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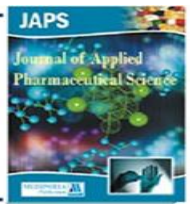

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Disintegrant activities of natural and pregelatinized trifoliate yams, rice and corn starches in paracetamol tablets

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ABSTRACT

Natural and pregelatinized starches from white and yellow trifoliate yams and rice were comparatively studied with official corn starch, in a paracetamol tablet formulation to assess their relative effectiveness as disintegrants. Disintegration time (D_t) and the (crushing strength/friability)/disintegration time ratio ($C_s/F_r)/D_t$ were employed as assessment parameters. Generally, the rankings of $(C_s/F_r)/D_t$ for the natural and pregelatinized starch disintegrants were white T. yam > corn > yellow T. yam > rice; and white T. yam > yellow T. yam > corn > rice, respectively. Pregelatinized starches produced better combined disintegrant properties of $(C_s/F_r)/D_t$ than natural starches. Tablets formulated with official corn starch disintegrant exhibited the lowest disintegration time values, but generally all the tablets containing the experimental starches also passed the official disintegration time test, and can therefore be used as alternative disintegrants in tablets.

Keywords: Disintegrants; natural starch; pregelatinized starch; trifoliate yams; rice.

INTRODUCTION

The position of disintegrants in tablet formulation – as endo-disintegrants, exo-disintegrants or endo-exo-disintegrants (Adebayo and Itiola, 1998) – determines their effectiveness (Alderborn, 2002). The capillary microstructure (porosity) of tablets, to a great extent, determines the degree of liquid penetration into, and disintegration of the tablets (Nogami, *et al.*, 1966). Capillary action due to the pore structure of the tablet as well as swelling are generally accepted as the main modes of action of such disintegrants as starch and cellulose derivatives (Ibezim, *et al.*, 2008). Also, pregelatinization of natural starches often leads to increase in their swellability and water absorbtivity (Alebiowu and Itiola, 2002). Hence the importance of such parameters as swelling capacity, water absorption capacity, moisture content as well as solubility determined for these materials, on their efficiency as disintegrants. The (crushing strength/friability)/ disintegration time ratio $\{(C_\delta /F_\gamma) /D_t\}$ has been suggested as a better index of assessing tablet performance as regards disintegrant activity, especially when compared with the crushing strength: friability ratio (C_s/F_r). This is because, in addition to measuring tablet strength (crushing strength) and weakness (friability), it simultaneously assesses the net effect of these parameters on disintegration time (Upadrashta, *et al.*, 1992). Generally, the higher the value of $\{(C_\delta/F_\gamma) /D_t\}$ the better the combined effects of binding and disintegrant activities in a tablet. Quite a number of workers have attempted to develop some natural and modified starches as multipurpose tableting excipients. It seems however that none has investigated the disintegrant activities of natural and

pregelatinized starches from trifoliate yams and rice in paracetamol tablet formulations, especially relative to some physicochemical properties of the starch materials. This work is thus aimed at investigating natural and pregelatinized starches from white and yellow trifoliate yams (*Dioscorea dumetorum* Pax) and rice (*Oryza sativa* Linn) as disintegrants in a paracetamol tablet formulation with respect to their misture content, solubility, swelling capacity and water absorption capacity.

MATERIALS AND METHODS

Materials

The materials used included paracetamol B.P. (BDH Chemicals Ltd, Poole, UK), Corn starch B.P.(BDH Chemicals Ltd, Poole, UK) and Polyvinylpyrrolidone, PVP (molecular weight 40,000; Aldrich Chemical Co. Ltd, Gillingham, Dorset, UK). Other materials used included the starches of white trifoliate yam, yellow trifoliate yam and rice extracted and purified following some established procedures (Young, 1984).

Corn starch BP and the experimental starches were fully pregelatinized using the method described by the British Pharmaceutical Codex (1979) and Herman *et al.* (1989).

Methods

Water absorption capacity

The method adapted by Solsulski (1962) was employed to determine the water absorption capacity (WAC). To 2.5g of each starch sample in a weighed 50ml centrifuge tube, 30ml of distilled water was added. This was then agitated on a vortex mixer for 2 minutes, centrifuged at 400rpm for 20minutes (Optima Centrifuge, Type BHG 500, Germany) and the supernatant decanted. The residue was weighed (w_1). The adsorbed drops of water were removed by drying the residue at 60^0 to constant weight (w_2) in an oven. The water absorption capacity (WAC), was then expressed as the weight of water bound by 100g dry powder:

$$WAC = [(w_1 - w_2)/ 2.5]. 100 \qquad (1)$$

Solubility

Percent solubility was determined for each starch powder by the method described by Leach *et al*. (1959). A quantity (1g) of finely powdered and dried sample (w) was weighed into a 100ml conical flask. 15ml of distilled water was added and shaken slowly for 5 minutes, then transferred into a water bath and heated for 20 minutes at about 80^0C with constant stirring. It was then transferred into a pre-weighed centrifuge tube (w_1), 7.5ml of distilled water was added and centrifuged (Optimal Centrifuge, Type BHG500, Germany) at 2200rpm for 20 minutes. The supernantant was then carefully decanted into a pre-weighed dish (w_2), dried at 100^0C to constant weight (w_3) and cooled for 30 minutes. From the weights taken, the following calculation was made:

