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A COMPARATIVE STUDY OF THE USE OF ENSET AND POTATO STARCHES IN TABLET FORMULATIONS.

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ABSTRACT

Enset and potato starches have been compared as binding agents and disintegrants in tablets made with paracetamol and chloroquine phosphate. Tablet crushing strengths, friabilities and disintegration times have been measured. The results show that enset starch can be used both as a binding agent and disintegrant. It has a better binding ability than potato starch, giving tablets of lower porosity. However because of this, tablets containing enset starch disintegrate more slowly.

INTRODUCTION

Starch is a common tablet excipient, being employed both as a binder and as a disintegrant. Potato starch and corn starch are widely used in Europe and the USA respectively. Wheat, rice and tapioca starches are used to a lesser extent, the latter two mainly in tropical countries. Many tropical countries have native species which might be used as a source of starch for pharmaceutical purposes, and some of these have been investigated (1). A potential source indigenous to Ethiopia is *Ensete ventricosum* Musaceae, related to the banana tree (2). This plant is widely used as a food source in Ethiopia (3). The isolation of starch from *E. ventricosum* (enset starch) has been described by Gebre-Mariam and Nikolayev (4), who also give a preliminary report on its use in tabletting. In the present work, the use of enset starch as a binder and disintegrant in tablets containing chloroquine phosphate and paracetamol has been investigated. For comparative purposes, identical tablets using potato starch have been prepared.

MATERIALS

Paracetamol (Sterling Drug Company Cramlington, UK); chloroquine phosphate (Halewood Chemicals Ltd Staines, UK); potato starch (BDH Chemicals Ltd, Poole, UK); magnesium stearate (Fisons Scientific Equipment, Loughborough, UK). Enset

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starch was isolated from *E. ventricosum* by the method of Gebre-Mariam and Nikolayev (4). It complies with the specifications for starch in the British Pharmacopoeia. The starches were either used as dry powders or as freshly prepared aqueous mucilages.

METHODS

Preparation of Tablet Formulations and Granules

The composition of tablet formulations containing paracetamol and chloroquine phosphate are given in Table 1. For each batch of the formulation (100g), the drug and the internal disintegrant (50% of the specified amount of enset or potato starch) were weighed and dry-mixed in a cube mixer (Erweka Apparatebau, Offenbach/Main, Germany, Model KU1) for 10 min at 50 rpm. The mixture was then transferred into a Z-blade mixer (Erweka Apparatebau, Offenbach/Main, Germany, Model LK5) and the appropriate quantity of freshly prepared enset or potato starch mucilage (35 grams of mucilage for paracetamol and 23 grams of mucilage for chloroquine phosphate) was then added as granulating agent and mixed for 5 minutes. Uniform wet masses were obtained which were then passed through a 1.40mm sieve. The wet granules were dried at 50°C for 12h and then were passed through a 1.0mm sieve. Granules retained on a 700μm sieve were collected and thoroughly mixed for 10 min with the specified amounts of external disintegrant and finely sifted magnesium stearate in the cube mixer described above. Triplicate batches of each formulation were prepared.

Compression of Tablets

400mg of the granules were individually weighed and compressed using an eccentric tablet press (Manesty Type F3, Manesty Machines Ltd, Liverpool, UK) fitted with 12.5mm diameter flat-faced punches. Force transducers were fitted to the upper punch. Paracetamol tablets were compressed at 12.5, 15.0 18.5 and 22.5kN and chloroquine phosphate tablets at compression forces of 8.5, 10.5, 12.5 and 14.5kN respectively.

Measurement of tablet properties

Crushing strength. This was determined using a CT40 strength tester (Engineering Systems, Nottingham, UK) The mean of 10 determinations was calculated for each batch.

Friability determination. Ten tablets were agitated for 5 min in a friabilator rotating at 20 rpm (Erweka Apparatebau, Offenbach/Main, Germany, Model TAP) and the percentage loss in weight measured.

Tablet porosity. The dimensions and weights of six tablets from each batch were determined 24h after manufacture and their apparent densities calculated. The true densities of the solids were obtained by air pycnometry for paracetamol, liquid pycnometry using chloroform for the starches and a flotation method using chloroform and ethanol for chloroquine phosphate (5).

Disintegration time. This was determined according to the method of the British Pharmacopoeia 1988. (Manesty Machines Ltd, Liverpool, UK). The mean disintegration time of 12 tablets of each batch was determined.

