EVALUATION OF YAM STARCH AS TABLET: BINDER AND DISINTEGRANT PART I—BEFORE STORAGE

By
R.N. NASIPURI
Department of Pharmaceutics
University of Ife, Ile-Ife

Introduction:

Starch is a naturally occuring substance of very wide distribution. It is an important adjuvant in the formulation and production of tablets. Among other things, the desirable physico-chemical nature of the starch, its relative inertness, abundance and cheapness favour the choice of this substances from a list of excipients available to a tablet formulator. It is used for such functions as filling, binding, disintegration, lubrication and dye migration inhibition in tableting.

Because of abundance, importance and simplified nature of starch, interest has of late been stimulated to research into the usefulness of those starches of local origin, such as cassava, yam and cocoyam starches. A survey of published reports show that whereas considerable work has been done on the four starches of the British Pharmacopoeia, namely potato, maize, wheat and rice, very little work is reported on yam and cassava starches.

Mital and Ocran (1) reported the suitability of cassava and yam starches as tablet disintegrants for the first time in 1968. Thereafter in 1975, the use of cassava starch as a binder and disintegrant in the formulation of tablets was reported by Nasipuri (2). Very recently, Jaiyeoba and Opakunle investigated the usefulness of both yam and cassava starches as diluents (3) and glidants (4).

Yams (several species of the genus Dioscorea) are important food crops in many tropical countries and in some sub-tropical regions. The greatest yam growing area of the world, the eastern part of West Africa produces about two-thirds of all the yams grown in the world while Nigeria alone produces almost half the global figure (5). Three species of yam are usually cultivated: the water yam (*D. alata*), the yellow yam (*D. cayenesis*) and the white yam (*D. rotandata*). The white yam is the most popular and most widely grown species.

Although the disintegrating property of yam starch has been reported in the formulation of tablets containing lactose, sodium hydrogen carbonate and calcium carbonate (1), no work has been reported in the literature about the suitability of this starch as a binder in the formulation of tablets.

The purpose of this investigation was to study the usefulness of yam starch both as a binder as well as disintegrant in the formulation of tablets containing organic medicinal substances and to compare the physical properties of the produced tablets with those prepared using acacia as a binder and potato starch as binder and disintegrant.

MATERIALS AND METHOD

Materials:

Sulphadimidine (ICI) and promethazine hydrochloride (M&B) were of British Pharmacopoeial grade and were used in this study as received. Potato starch and acacia were obtained from B.D.H. Chemicals Limited and M.&B. Limited, England respectively. Talc (BDH) and magnesium stearate (BDH) were of B.P. grade. Yam starch was prepared in the laboratory by the method described below.

The starches were used as binders in the form of 10% w/w pastes and as disintegrants in the form of dried powders. Acacia, on the other hand, was used in the form of a 20% w/v mucilage as a binder.

Preparation of Yam Starch:

Tubers of *Diascorea rotundata* were washed, peeled, rewashed, cut into small pieces and reduced to a fine paste using a Stephan Cutting Machine (Stephan Universal Machine, A. Stephan u. Sohne, Hameln, W. Germany). After adding water rasping was continued at high speed until very fine slurry was obtained. The slurry was passed through a 200 um mesh sieve with the addition of water to discard the coarse residue. The starch milk was allowed to settle and then washed several times with 0.01N sodium hydroxide to neutralise the slight acidity. Excess alkali was removed by washing repeatedly with distilled water. The clean starch milk was then centrifuged in a Basket Centrifuge (M.S.E., England) and then spin-dried in the same equipment. The spin-dried starch was finally dried in a Fluidized Bed Dryer (Glatt, West Germany) at a temperature range of 45-48° for 20 minutes. The dried starch was reduced to a fine powder with a Disc Grinder (Pascall Engineering Co. Ltd., England).

Preparation of Starch Mucilage (10% w/w):

Required quantity of starch powder was suspended in two parts of cold water and four times as much boiling water was added with continuous stirring to make the paste. While still hot, sufficient quantity of hot water was added to make up the required weight. The mucilage so prepared was used while still hot and pourable.

