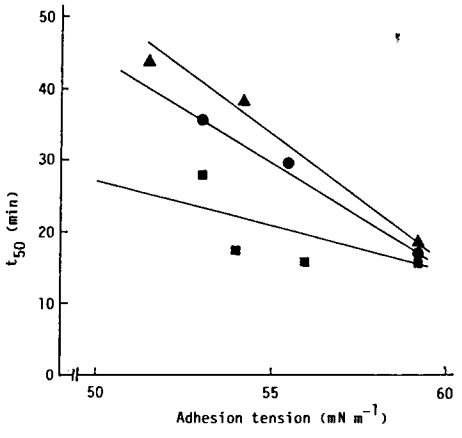

FIG. 4. Correlation of t_{50} (min) of paracetamol tablets ($P_f = 0.90$) containing between 0 and 10% w/w of binder with adhesion tension (mNm^{-1}) of water on the tablets. Symbols as in FIG. 1.

Discussion

The bioavailability of a drug in tablet form has been closely associated with the preparation's disintegration and dissolution rate. Although dissolution of drug occurs from an intact tablet when it is added to a dissolution medium, a considerable amount of dissolution occurs from the small particles and the aggregates or granules after disintegration (Wagner 1969). Thus, the disintegration of a tablet plays a considerable part in the dissolution process.

As expected from previous reports (Esezobo & Pilpel 1976; Adeyemi & Pilpel 1984) and shown in the present study (see Fig. 1), the disintegration times of the tablets increased with increase in their packing fractions; the increase being slight at lower packing fractions but increasing greatly at higher packing fractions. An explanation for this is that when granules are compressed in a die, the fragmentation that occurs leads initially to an increase in their specific surface area. At higher packing fractions, these fragments presumably reform into compacts by the process of cold bonding between the particles. Thus, the rate of liquid penetration into the tablets' interstitial void spaces to produce the swelling of disintegrant and the disruption of the tablets is reduced at the higher packing fraction, thereby prolonging the disintegration time of the tablets.

Fig. 1 also shows that gelatin prolonged the disintegration times of the tablets more than polyvinylpyrrolidone (PVP) and this has been ascribed to the greater binding property of gelatin than PVP (Zubair et al 1988). The inclusion of tapioca in the paracetamol tablet formulations produced tablets with the shortest disintegration times. This is expected since tapioca produced tablets of the least tensile strengths at all concentrations (see Table 1).

From Table 1 it will be seen that in all cases the disintegration times of the tablets were less than their t_{50} times. This is to be expected since the degree of agitation in the disintegration test is much higher than in the dissolution test (Esezobo & Pilpel 1977). In addition, the disintegration times, D, were less than the t_1 values. It is known that the adsorption and penetration of water into tablets initiates the disintegration process and the shorter values of D are

probably due to the rapid water absorption by (or penetration into) the tablets and their subsequent breaking up into particles that passed through the 1·70 mm sieve aperture of the disintegration test apparatus.

The straight lines obtained with tablets containing 2·5 and 5% w/w of tapioca (Table 1 and Fig. 3) may be ascribed to its water absorbing property, swelling and the formation of a mucilagenous mass in the presence of water. This would result in the rapid break up of the tablets in the dissolution medium into smaller particles to produce a maximum surface area for dissolution after which the surface area decreases progressively with time (Igwilo & Pilpel 1987). However, at a higher concentration (say at 10% w/w tapioca) two straight lines with slopes k_1 and k_2 were obtained (Table 1). It may thus be inferred that a concentration of 10% w/w or more of tapioca is required to produce noticeable binding properties.

The increase in disintegration and t_{50} times of tablets at higher binder concentrations (see Table 1) is probably due to the influence of the binders on the wettability and penetration of liquid into the capillaries of the tablets. Tables 1 and 2 indicate that a good correlation exists between disintegration times and wettability of tablets as determined by the adhesion tension, AT, of water on them; while Fig. 4 illustrates the correlation between t_{50} times and adhesion tension, AT. The penetration of liquid into the capillaries of tablets has been shown to be necessary for the process of disintegration and dissolution of tablets to occur (Jones 1981; Alkan & Groves 1982; Adeyemi & Pilpel 1984; Itiola & Pilpel 1986). The presence of binders in tablet formulations would be expected to reduce the size and number and alter the shapes of the capillary spaces between the particles which are contributing to the transport of water. They therefore affect the penetration of water into tablets. In fact, Huber et al (1966) have suggested that binders form thin films around granules during the granulation process and form viscous barriers to the penetration of test fluid thus prolonging disintegration and dissolution times of tablets. These effects are expected to be magnified at higher concentrations of binding agents and may be responsible for the observed decrease in the values of AT of water on the tablets with increase in the amount of binder (see Table 2).

Conclusions

Tapioca acts as a weaker binder than either PVP or gelatin in paracetamol tablet formulations, giving tablets with shorter disintegration and dissolution times even at a concentration of 10% w/w. It might be considered as a binder in the formulation of pharmaceutical tablets.

This study has shown that the nature and quantity of the binder affects the wettability of tablet surfaces and hence their adhesion tension. This has been used to explain the disintegration and dissolution characteristics of paracetamol tablets.

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