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Comparative evaluation of starches obtained from *Dioscorea* species as intragranular tablet disintegrant

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Starches from four Dioscorea *species namely* Dioscorea dumetorum *(bitter yam),* D. oppositifolia *(Chinese yam),* D. alata *(water yam) and* D. rotundata *(white yam) have been evaluated as disintegrants in chloroquine phosphate tablet formulations in comparison with official corn starch. The mechanical and drug release properties of the tablets were assessed. The results showed that the ranking of the effectiveness of the starches as intragranular disintegrant was water > white > corn > Chinese> bitter. The disintegrant concentration had significant ($p < 0.001$) effects on the disintegrant efficiency. The four experimental starches compared favorably and in some cases showed better efficiency as intragranular disintegrant than corn starch and could be further developed for use in commercial tablet formulation.*

Key words: Dioscorea – Yam – Corn starch – Crushing strength – Friability – Disintegration time – Dissolution time.

Disintegrants are important components of tablet formulations required to facilitate break up of tablet compact to release the active drug in the tablet, making it available for rapid dissolution and absorption. Disintegrants may act by swelling e.g. starches; capillary action e.g. starch and cellulose; evolution of gas by a chemical reaction when the tablet comes in contact with water e.g. reaction of sodium carbonate with citric acid and tartaric acid or by a combination of these mechanisms [1].

Yams tubers (family *Dioscoreaceae*) commonly cultivated in many parts of Africa and South East Asia, are another potential starch source that could be used in food and pharmaceutical industries that has not been explored. The tubers have high starch content (70-80% dry basis) and are readily available. Recent studies have shown the potential of starches from four different Dioscorea (yam) species as direct compression excipients and binding agents in tablet [2]. The starches from the four species varied considerably in their physicochemical and material properties [2]. However, no known work has been done to evaluate these four *Dioscorea* starches as intragranular disintegrants in pharmaceutical tablets. Thus, the suitability and relative efficiencies of starches obtained from the four *Dioscorea* species namely *Dioscorea dumetorum* (bitter yam), *D. oppositifolia* (Chinese yam), *D. alata* (water yam) and *D. rotundata* (white yam), as intragranular disintegrants has been investigated in comparison with official cornstarch. Chloroquine phosphate used as the model drug is an important antimalarial drug which is only slightly soluble in water and disintegration would play a significant role in the dissolution process of its tablets.

I. MATERIALS AND METHODS

The materials used were chloroquine phosphate BP, corn starch BP and polyvinylpyrrolidone (PVP), molecular weight 44,000 (BDH Chemicals Ltd., Poole, UK). Tubers of four different *Dioscorea* species namely *Dioscorea rotundata* L., *D. dumetorum* Kunth, *D. oppositifolia* L. and *D. alata* L. DIAL2 subsequently referred to as white, bitter, Chinese and water, respectively, were obtained from local farmers in Ibadan, Nigeria and authenticated. The starches were extracted from the relevant tubers using established procedures [3]. The swelling and water retention capacities of the starches were determined using established procedures [4, 5].

Batches (200 g) of chloroquine phosphate granules were prepared by wet granulation using 2%w/w of polyvinylpyrrolidone as binder to produce samples containing 5-20%w/w starch disintegrants. The wet masses were granulated manually using a mesh 12 sieve (1,400 μm), the granules dried in an oven at 50°C for 18 h and dry screened through a mesh 16 sieve (1,000 μm). The moisture content of the granules was between 2-4% w/w. Particle densities were determined by the liquid pycnometer method with xylene as the displacement fluid [6]. Tablets (500 mg) were prepared from the 500-1,000 μm granules in a 10.5-mm die and flat-faced punches lubricated with a 1% w/v dispersion of magnesium stearate in acetone for 30 seconds on a Carver hydraulic press (Model C, Carver Inc., Menomonee Falls, Wisconsin, USA). The packing fraction (P_f) of the tablets was calculated [7].