$$Solubility (\%) = [(w_2 - w_3) / w]. 100 \qquad (2)$$

Swelling power

The swelling power of each starch sample was determined by the method described by Bowen and Vadino (1984). A quantity (5g) of powdered and dried sample was poured into a 100ml measuring cylinder (V_1). 90ml of deionised water was added and the dispersion was well shaken for 5minutes. The dispersion was then made up to 100ml with deionised water and allowed to stand for 24 hours before sedimentation volume was obtained (V_2). The swelling power was then calculated as follows:

$$Swelling\ power = V_2 / V_1 \qquad (3)$$

Determinations were made in triplicate.

Granulation for evaluation of starches as disintegrants

To evaluate the starches as disintegrants, 280g quantities were prepared of a paracetamol formulation containing either 3.0%w/w, 6.0%w/w 9.0%w/w or 12.0%w/w of starch added as endo- (I), or exo- (II) or 50% endo- + 50% exo- (III) disintegrants. To prepare type I granules, the required quantities of paracetamol and starch were dry-mixed for 5 minutes in a Kenwood planetary mixer and then moistened with polyvinylpyrrolidone, PVP (MW = 40, 000) solution to produce 5%w/w of PVP binder in the final granulation. The masses were then wet-screened using a number 12 mesh sieve (1400µm), dried at 60^0C for 6 hours in a hot air oven and then dry-screened using a number 16 mesh sieve (1000µm).

For type II granules, the required amount of paracetamol was moistened with PVP solution to produce 5%w/w of the binder in the final granulation. The masses were then wet-screened, dried and dry-screened as for type I. The required quantity of starch was then added as exo-disintegrant and mixed with the granules in a bottle. The type III granules were prepared by dry-mixing the required quantity of paracetamol with 50% of the starch, moistened with PVP solution as before for Types I and II granulations and then wet-screened, dried and dry-screened The remaining 50% of the starch was then added and mixed as exodisintegrant with the granules in a bottle.

A blank preparation containing no starch disintegrant was also prepared. The degree of mixing, M was calculated using the following expression (Shotton and Ridgeway, 1974):

$$M = 1- \delta/ \delta_0 \qquad (4)$$

Where δ is the standard deviation estimated from the analysed samples and δ_0 is the standard deviation of the completely unmixed system. δ_0 is a function of the proportion of paracetamol in the mixture (y) and is obtained thus:

$$\delta_0 = [y (1-y)]^{1/2} \qquad (5)$$

The moisture content of 10g of each type of granule was determined on a wet-weight basis on an Ohaus moisture balance (Ohaus Scale Corporation, New Jersey, USA). Quantities (500mg) of each batch of granules of size 500-1000µm were compressed using pre-determined loads. The weights (w) and dimensions of the tablets were then measured to within $\pm$1mg and $\pm$0.01mm, respectively and their relative density, R was calculated, using the Equation:

$$R_0 = \rho_0/\rho_p \qquad (6)$$

Crushing strength test

The crushing strength of the tablets was determined using the Monsanto hardness tester. Determinations were made in quadruplicate.

Friability test

The friability (%) of the tablets for the evaluation of the starches as disintegrants was determined using an Erweka friabilator (Erweka, Apparatebau, Offenbauch / Main, Germany). Ten tablets were weighed and then placed inside the compartment on the instrument and caused to tumble at the rate of 25 rpm for 4 minutes. The tablets were then reweighed and the loss in weight, expressed as a percentage of the original weight, was recorded as the friability. Determinations were done in quadruplicate.

Disintegration time test

The disintegration time of the tablets was determined in distilled water at 37 $\pm$ 0.5^{0}C using a B.P. Manesty disintegration test unit (Manesty Machines Ltd; Poole, UK). A tablet each was placed on the wire mesh just above the surface of the distilled water in the test tubes and the unit was switched on simultaneously with a stop clock. The time taken for the tablets to disintegrate and all particles to pass through the wire mesh was recorded as the disintegration time. Determinations were made in quadruplicate.

Statistical analysis was carried out on all the parameters obtained in evaluating the disintegrant activity of the starches using two-way Analysis of Variance (ANOVA) on a computer software GraphPad Prism® 4 (GraphPad Software Inc., San Diego, USA). Post-hoc (Turkey-Kramer multiple comparison) test was employed to compare the individual differences between the samples. At 95% confidence interval, probability, *p* values greater than 0.05 (that is, 5%) were considered insignificant. Correlations between various parameters for evaluation of starch disintegrants in the paracetamol tablets are presented in Table III.

Table I : Physicochemical properties of the starches.