Preparation of Granules :

Wet granulation method was used to prepare granules of both sulphadimidine and promethazine hydrochloride. Tablets were formulated to contain either 500mg of

sulphadimidine or 25mg of promethazine hydrochloride. Three different binders (10% w/w yam starch paste or 20% w/v acacia mucilage or 10% w/w potato starch) were used for each substance.

Sulphadimidine Granules: Sulphadimidine powder was mixed with part of the disintegrant (either yam or potato starch, 12.5mg per tablet) as intra-granular disintegrant and then kneaded in a Erweka Kneader (Z-blade mixer) for 20 minutes with pre-determined quantity of one of the binders (granulating fluids) as mentioned above. The wet mass was then forced through No. 10 mesh sieve using a Jackson. Crockatt granulator. The granules were dried at 50°C for 3 hours in a tray dryer and then passed through a No. 12 mesh sieve super-imposed on a No. 60 sieve. The granules retained by No. 60 mesh sieve were used.

Promethazine Hydrochloride Granules: The drug was mixed with lactose (75mg per tablet) and part of the starch (1.25 mg per tablet). Granules were prepared by wet granulation method using a No. 12 mesh sieve and passing the dried granules through 16/60 mesh sieve in the same was as described under sulphadimidine granules using one of the three binders mentioned above.

Moisture Content in the Granules :

Moisture content in the granules was determined using Ohaus Moisture Determining Balance. Table I gives the values of moisture content in the granules.

Incorporation of Extra-Granular Disintegrant and Lubricant:

Disintegrant used in this study were either yam starch or potato starch. As mentioned earlier, part of the starch was added to the powdered drug as extra-granular disintegrant before granulation. The remaining part was mixed with the dried granules prior to compression. For this purpose amounts added were—2.5% w/w for sulphadimidine granules and 1.25% w/w for promethazine hydrochloride granules.

For the granules prepared with acacia mucilage as granulating agent, yam starch or potato starch was used as disintegrant in separate formulations. But only yam starch was added to granules prepared with yam starch paste as the binder while only potato starch was mixed with granules prepared with potato starch paste as binder, thus having the same starch combination in the last two cases.

Lubricant used was a mixture of talc and magnesium stearate (1:1). 1% w/w of this combination was added to each formulation.

Compression :

The granules were compressed to tablets in a triple-punch rotary tablet machine (Korsch—Pharmapress 100). The machine was set to produce flat, bevelled-edged 11mm diameter sulphadimidine tablets or 6mm diameter promethazine tablet at a pre-determined compression pressure and speed.

Tests on Tablets :

Tablet crushing strength was measured using a pfizer hardness tester.

Friability Value: This was determined by "Roche" friabilator (Erweka). Twenty tablets were placed in the drum which was then set in motion to rotate for four minutes at a rate of 25 r.p.m.

Disintegration Time: Disintegration time of tablets were assessed using the standard Brit. Ph. apparatus (manesty tablet disintegration tester). Distilled water was used as the medium at a temperature between 36-38°C. Five tablets were used at a time for each test.

Dissolution Rate: A rotating busket type dissolution rate tester (Erweka, Type DT) was used for this purpose. For sulphadimidine tablets, dissolution medium used was 500ml of 1N hydrochloric acid whereas 300ml. distilled water was used for promethazine tablets. One tablet was placed in the busket and a rotation speed of 120 r.p.m. was used. All dissolution rate studies were carried out at $37° \pm 0.5°C$. Samples of the medium were withdrawn at appropriate intervals and filtered through a sintered glass filter (No. 3). An equal amount of the fresh medium was added to replace the aliquot withdrawn. Determinations of sulphadimidine and promethazine hydrochloride in the filtrate were made spectrophotometrically at 230nm and 249nm respectively. Adjustments were made in the calculations for the removal of the dissolution medium containing dissolved drug and subsequent replacement of fresh medium. Three replicates were made and averaged.

Results and Discussion

Values of moisture contents in the granules prepared with the three different granulating agents (Table 1) show that 3 hours drying in a tray dryer at 50°C may be just sufficient for the granules to retain adequate residual amount of moisture for compression into suitable tablets. The residual moisture in the granules for both sulphadimidine and promethazine hydrochloride were virtually the same.