The crushing strength of the tablets was determined at room temperature by diametral compression [8], using a hardness tester (Ketan Scientific & Chemicals, Ahmedebad, India). The percent friability of the tablets was determined using a Veego friability test apparatus (Veego Scientific devices, Mumbai, Maharashtra, India) operated at 25 rpm for 4 min. The disintegration time, DT, of the tablet was determined in distilled water at 37 ± 0.5°C using a Veego disintegration tester (Veego Scientific devices, Mumbai, Maharashtra, India). The dissolution test was carried out on the tablets using the USP 20 III basket method (Hanson Model 72RL, USA) rotated at 100 rpm in 900 mL of 0.1M HCl, maintained at 37 ± 0.5°C. The amount of chloroquine released was determined using a UV spectrophotometer (PU8610 Kinetics, Sarose Scientific Instruments, Cambridge, UK) at the wavelength of 255 nm.

Statistical analysis to compare individual differences between the starches was carried out using the software of GraphPad Prism4 (GraphPad Software Inc., San Diego, USA).

II. RESULTS AND DISCUSSION

The swelling capacity was 0.80, 0.82, 1.29, 1.22 and 1.20 while the water binding capacity was 1.20, 1.15, 0.69, 0.59 and 0.95 for bitter, Chinese, water, white and corn starches, respectively. The ranking of the swelling capacity of the starches was water > white > corn > Chinese > bitter while the ranking was generally reversed for the water binding capacity. The difference may be attributed to factors such as the amylose/amylopectin content, molecular weight, conformation, degree of polymerization and degree of branching of amylopectin [9].

The mechanical properties of pharmaceutical tablets are quantifiable by the crushing strength (CS) and the friability (F) of the

Table I - Mechanical and release properties of chloroquine phosphate tablets at packing fraction = 0.90 (mean ± SD, n = 4).

Starch	Conc. (% w/w)	Crushing strength (N)	Friability (%)	CSFR	DT (min)	CSFR/ DT	t_{50} (min)	t_{80} (min)	t_1 (min)	k_1	k_2
	0.00	74.67±2.31	2.13±0.15	35.06	12.80±0.00	2.74	35.50± 0.71	58.50 ±0.71	49±1.41	0.01± 0.00	0.02±0.00
Bitter	5.00	119.33±0.58	1.13±0.03	105.60	11.10±0.05	9.51	35.00±1.41	59.50±0.71	42.50 ±2.12	0.02±0.00	0.04± 0.01
	10.00	119.83±0.28	1.03±0.11	116.34	10.22±0.02	11.38	31.00±1.41	54.00±1.41	41.00± 1.41	0.02±0.00	0.06± 0.02
	15.00	122.50±4.90	0.99±0.01	123.73	9.52±0.04	13.00	30.00±0.00	47.00±1.41	39.00± 1.41	0.02±0.00	0.06± 0.01
	20.00	123.70±4.20	0.91±0.03	135.93	8.83±0.03	15.39	26.50±0.71	45.00±1.41	37.50± 0.71	0.03±0.00	0.08± 0.03
Chinese	5.00	126.93±1.85	0.99±0.06	128.21	12.03±0.21	10.66	45.00±1.41	75.00±1.41	54.00 ±2.83	0.02±0.00	0.03±0.00
	10.00	130.77±1.72	0.88±0.01	148.60	10.51±0.02	14.14	32.00±0.00	50.50±2.12	43.50±4.95	0.02±0.00	0.04±0.00
	15.00	132.27±1.01	0.87±0.02	152.03	10.29±0.01	14.77	27.00±1.41	45.00±1.41	42.50 ±4.95	0.03±0.00	0.10±0.03
	20.00	131.02±0.80	0.82±0.02	159.78	8.59 ±0.09	18.60	26.00±0.00	43.25±0.35	39.00 ±1.41	0.03±0.01	0.13±0.06
Water	5.00	72.00±4.00	2.24±0.04	32.14	8.79±0.07	3.66	19.00±1.41	37.50±0.71	27.00± 2.83	0.04±0.00	0.06±0.00
	10.00	80.00±2.00	2.12±0.08	37.74	8.22±0.06	4.59	16.00±0.00	32.50±0.71	21.50±0.71	0.04±0.00	0.08±0.01
	15.00	87.60±5.41	2.01±0.08	43.58	7.75±0.07	5.62	14.50±0.71	30.00±1.41	20.00 ±0.00	0.05±0.00	0.09±0.00
	20.00	94.00±1.00	1.93±0.40	48.70	7.42±0.23	6.56	12.50±0.71	27.25±1.06	19.50 ±0.71	0.06±0.00	0.20±0.00
White	5.00	92.33 ±0.58	2.00±0.02	46.17	9.78±0.22	4.72	20.50±0.71	39.50±0.71	38.00±0.00	0.03±0.01	0.20±0.00
	10.00	96.67 ±1.15	1.99±0.01	48.58	9.20 ±0.00	5.28	16.75±0.35	33.50±0.71	29.75±0.35	0.05±0.00	0.10±0.01
	15.00	99.00 ±2.65	1.98±0.03	50.00	8.37 ±0.06	5.97	15.00±0.00	31.00±1.41	28.00±0.00	0.05±0.00	0.14±0.01
	20.00	100.05±2.78	1.66±0.05	60.27	8.02 ±0.02	7.52	13.00±0.00	28.00±1.41	26.00±1.41	0.06±0.01	0.21±0.06
Corn	5.00	100.00±0.00	1.51±0.01	66.23	10.20±0.04	6.49	25.50±0.71	42.50± 0.71	38.00±1.41	0.04±0.00	0.15±0.07
	10.00	105.33±0.58	1.41±0.01	74.70	9.65 ±0.03	7.74	21.00±0.00	38.50± 0.71	35.00±2.83	0.04±0.00	0.16±0.06
	15.00	107.00±2.00	1.40±0.04	76.43	9.42 ±0.04	8.11	19.50±0.71	35.50± 0.71	31.00±1.41	0.04±0.00	0.19±0.09
	20.00	116.33±1.53	1.39±0.02	83.69	9.05 ±0.06	9.25	17.00±0.00	32.50± 0.71	28.50±0.71	0.05±0.00	0.19±0.02

