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Evaluation of starch obtained from *Ensete ventricosum* as a binder and disintegrant for compressed tablets

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Abstract—The binding and disintegrant properties of starch obtained from *Ensete ventricosum* Musaceae have been evaluated. The effect of the starch on the physical properties such as crushing strength, friability and disintegration time of tablets of chloroquine phosphate, dipyrone and paracetamol was compared with tablets prepared with potato starch. The results show that enset starch can be used both as a tablet binder and disintegrant and the indication is that enset starch has a better binding ability and less disintegrating power than potato starch.

Ensete ventricosum Musaceae is a plant indigenous to Ethiopia, closely related to the banana tree (Simmonds 1985). The plant is cultivated in many parts of the country, particularly in the south and south-west. Approximately one-sixth of the native population depend on it either wholly or partially for their food supply (Besrat et al 1979). The two main products utilized as food are locally known as boulla and kocho. In the preparation of these two products, the pseudostem and corms are cut and crushed, and the exuding liquid containing starch is collected. Most of the water is allowed to drain away and the main product, the wet starch, boulla, is collected leaving the fibrous material, kocho, behind. It has been reported that purified air-dried boulla contains 85% starch, 14% moisture, 0·2% ash and no fibrous material (Rama et al 1983). Since enset is locally produced in abundant quantities and starch can easily be obtained from it, we have studied its application both as a binder and disintegrant for tablets of chloroquine phosphate, dipyrone and paracetamol, each containing 250 mg of the respective drugs. The physical characteristics of these tablets were compared with those of tablets prepared using potato starch.

Materials and methods

Materials. Chloroquine phosphate, dipyrone and paracetamol were of pharmaceutical grades and were obtained from Ethiopian Pharmaceutical Manufacturing Plant. Potato starch, magnesium stearate and talc were from BDH Ltd, UK.

Preparation of enset starch. Fresh wet boulla was purchased from the local market and suspended in large quantities of distilled water containing 0·075% w/v sodium metabisulphite (Willigen 1964). The material was then passed through fine muslin to remove the cell debris and the translucent suspension collected, filtered through a fine sieve and allowed to settle. The sedimented starch was washed several times with distilled water followed by sieving after each washing until the wash-water was clear and free of suspended impurities. The resulting starch was sieved and dried in air. It was then screened through a 150 μm sieve and collected. The starch so obtained complied with the specifications of the British Pharmacopoeia (1988) for starches.

Preparation of tablet formulations and granules. The compositions of the three tablet formulations (chloroquine phosphate, dipyrone and paracetamol) are given in Table 1. For each batch of the formulation (50 g), the drug and the appropriate quantities of the disintegrant, enset or potato starch were weighed and dry-mixed by the geometric dilution method using a porcelain mortar and pestle. An appropriate quantity of freshly prepared enset or potato starch mucilages was then added as the granulating agent and mixed until a uniform wet mass was obtained. The wet masses were then granulated by passing through a 1·40 mm sieve. The granules were dried at 50°C for 12 h and the resulting dry granules were passed through a 1·00 mm sieve. Sieved granules retained on an 850 μm sieve were collected and thoroughly mixed with the specified amount of finely sifted talc and magnesium stearate.

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Compression of tablets. Approximately 280 mg of the granules was compressed in a 9·5 mm diameter stainless steel die fitted with normal concave punches using a single punch tablet machine (Diaf, Denmark). The machine compression force dial was kept constant at 7·5 units.

Crushing strength. The Pfizer Tablet Hardness Tester was employed for determining the crushing strength of the tablets. Ten tablets from each batch were used in each determination and the mean value and the standard error were calculated for three batches.

Friability. The Erweka type friabilator was used for determining friability. Ten tablets from each batch were placed in the friabilator and allowed to run for 5 min at the rate of 20 rev min^{-1}. The percent loss in weight was calculated as the friability.

Disintegration time. The disintegration times of the tablets were measured in distilled water at 37 ± 1°C in a Manesty Disintegration Tester according to the British Pharmacopoeia (1988). The tablets were considered completely disintegrated when all the particles passed through the wire mesh. The mean value and the standard error were calculated for at least 12 tablets from each batch.

Statistics. Differences between formulations was assessed using Student's *t*-test with $P < 0.05$ being considered significant.