TABLE 1

Formulations of Paracetamol and Chloroquine Phosphate Tablets incorporating Enset and Potato Starches.

A. Enset and potato starches used as mucilages, and the corresponding concentration of starch remaining after drying.

	Paracetamol	Chloroquine phosphate
Starch (%) (as disintegrant)*	15.0	10.0
Starch mucilage (%) (as binder)	7.5, 10.0, 12.5, 15.0 2.63, 3.50, 4.38, 5.25	5.0, 7.5, 10.0, 12.5 1.15, 1.73, 2.30, 2.88
Magnesium stearate (%)	0.5	0.5

B. Enset and potato starches used as disintegrants.

	Paracetamol	Chloroquine phosphate
Starch (%) (as disintegrant)*	10.0, 12.5, 15.0, 17.5	7.5, 10.0, 12.5, 15.0
Starch mucilage (%) (as binder)**	10.0 3.5	5.0 1.15
Magnesium stearate (%)	0.5	0.5

* % w/w of drug.
** % of starch remaining in the mass (drug plus internal disintegrant) as binder following drying.

RESULTS AND DISCUSSION

In a tablet formulation, starch can play two roles, that of binding agent and as a disintegrating agent. In this work, an attempt has been made to distinguish these two roles. Furthermore both these roles may be expected to be influenced by the solubility of the other components of the tablet. In the wet granulation process, liquid bridges are developed between particles. If the solid is appreciably soluble in the granulating fluid, it will dissolve and then recrystallise as the liquid phase is removed on drying. The formation of crystal bridges has been shown to be a major influence on the physical strength of tablets (6). It was for this reason that both a freely soluble solid (chloroquine phosphate, soluble 1 in 4) and a sparingly soluble solid (paracetamol, soluble 1 in 70) were chosen. Also tablets containing solids of high solubility would be expected to disintegrate more readily than those of lower solubility.

The relationship between tablet crushing strength and binder concentration is shown in Figure 1. Binder concentration is expressed in terms of the weight of the dried binder as a percentage of the weight of the drug. The disintegrant concentration is kept constant. For both drug substances, increasing the binder concentration increased the crushing strength of the tablets prepared at any given force. This is in agreement with previous work on starches and other binders (4, 7). In wet granulation, liquid bridges are developed between particles, and the tensile strength of