tablets [10-12]. Representative plots of CS for chloroquine tablets containing 10%w/w starch disintegrant are presented in *Figure 1*. It is well known that the CS of tablets tends to increase and their friability tends to decrease with an increase in packing fraction. The values of CS and F for the tablets at packing fraction of 0.90 obtained from the graph are presented in *Table I*. The ranking for the crushing strength of the tablets was Chinese > bitter > corn > white > water while the ranking was reverse for friability. Tablets containing water and white did not conform to official requirements by showing friability values of 1%w/w or less at all the concentrations used whereas bitter and Chinese starch at concentrations of 5%w/w and above conformed to the requirements.

The mechanical strength of tablets has also been measured using the crushing strength-friability ratio (CSFR) [6, 11]. Generally, the higher the CSFR values, the stronger the tablet. The CSFR values generally increased with the concentration of starch disintegrant (*Table I*). This could be due to the fact that there were more particle-particle contact points, particularly with the particles of the starches which help create more solid bonds, resulting in tablets with higher CSFR values at high starch concentrations [12]. The ranking of the CSFR was Chinese > bitter > corn > white > water. There were significant ($p < 0.05$) differences in the CSFR values of the tablets containing the various starches.

Representative plots of disintegration time (DT) versus packing fraction are shown in *Figure 2* while the values of DT for the tablets at packing fraction of 0.90 are also presented in *Table I*. The disintegration time of chloroquine tablets generally increased with packing fraction of the tablets but decreased with increase in the concentration of starch disintegrant. The effects of packing fraction on DT could probably result from the decrease in tablet porosity or reduction in capillary microstructure of the tablets brought about by the closure of the inter- and intra- granular pore spaces through particle rearrangement, fragmentation and particle deformation [6, 11]. At high packing fraction, the low tablet porosity would imply reduced solvent penetration resulting in reduced swelling and therefore increased disintegration time. The effect of the concentration of disintegrant