Hardness and friability values of both sulphadimidine and promethazine tablets prepared with different binder/disintegrant combinations are given in Table 2. Results show that there was not much variation in the hardness of tablets immediately after compression; the range was almost same. This, in part, may be due to almost equal amount of residual moisture present in the granules (Table 1). Results also indicate that just after preparation the tablets did not show much variation in the average percentage loss when subjected to friability test using Roche Friabilator.

Results of the disintegration time of the formulated tablets (Table 2) show that with water as the medium, disintegration time of sulphadimidine tablets are somewhat higher than promethazine hydrochloride tablets although the hardness values of all tablets were almost within the same range. This may be due to much higher solubility of promethazine hydrochloride in water than sulphadimidine. Moreover, tablets prepared with starch paste as binding agent gave comparatively lower disintegration time than those prepared with acacia mucilage as the binding agent. Although **in-vitro** disintegration time does not necessarily bear a relationship to the **in-vivo** tests and does not also reflect on the rate of solution of drugs and their subsequent absorption by the body system, but disintegra-

TABLE 1

VALUES OF MOISTURE CONTENT IN THE GRANULES PREPARED WITH VARIOUS GRANULATING AGENTS

Granules of	Moisture Content in Granules prepared		
	with 20% w/v Acacia Mucilage	10% w/w yam starch Paste	10% w/w Potato starch Paste
Sulphadimidine	1.25	1.10	1.10
Promethazine HCL	1.25	1.20	1.15

TABLE 2

HARDNESS, FRIABILITY VALUES AND DISINTEGRATION TIME OF TABLETS

Tablets of	Binder	Disintegrant	Hardness kg/cm^2	Friability values (percent)	Disintegration Time in Seconds
Sulpha-dimidine	a	a	3.5-6.8	0.92	330
	c	a	3.6-6.4	0.85	690
	c	b	3.3-6.7	0.83	465
	b	b	3.4-6.6	0.95	290
Promethazine Hydrochloride	a	a'	3.5-7.0	0.75	115
	c	a'	3.2-6.7	1.00	255
	c	b'	3.2-6.7	0.84	240
	b	b'	3.3-6.4	0.92	160

Binder

a = Yam Starch Paste (10% w/w)
b = Potato Starch Paste (10% w/w)
c = Acacia Mucilage (20% w/v)

Disintegrant

a = Dried Yam Starch 5%
b = Dried Potato Starch 5%
a' = Dried Yam Starch 2.5%
b' = Dried Potato Starch 2.5%

TABLE 3

DISSOLUTION TIMES ($T_{50\%}$ and $T_{90\%}$) OF SULPHADIMIDINE AND PROMETHAZINE HYDROCHLORIDE FROM THE FORMULATED TABLETS

Tablets of	Binder	Disintegrant	Dissolution Times (Min.)	
			$T_{50\%}$	$T_{90\%}$
Sulphadimidine	a	a	6	14
	c	a	8	21
	c	b	8	17
	b	b	5.5	12
Promethazine Hydrochloride	a	a'	8	11
	c	a'	4.5	14
	c	b'	5	17.5
	b	b'	3	10

a, b, c, under binder and

a, b, a', b', under disintegrant have the same meaning as given under Table 2

tion of tablets into small particles within a low period of time would definitely increase the rate of solution of drugs present in the tablets. As could be seen in Table 2, the disintegration time varied between 115 to 255 seconds for promethazine tablets and 290 to 690 seconds for sulphadimidine tablets. This comparatively-low disintegration time offer advantage to any formulated tablet. In the present investigation, the incorporation of starch as a combination of intra-granular and extra-granular disintegrant may be responsible for this.

The effects of different binder/disintegrant combination on the dissolution rate of sulphadimidine and promethazine tablets are shown in Figures 1 and 2 respectively. The results reported are the average of three determinations and the maximum inter-tablet variation within a batch was $\pm 6.5\%$ for sulphadimidine tablets and $\pm 8\%$ for promethazine hydrochloride tablets. Values of $t_{50\%}$ and $t_{90\%}$ for the tablets are given in Table 3. Results show that the rate of dissolution of the active drugs from tablets prepared with either yam starch or potato starch as binder/disintegrant was almost same. Tablets prepared with gum acacia as the binder and either yam or potato starch as the disintegrant, on the other hand, gave lower rate of dissolution; $t_{90\%}$ were found to be somewhat higher in these cases.