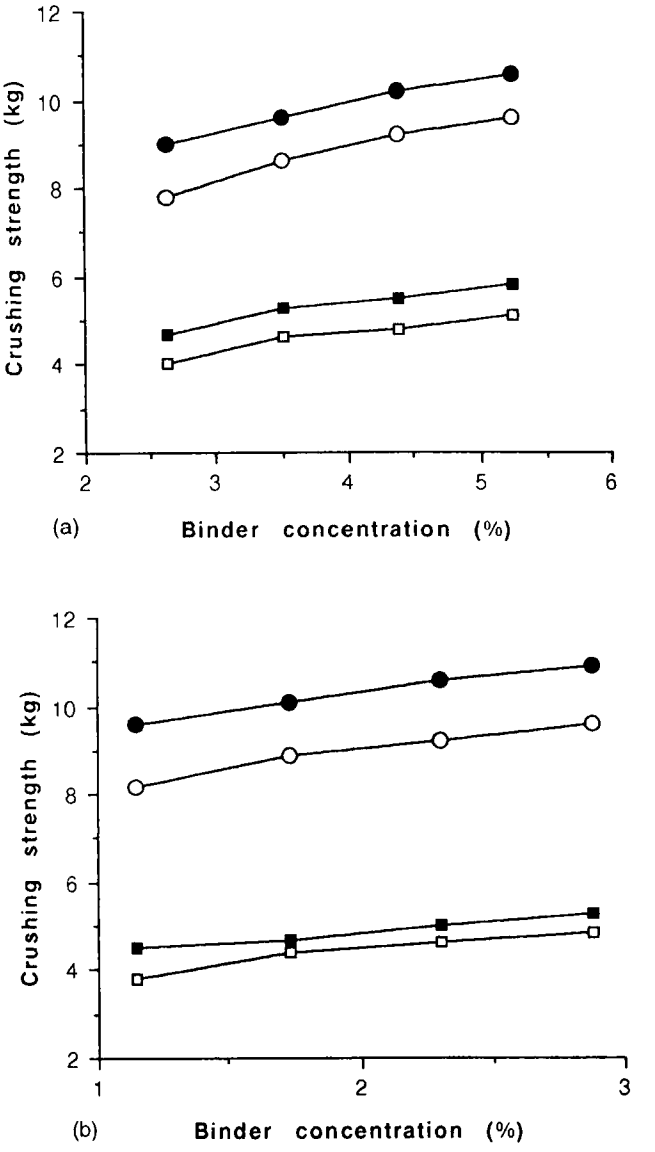

FIGURE 1

Effect of concentration of starch employed as a binder on the crushing strength of tablets. Closed symbols, enset starch; open symbols, potato starch.
A. Paracetamol tablets. □, ■; compression force 12.5kN. o, ●; compression force 22.5kN.
B. Chloroquine phosphate tablets. □, ■; compression force 8.5kN. o, ●; compression force 14.5kN.

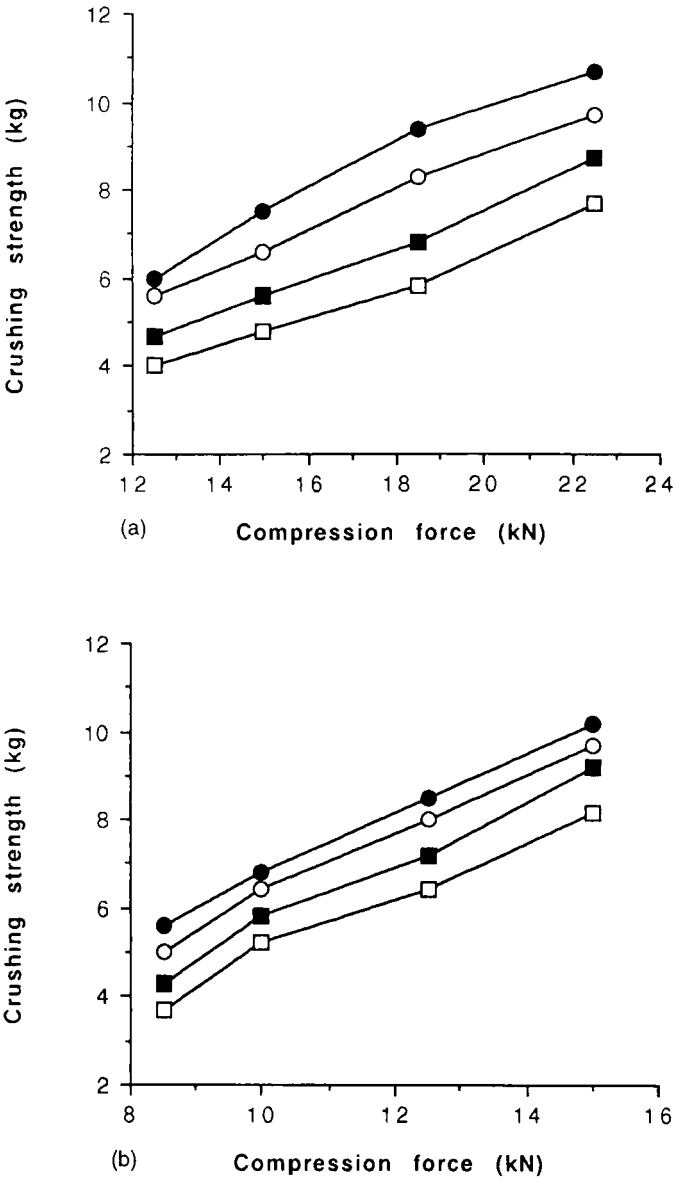

FIGURE 2
Effect of compression force on the crushing strength of tablets. Closed symbols, enset starch; open symbols, potato starch.
A. Paracetamol tablets prepared with 2.62% binder (□,■) and 5.25% binder (o, ●).
B. Chloroquine phosphate tablets prepared with 1.15% binder (□,■) and 2.88% binder (o, ●).