Results and discussion

The crushing strength of the tablets (chloroquine phosphate, dipyrone and paracetamol) were plotted as a function of binder (starch mucilage) concentration keeping the amount of disintegrant constant (Fig. 1). Increasing the binder concentration increased the crushing strength of the tablets. This is in agreement with previous work on starches as binders (Esezobo & Pilpel 1976; Stanley-Wood & Shubair 1979). In wet granulation, liquid bridges are developed between particles, and the tensile strength of these bonds increases as the amount of liquid (mucilage) added is increased; during drying, interparticulate bonds result from fusion or recrystallization and curing of the binding agent (Banker & Anderson 1986). It has also been shown (York & Pilpel 1973) that the amount of bonding that takes place between the particles due to asperity melting and plastic and elastic deformation of the particles, and hence the hardness of the tablets, depends on the amount of binding agent present and the compression force applied. Since in the present

Table 1. Formulations of chloroquine phosphate, dipyrone and paracetamol tablets (250 mg).

Starch mucilage	Starch as disintegrant*	Talc**	Magnesium stearate**
A. Enset and potato starch mucilages used as binders (% w/w)			
Chloroquine phosphate 2·5, 5·0, 7·5, 10·0, 12·5, 15·0	10·0	3·0	1·0
Dipyrone 2·5, 5·0, 7·5, 10·0, 12·5, 15·0	5·0	3·0	1·0
Paracetamol 2·5, 5·0, 7·5, 10·0, 12·5, 15·0	10·0	3·0	1·0
B. Enset and potato starch used as disintegrants (% w/w)			
Chloroquine phosphate 5·0	2·5, 5·0, 7·5, 10·0, 12·5, 15·0	3·0	1·0
Dipyrone 5·0	2·5, 5·0, 7·5, 10·0, 12·5, 15·0	3·0	1·0
Paracetamol 10·0	2·5, 5·0, 7·5, 10·0, 12·5, 15·0	3·0	1·0

*% w/w of drug. **% w/w of dry granule.

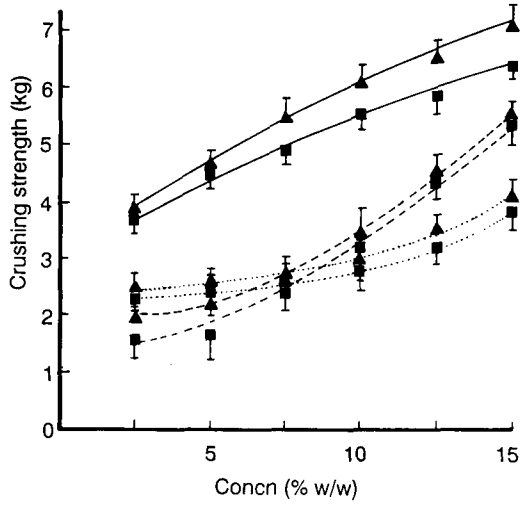

FIG. 1. Effects of concentration of starch mucilages employed as binders on the crushing strength of tablets (——chloroquine phosphate; . . . . .dipyrone; – – –paracetamol; ▲ enset starch; ■ potato starch). Significant differences were as follows: for chloroquine phosphate $P<0.01$, for dipyrone $P<0.01$, for paracetamol $P<0.05$.

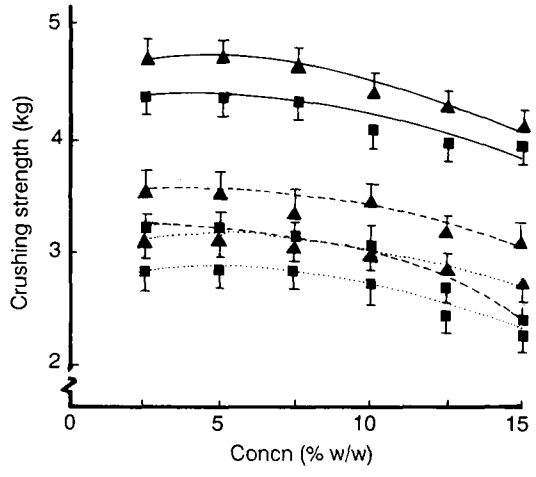

FIG. 2. Effects of concentration of starches employed as disintegrants on the crushing strength of tablets (——chloroquine phosphate; . . . . .dipyrone; – – –paracetamol; ▲ enset starch; ■ potato starch). Significant differences were as follows: for chloroquine phosphate $P<0.01$, for dipyrone $P<0.05$, for paracetamol $P<0.01$.

study constant compression force was applied, it is assumed that the greater the concentration of starch mucilage used, the greater the amount of bonding took place, and, therefore, the harder the tablets. Fig. 1 also shows that for all three drugs, enset starch mucilage gave tablets with greater crushing strength than those made with potato starch mucilage.