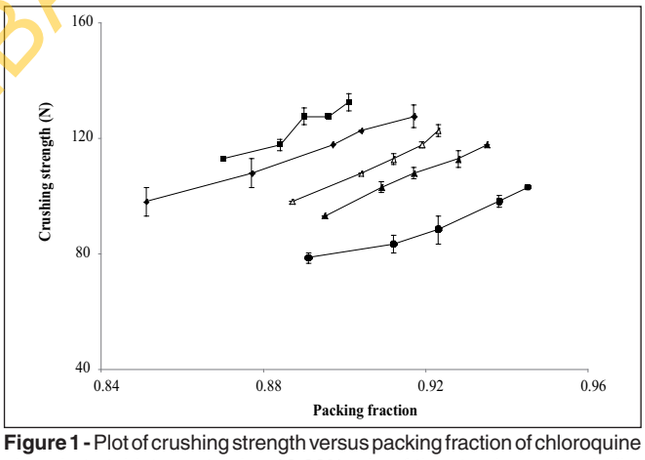

Figure 1 - Plot of crushing strength versus packing fraction of chloroquine phosphate tablets containing 10.00% w/w of the starches as endodisintegrant. ◆, bitter; ■, Chinese; ●, water; ▲, white; Δ, corn.

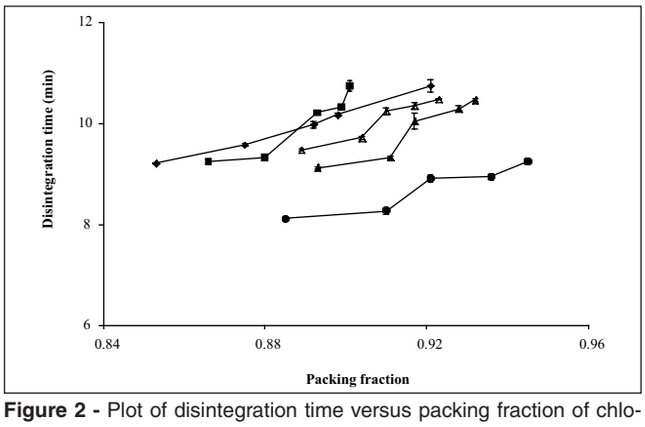

Figure 2 - Plot of disintegration time versus packing fraction of chloroquine phosphate tablets containing 10.00%w/w of the starches as endodisintegrant. ◆, bitter; ■, Chinese; ●, water; ▲, white; Δ, corn.

on DT could be due to the fact that the higher the amount of starch disintegrant exposed to the disintegrating fluid, the higher the amount of water absorbed and subsequent generation of higher swelling force to facilitate disintegration [1]. The ranking of DT for the formulations was Chinese > bitter > corn > white > water. All tablets containing the four Dioscorea starches conformed to the BP requirements on disintegration for uncoated tablets i.e. disintegration within 15 min [10-12].

Disintegration has been viewed as the net balance of the interaction between the adhesive and disintegrating forces [1]. The CSFR/DT ratio has been suggested as a better index of measuring tablet quality because in addition to measuring tablet strength (crushing) and weakness (friability), it simultaneously evaluates all negative effects of these parameters on disintegration time [13]. In general, high values of the CSFR/DT ratio indicate a better balance between binding and disintegration properties. A low value of CSFR/DT implies higher disintegrant effect with disintegration time having unduly high effect on the system. The ranking of CSFR/DT (*Table I*) was water < white < corn < bitter < Chinese. On activation, disintegrants act by improving the hydrophilicity of the tablet matrix and facilitate solvent penetration by capillary action [1]. The disintegrant concentration had a significant ($p < 0.001$) effect on the disintegrant properties. Furthermore, tablets formulations containing Chinese and Bitter had significantly ($p < 0.05$) higher CSFR/DT ratio than tablets containing the other starches.

The dissolution times, t_{50} and t_{80} (i.e. time required for 50% and 80% of chloroquine phosphate to be released, respectively) at packing fraction 0.90 are presented in *Table I*. Values of Ln [Cs/ (Cs-C)] versus t were plotted [14] from the integrated form of the Noyes and Whitney equation [15]. In all cases, two straight regression lines of slopes k_1 and k_2 were obtained and the time at which the lines intersect is denoted by t_1. The dissolution parameters at the packing fraction of 0.90 are presented in *Table I*. It can be observed that the values of t_{50}, t_{80} and t_1 decreased with an increase in disintegrant concentration while k_1 and k_2 generally increased. The ranking of t_{50}, t_{80} and t_1 for the tablets containing the different starches was Chinese > bitter > corn > white > water. Tablets formulations containing Chinese and bitter had significantly ($p < 0.05$) higher dissolution times than tablets containing the other starches. In addition, the values of k_1 were lower than the values of k_2, implying a faster dissolution rate of the drug after t_1. The change from k_1 to k_2 at time t_1 is attributable to a change in the surface area due to the break up of the tablets into fragments [6, 7]. It is notable that tablets containing water and white which exhibited low mechanical strength, gave the fastest rate of release of chloroquine phosphate while Chinese and bitter with higher mechanical strength gave slower release rates. Thus, the type, concentration and efficiency of disintegrant affected the dissolution properties of the tablets.