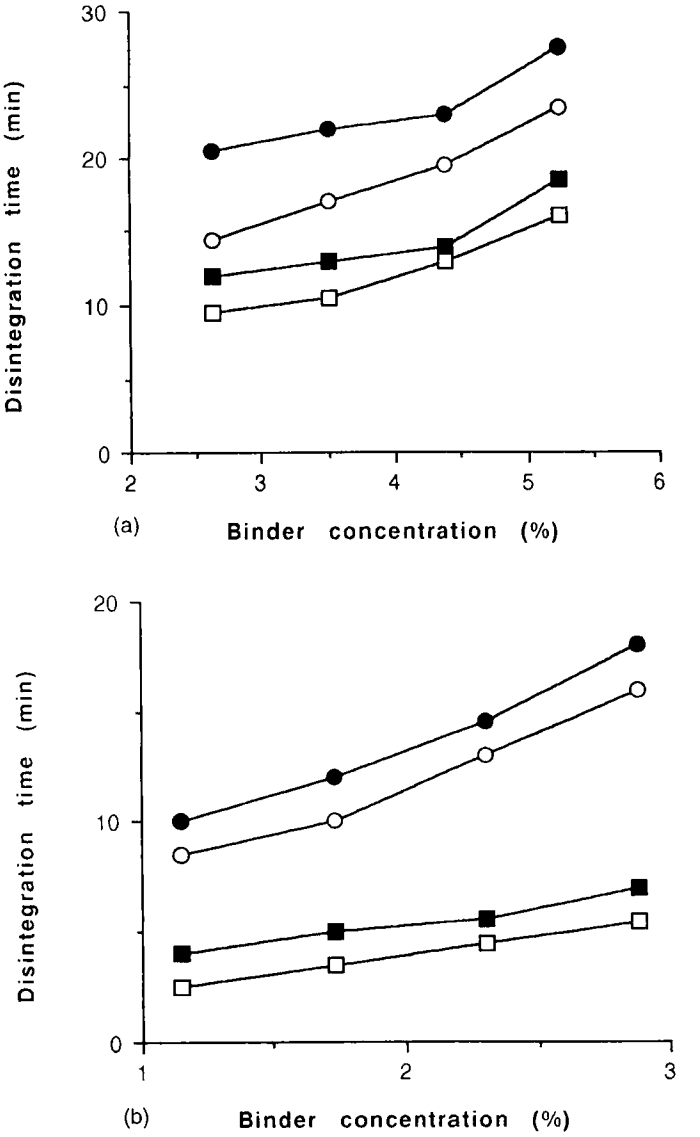

FIGURE 3

Effect of concentration of starches employed as binders on the disintegration time of tablets. Closed symbols, enset starch; open symbols, potato starch.

A. Paracetamol tablets. □, ■; compression force 12.5kN. o, ●; compression force 22.5kN.

B. Chloroquine phosphate tablets. □, ■; compression force 8.5kN. o, ●; compression force 14.5kN.

TABLE 2

The Effect of Disintegrant Concentration and Compression Force on Disintegration Time of Tablets (E = Enset starch, P = Potato starch).

A. Paracetamol tablets

	Disintegrant concentration (% by weight of drug)							
	10.0		12.5		15.0		17.5	
	Disintegration time (min)							
Compression force (kN)	E	P	E	P	E	P	E	P
12.5	15.0	14.0	13.9	12.8	12.6	12.0	11.0	9.5
15.0	17.3	15.3	15.7	14.0	14.5	13.1	12.5	11.8
18.5	20.0	17.6	18.4	16.9	17.0	15.9	15.2	13.9
22.5	25.7	20.4	24.0	19.6	22.0	18.8	19.1	16.3

B. Chloroquine phosphate tablets.

	Disintegrant concentration (% by weight of drug)							
	7.5		10.0		12.5		15.0	
	Disintegration time (min)							
Compression force (kN)	E	P	E	P	E	P	E	P
8.5	4.2	3.7	3.6	3.2	3.0	2.8	2.8	2.7
10.5	5.8	5.5	4.9	4.7	4.2	3.7	3.9	3.6
12.5	8.5	7.3	7.7	6.5	5.2	4.4	4.4	4.1
15.0	11.4	10.3	9.6	8.6	8.2	7.8	7.2	6.7

these bonds increases as the amount of liquid is increased. During drying, interparticulate bonds result from fusion or recrystallisation and curing of the binding agent (8). It is therefore assumed that as the amount of starch mucilage used is increased, a greater amount of bonding takes place. Though tablets made from the two drug substances show similar relationships between crushing strength and binder concentration, any given physical strength of chloroquine phosphate tablets is achieved at lower forces than for paracetamol. This is indicative of the role played by crystal bridging with the more soluble material. Figure 1 also shows that for both paracetamol and chloroquine phosphate, enset starch gave tablets of greater crushing strength than those made with potato starch.