The effects of the starches as disintegrant on the crushing strength of the tablets with one binder concentration (i.e. starch mucilages) are shown in Fig. 2. When the concentration of the starch mucilages was kept constant, an increase in disintegrant concentration (2·5–7·5%) showed no significant change in the crushing strength of the tablets. However, when the starch concentration exceeded 7·5%, a reduction in the crushing strength of the tablets was noted. 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 different starches as disintegrants on the crushing strength of the tablets, however, differed significantly.

Friability is a measure of interparticular cohesiveness in tablets. Since interparticulate cohesiveness increases with an increase in binder concentration, the friability of chloroquine phosphate and dipyrone tablets decreased, with an increase in binder concentration (Table 2). Paracetamol, however, showed capping at binder concentrations below 7·5% when tested for friability. Capping in paracetamol tablets has been attributed to a low degree of plastic flow and bonding (Obiorah & Shotton 1976; Doelker & Shotton 1977) and it has been suggested that capping could be eliminated if strong interparticulate bonding is formed between the particles (Krycer et al 1982) by using the appropriate amount of binding agent (Yu et al 1988). Hence, in this study the capping tendency of paracetamol was eliminated at higher binder concentrations (Table 2). For all three drugs, tablets prepared with enset starch mucilage were generally less friable than those made with potato starch mucilage and the results agree well with those of the crushing strength of tablets.

Fig. 3 shows the effects of binder concentration on the disintegration times of tablets. Increasing the starch mucilage concentration increased the disintegration time of the tablets.

Table 2. Effects of enset or potato starch as a binder on the friability of tablets.

Binder concn (%w/w)	Friability (%) Chloroquine phosphate Enset	Potato	Dipyrone Enset	Potato	Paracetamol Enset	Potato
2·5	0·53	0·61	0·81	0·85	Capping	Capping
5·0	0·38	0·46	0·64	0·67	Capping	Capping
7·5	0·36	0·37	0·60	0·66	4·55	6·42
10·0	0·31	0·35	0·57	0·60	0·55	1·15
12·5	0·23	0·24	0·46	0·52	0·40	0·83
15·0	0·20	0·21	0·42	0·47	0·40	0·77

Each result is the mean of three replicates.

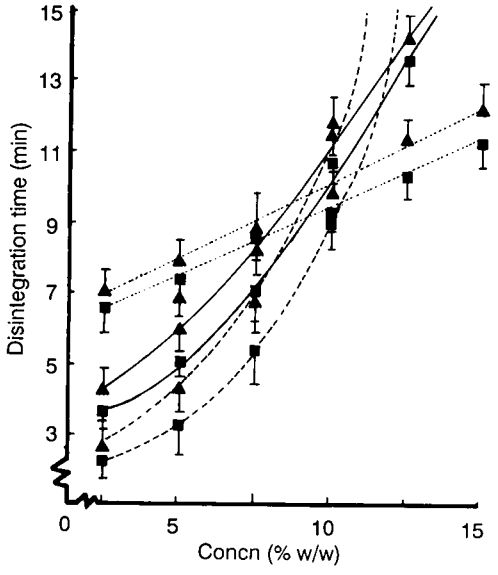

FIG. 3. Effects of concentration of starch mucilages employed as binders on the disintegration times of tablets (——chloroquine phosphate; . . . . .dipyrone; – – – – –paracetamol; ▲ enset starch; ■ potato starch). Significant differences were as follows: chloroquine phosphate $P < 0{\cdot}01$, dipyrone $P < 0{\cdot}01$, paracetamol $P < 0{\cdot}05$.

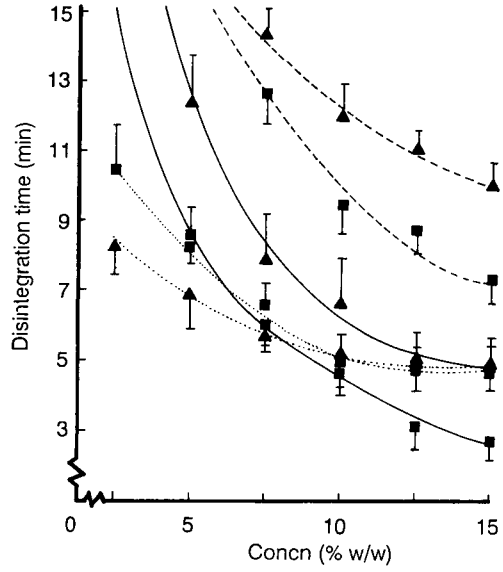

FIG. 4. Effects of concentration of starches employed as disintegrants on the disintegration times of tablets (——chloroquine phosphate; . . . . .dipyrone; – – – – –paracetamol; ▲ enset starch; ■ potato starch). Significant differences were as follows: chloroquine phosphate $P < 0{\cdot}01$, paracetamol $P < 0{\cdot}05$. The difference between dipyrone formulations was not significant ($P > 0{\cdot}05$).