Considering all the results it may be concluded that yam starch can be used as a binder as well as a disintegrant for the formulation of tablets containing both soluble and insoluble organic drugs. It is equally good as potato starch in respect of its binding and disintegrating properties and may be considered slightly better than gum acacia as binder for its ability to give a higher dissolution rate.

Summary

The suitability of yam starch as a tablet binder as well as a disintegrant has been investigated. A comparative study on the binding properties of gum acacia, yam starch and potato starch and also on the binding and disintegrating properties of the two starches have been made. Yam starch was found to be an efficient binder/disintegrant in the formulation of tablets containing both soluble and insoluble organic medicinal substances.

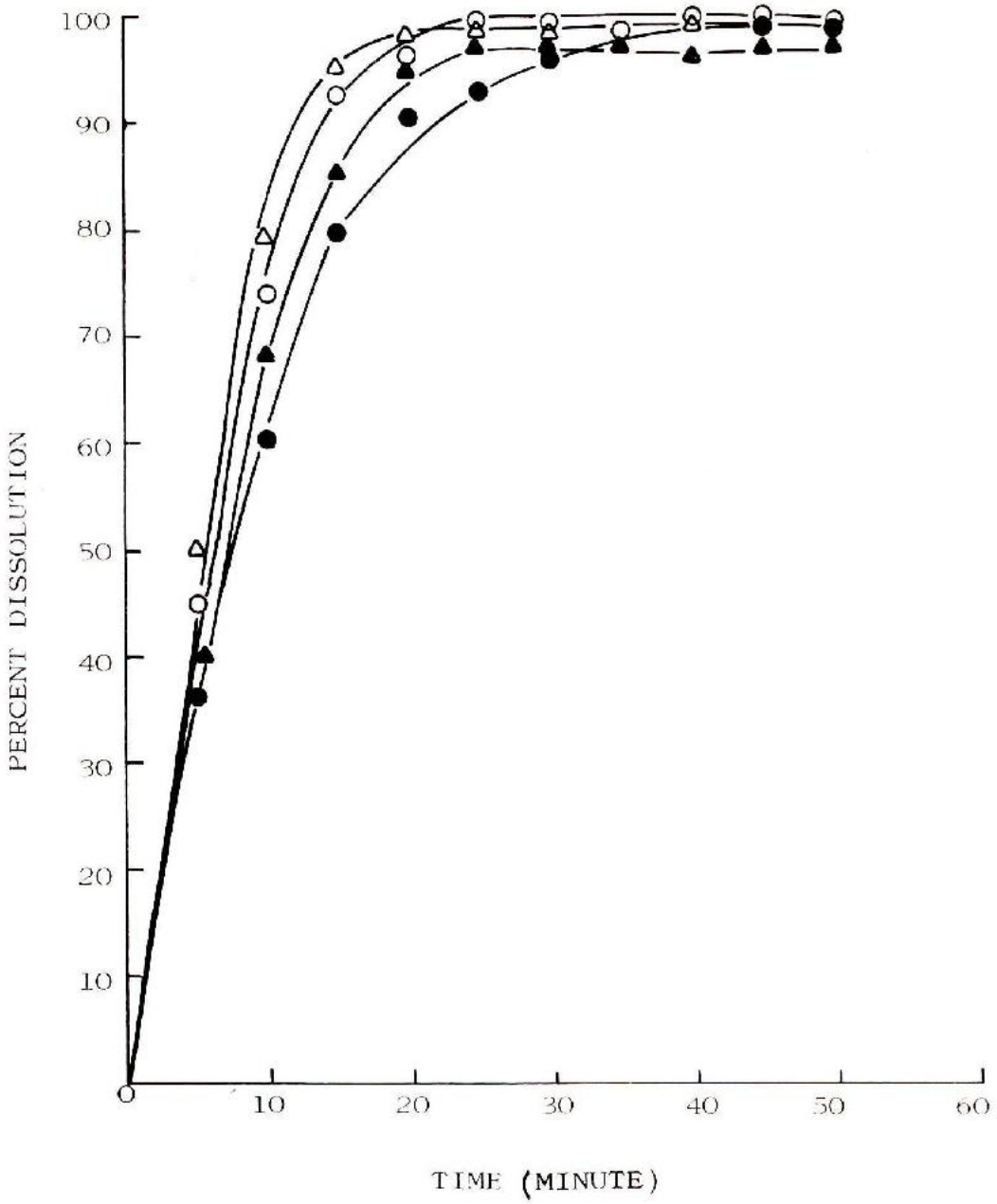

FIGURE 1

DISSOLUTION RATES OF SULPHADIMIDINE FROM FORMULATED TABLETS

Key :	*Binder*	*Disintegrant*
O——O	Yam Starch Paste (10% w/w)	Yam Starch 5% w/w
●——●	Acacia Mucilage (20% w/v)	Yam Starch 5% w/w
△——△	Potato Starch Paste (10% w/w)	Potato Starch 5% w/w
▲——▲	Acacia Mucilage (20% w/v)	Potato Starch 5% w/w

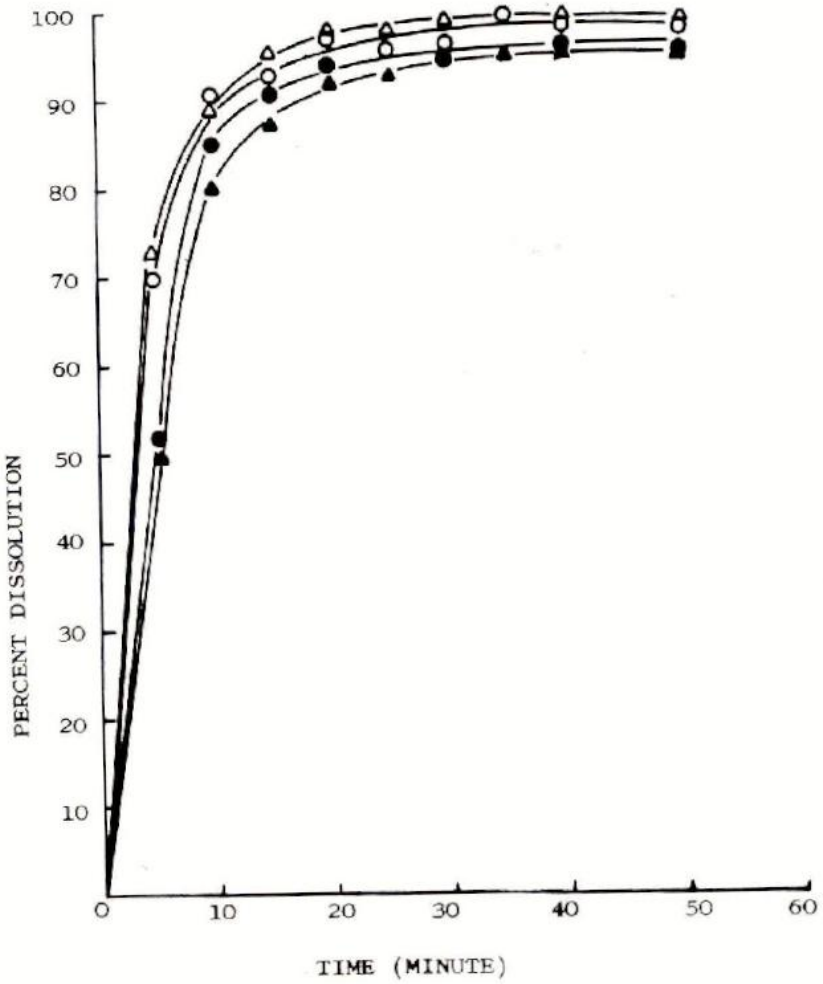

FIGURE 2

DISSOLUTION RATES OF PROMETHAZINE HYDROCHLORIDE FROM FORMULATED TABLETS

Key:	*Binder*	*Disintegrant*
O——O	Yam Starch Paste (10% w/w)	Yam Starch 2.5% w/w
●——●	Acacia Mucilage (20% w/v)	Yam Starch 2.5% w/w
△——△	Potato Starch Paste (10% w/w)	Potato Starch 2.5% w/w
▲——▲	Acacia Mucilage (20% w/w)	Potato Starch 2.5% w/w

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