The relationship between the compression force and the crushing strength of paracetamol and chloroquine phosphate tablets with two different binder concentrations is shown in Figure 2, from which it can be seen that the crushing strength of both tablets increased with an increase in compression force. Figure 2 also shows that at all levels of compression force, tablets made with enset starch have greater crushing strength than those made with potato starch.

Because an increase in the binder concentration gives tablets of greater physical strength, this might in turn affect the disintegration times of the tablets. It has been

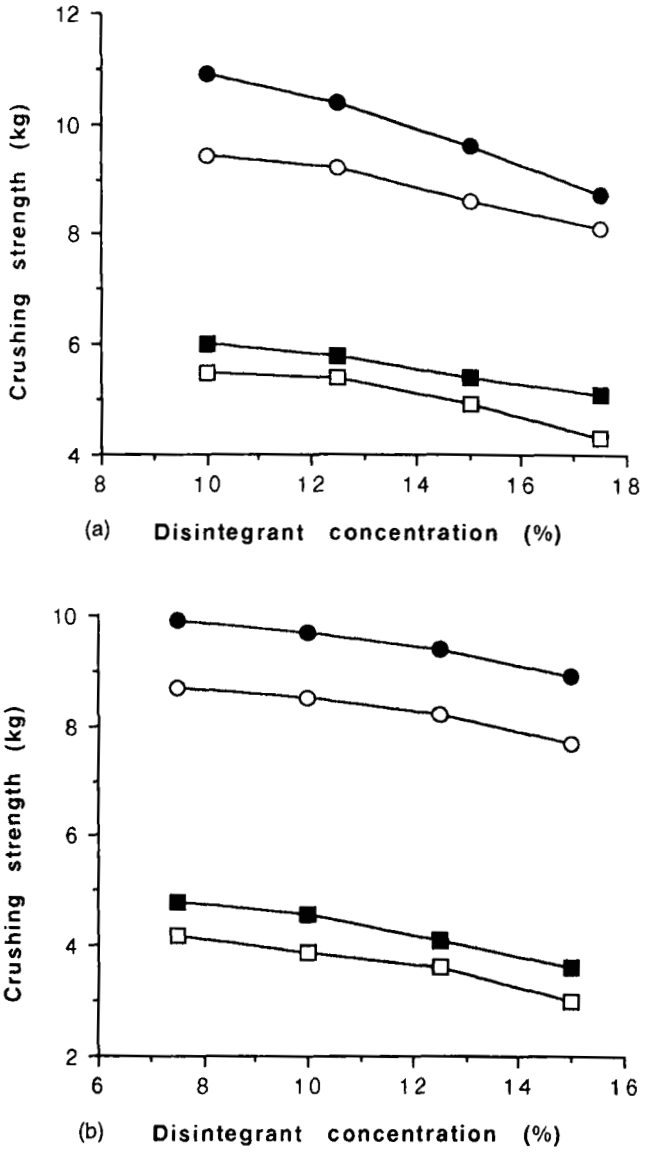

FIGURE 4

Effect of concentration of the starches employed as disintegrants on the crushing strength of the tablets. Closed symbols, enset starch; open symbols, potato starch. A. Paracetamol tablets. □, ■; compression force 12.5kN. o, ●; compression force 22.5kN.