The most widely reported mechanisms of disintegrant action of starches are believed to depend on swelling and wicking [1, 13]. The swelling power and water binding capacity of starch powders have been shown to have significant effects on their disintegrant properties [10]. Thus, the faster disintegration and dissolution times observed for tablets containing water, white and corn could be as a result of their higher swelling power which facilitates disintegration and hence could be more useful as disintegrant. However, when the mechanical properties of the tablets were considered, Chinese and bitter would appear to be more useful disintegrants since they also produced tablets with better ability to withstand the rigors of shipping and handling during use. Moreover, there appeared to be a better balance between binding and disintegration properties of the tablets containing the two starches. Furthermore, the disintegration time of the tablets was within the limit specified by the BP on the requirement on disintegration

The results show that the four experimental starches compared favorably and in some cases showed better efficiency as intragranular disintegrant than corn starch in chloroquine tablet formulations. Thus the experimental starches could be further developed for use in commercial tablet formulation.

REFERENCES

1. Wan L.S.C., Prasad K.P.P. - Uptake of water into tablets with low substituted carboxymethylcellulose sodium as disintegrants. - Int. J. Pharm., **55**, 155-171, 1989.
2. Odeku O.A., Picker-Freyer K.M. - Analysis of the material and tablet formation properties of four *Dioscorea* starches. - Starch/Stärke, **59**, 430-444, 2007.
3. Radley J.A. (Ed.) - Starch Production Technology. - Applied Science Publishers Ltd., London, 1976, pp. 189-229.
4. Bowen F.E., Vadino W.A. - A simple method for differentiating sources. - Drug Dev. Ind. Pharm., **10**, 505-511, 1984.
5. Ring S.G. - Some studies on gelatin. - Starch/Stärke, **37**, 80-87, 1985.
6. Odeku O.A., Itiola O.A. - Evaluation of the effects of Khaya gum on the mechanical and release properties of paracetamol tablets. - Drug Dev. Ind. Pharm., **29** (3), 311-320, 2003.
7. Akin-Ajani O.D., Itiola O.A., Odeku O. A. - Effects of plantain and corn starches on the mechanical and disintegration properties of paracetamol tablets. - AAPS PharmSciTech., **6** (3), 458-463, 2005.
8. Fell J.T., Newton J.M. - Determination of tablet strength by the diametral compression test. - J. Pharm. Sci., **59**, 688-691, 1970.
9. Mélo E.A., Stamford T.L.M., Silva M.P.C., Krieger N., Stamford N.P. - Functional properties of yam bean (*Pachyrhizus erosus*) starch. - Biores. Tech., **89**, 103-106, 2003.
10. British Pharmacopoeia, HMSO, London, P. A262, 1998.
11. Odeku O.A. - Assessment of *Albizia zygia* gum as binding agent in tablet formulations. - Acta Pharm., **55**, 263-276, 2005.
12. Odeku O.A., Alabi C.O. - Evaluation of native and modified forms of *Pennisetum glaucum* (millet) starch as disintegrants in chloroquine tablet formulations. - J. Drug Del. Sci. Tech., **17** (2), 155-157, 2007.
13. Luangtanan-Anan M., Fell J.T. - Bonding mechanisms in tableting. - Int. J. Pharm., **60**, 197-202, 1990.
14. Kitazawa S., Johno I., Ito Y., Temura S., Okada J. - Effects of hardness on disintegration times and dissolution rate of uncoated caffeine tablets. - J. Pharm. Pharmacol., **27**, 765-770, 1975.
15. Noyes A.A., Whitney W.R. - The rate of solution of solid substances in their own solutions. - J. Am. Chem. Soc. ,**19**, 930-934, 1897.

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