The increase in disintegration time with binder concentration was expected as it has been shown by various workers (Esezobo & Pilpel 1976; Pilpel et al 1978) that a thin film of the starch 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 mucilagenous, viscous barrier between the granules and the water, retarding the disintegration of the granules (Huber et al 1966; Pilpel et al 1978). Accordingly, it is assumed that at given equal concentrations of enset and potato starches, enset starch forms a thicker film round the granules, thus causing a longer disintegration time than potato starch. The differences in disintegration times between tablets prepared with enset starch and those made with potato starch were statistically significant.

For all the tablets prepared with enset or potato starch, disintegration time decreased with increased amount of starch added as disintegrant (Fig. 4). Chloroquine phosphate paracetamol tablets formulated with enset starch, however, gave slower disintegration times than those formulated with potato starch.

It would appear that enset starch is a better binder than potato starch as it gave greater crushing strength and less friable tablets. As a disintegrant, however, it is less effective. Nonetheless, the disintegration times for all the three tablets formulated with enset starch fall within the British Pharmacopoeia (1988) limits for disintegration times of uncoated tablets. Since enset starch compares favourably with potato starch it is suggested that it could be used as an alternative source in the formulation of chloroquine phosphate, dipyrone and paracetamol tablets.

The authors wish to thank the Ethiopian Pharmaceutical Manufacturing Plant for the gift of materials and also for allowing them to use some of the laboratory equipment. We are also grateful to the Quality Control Unit of the National Health Research Institute for giving us access to laboratory facilities. We would like to thank Mr Bisrat Fantaye and Mr Kedir Tahir for carrying out part of the preliminary work.

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Book Review

Plants in Cardiology
by A. Hollman
Published 1992 British Medical Journal, London
vii + 40 pages
ISBN 0 7279 0744 1 £5.95 UK, £7.50 overseas

The welcome renewal of interest in plants as sources of new drugs is sometimes understood only in terms of their providing new molecules which might eventually end up as the active compound in a medicine.

This small book, originally published as a series of articles on plant constituents of cardiological interest in the *British Heart Journal*, contains several examples of other ways in which natural products are useful in the wider sphere of drug discovery. Thus khellin from *Ammi visnaga* is an example of a drug molecule which has acted as a template for new coronary vasodilators such as nifedipine. Other compounds have found use as pharmacological tools such as aconitine from *Aconitum* species which induces atrial fibrillation. Toxicological interest is exemplified by such plants as species of *Senecio* and members of the Boraginaceae which contain pyrrolizidine alkaloids which cause hepatic veno-occlusive disease.

This book provides some interesting historical accounts of the development of drugs from plants but it is deficient in not having any chemical structures which would illustrate the chemical links between natural products and drugs derived from them. The treatment is somewhat imbalanced, e.g. the cardiac glycoside-containing plants, the source of very important drugs, are only given one page, the same as the xanthine alkaloids, which are described as obsolete.

In spite of the title, some mention is made of other pharmacological effects and uses of compounds from the plants described. There are some important omissions in this respect, e.g. the use of theophylline as a bronchodilator. A substantial amount of the experimental work cited is several decades old and comparatively few modern references occur.

This book is useful to those interested in the background to the drugs mentioned but readers will have to look elsewhere for the fuller picture and especially the chemical relationships involved.

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Book Review

Oxford Textbook of Clinical Pharmacology and Drug Therapy
Second edition
Edited by D. G. Grahame-Smith and J. K. Aronson
Published 1992 Oxford University Press, Oxford
XVII + 756 pages
ISBN 0 19 261675 7 £25.00 (paperback)

The first edition of this Oxford-based textbook of clinical pharmacology and therapeutics quickly established itself as a major text among undergraduate pharmacy, medical students and prescribing doctors, and has been reprinted four times since 1984. The subject has moved on, however, and important advances have been made in therapeutics and so this second edition is welcome. It is larger than the first but retains its basic format, and the authors have wisely enlisted the help of specialist colleagues to assist in writing the chapters on various areas of therapeutic practice.

An attractive feature of the book, particularly the earlier chapters on the basic science of clinical pharmacology and pharmacokinetics, is the use of seminal research papers to illustrate fundamental principles, to which the enquiring student may refer for further reading.

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