B. Chloroquine phosphate tablets. ◫, ■; compression force 8.5kN. o, ●; compression force 14.5kN.

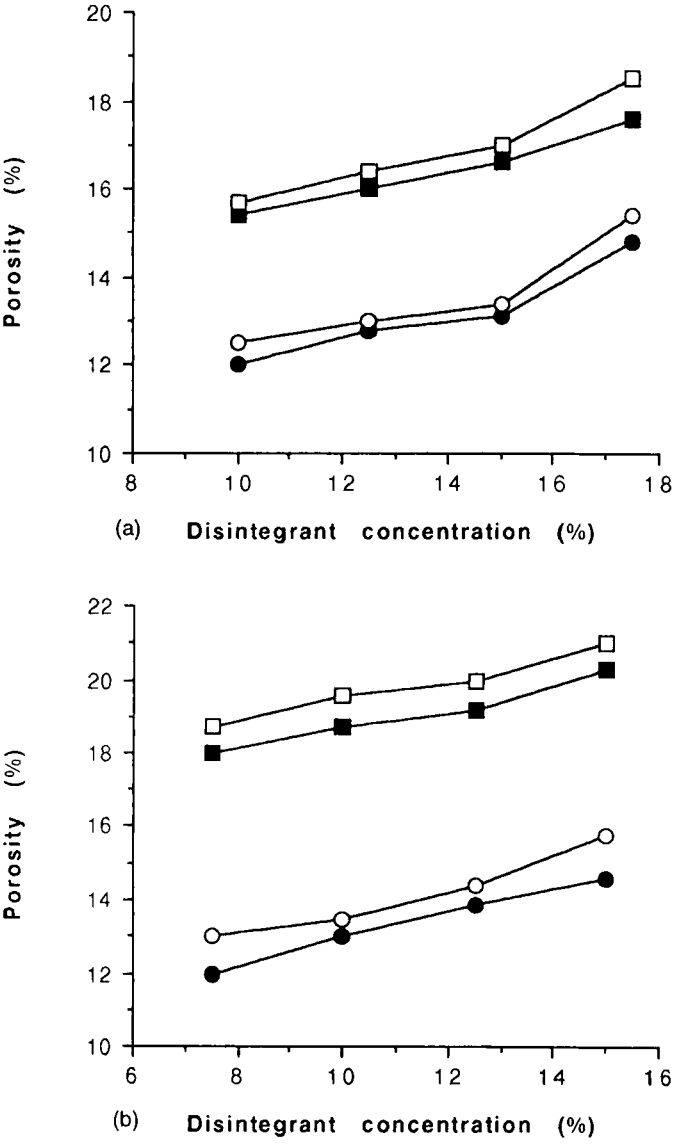

FIGURE 5

Effect of concentration of starches employed as disintegrants on the porosity of tablets. Closed symbols, enset starch; open symbols, potato starch.
A. Paracetamol tablets. □,■; compression force 12.5kN. o, ●; compression force 22.5kN.
B. Chloroquine phosphate tablets. □, ■; compression force 8.5kN. o, ●; compression force 14.5kN.

shown by previous workers that a thin film of mucilage around the granules is formed with a thickness depending on the quantity of mucilage used. It has also been shown that in the presence of water this thin film is converted into a mucilaginous viscous barrier between the granules and the water retarding the disintegration of the granules (9). Figure 3 shows that this occurs to a similar extent with both enset and potato starches.

The effects of the starches as disintegrating agents on the crushing strength of the tablets at a constant binder concentration are shown in Figure 4. When the concentration of the binder was kept constant an increase in disintegrant concentration showed a gradual reduction in the crushing strength of the tablets. The decrease in crushing strength of the tablets at higher concentrations of disintegrant may be attributed to the poor compressibility of starch. The effect of the starches as disintegrants on the crushing strength of the tablets however differed significantly, in that tablets made with enset starch were invariably stronger than those made with potato starch. Changes in tablet friability were similar to those in tablet crushing strength.

For both paracetamol and chloroquine phosphate tablets prepared with enset or potato starch, disintegration time decreased with increased amount of starch added as disintegrant (Table 2) Tablets formulated with enset starch, however, gave somewhat longer disintegration times than those formulated with potato starch at all levels of compression force.

All these effects on disintegration time, crushing strength and friability can be explained by reference to the porosity of the tablets. The effects of the starches employed as disintegrants on the porosity of the tablets with one binder concentration are shown in Figure 5. An increase in disintegrant concentration up to 15% showed a gradual increase in the porosity of paracetamol tablets. An increase beyond 15% of disintegrant, however, showed a sharp increase in porosity of paracetamol tablets, which may be explained by the elasticity of the starch particles. Chloroquine phosphate tablets also showed increased porosity with increased disintegrant concentration. In both cases, enset starch gave less porous tablets than those prepared with potato starch. This would account for their longer disintegration times and greater physical strength of the former.

CONCLUSIONS

From the foregoing, it appears that enset starch is a better binder than potato starch in tablets of paracetamol and chloroquine phosphate as it gave less porous tablets with a greater crushing strength and lower friability tablets. As a disintegrant it is less effective. Nonetheless, enset starch can be used as a disintegrant when formulated in optimum concentration. It is therefore suggested that *Ensete ventricosum* could be used as an alternative source of starch for use in tablet formulation.

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