Nature of Starch	Form of starch	Moisture Content (%)	Swelling power	Solubility (%)	Water Absorption Capacity (g/100g)
White T. yam	Natural	9.26	4.51	3.88	18.09
	Pregelatinized	5.79	15.11	16.00	120.92
Yellow T. yam	Natural	8.54	5.28	4.85	27.14
	Pregelatinized	5.77	11.16	12.00	112.39
Rice	Natural	9.29	5.28	4.91	18.29
	Pregelatinized	5.86	10.93	7.00	94.77
Corn	Natural	9.30	5.78	4.88	32.08
	Pregelatinized	6.02	18.03	19.00	102.63

Table II : Values of (crushing strength/friability)/disintegration time ratio $\{(C_\delta/F_\gamma)/D_t\}$ for paracetamol tablets containing starch disintegrants at relative density (R) of 0.90.

Starch disintegrant	Concentration (% w/w)	(Crushing strength/friability)/disintegration time ratio $\{(C_\delta/F_\gamma)/D_t\}$					
		Natural			Pregelatinized		
		endo-dis-integrant	exo-dis-ıntegrant	endo-exo-dis-integrant	endo-dis-integrnt	exo-dis-integrant	endo-xo-dis-integrant
None	0.0	1.59	–	–	–	–	–
White T. yam	3.0	2.32	3.01	2.78	2.75	5.97	4.44
	6.0	3.24	4.39	4.16	4.71	8.23	6.99
	9.0	5.52	7.31	6.47	8.41	16.00	13.86
	12.0	11.16	16.14	13.35	11.76	27.84	17.79
Yellow T. yam	3.0	2.16	3.20	3.24	2.88	5.51	4.87
	6.0	3.06	4.23	4.10	3.66	7.17	6.42
	9.0	4.36	6.95	5.45	4.05	10.25	7.93
	12.0	7.20	11.21	9.65	4.68	16.20	10.06
Rice	3.0	1.75	2.40	2.04	1.27	2.56	2.30
	6.0	1.92	2.77	2.18	2.47	3.24	2.61
	9.0	2.83	3.88	3.22	2.76	5.01	3.73
	12.0	5.74	7.80	6.75	3.19	6.13	4.48
Corn	3.0	2.66	3.63	3.62	2.10	4.70	4.11
	6.0	3.754	5.01	4.41	2.48	6.47	4.46
	9.0	5.13	6.97	6.07	2.77	8.58	6.01
	12.0	8.60	13.22	10.10	4.18	13.60	7.92

RESULTS AND DISCUSSION

Values of moisture content, swelling power, solubility and water absorption capacity are presented in Table I. The pregelatinized starches showed much higher swelling ability, % solubility and water absorption capacity than the natural starches. Thus, as expected, pregelatinization increased the cold-water swellability of the starches (Alebiowu and Itiola, 2002). The rankings of swelling power and solubility for natural starches were corn > rice = yellow T. yam > white T. yam, and, rice > corn > yellow T. yam > white T. yam, respectively, and was corn > white T. yam > yellow T. yam > rice, for pregelatinized starches.

In contrast, the values of the water absorption capacity for natural and pregelatinized starches followed the rankings of corn > yellow T. yam > rice > white T. yam, and white T. yam > yellow T. yam > corn > rice, respectively.

The values of moisture content for the granules containing disintegrants are included in Table I. Increase in the disintegrant concentration showed no significant effect on moisture content. Granules containing pregelatinized starches generally possessed slightly higher moisture content than the corresponding ones formulated with natural starches.

Representative plots of crushing strength (C_s) versus relative density (R) for paracetamol tablets formulated with 6% w/w natural starch exo-disintegrants are presented in Fig.1. It can be seen that crushing strength is a direct function of relative density. The crushing strength increased as the relative density increased, probably as a result of decrease in porosity resulting in an increase in the number of contact points, and eventually, an increase in the formation of solid interpaticulate bonds (Bi, *et al.*, 1999; Itiola and Pilpel, 1996; Luangtana-Anan and Fell, 1990; Pilpel, *et al.*, 1978). The difference in rankings of crushing strength observed for paracetamol tablets formulated with natural starches, and with pregelatinized starches could be as a result of the difference in swelling ability of both forms. Also, the probable differences in the swelling ability of the starches in formulation and the swelling ability of the starches in pure form, would affect the strength of the bonds formed in the tablets. The rankings were the same for the three modes of incorporation of the disintegrants.

Table III : Correlations between various parameters for evaluation of starch exo- disintegrants in the paracetamol tablets.

Starch disintegrant	Exo-disintegrant	(y) Ordinate	(x) Abscissa	Equation for the line of best fit	Corr coeff (r)	Level of sig. (p)
White T. yam starch	Natural		C_s/F_r	$0.310C_s/F_r - 5.617$	0.997	<0.0005
	Pregel			$0.256C_s/F_r - 5.040$	0.996	<0.05
	Natural	$(C_s/F_r)/D_t$	C_s/F_r	$-0.040C_s/F_r + 7.233$	-0.987	<0.05
	Pregel			$-0.590C_s/F_r+31.156$	-0.897	<0.05
	Natural	$(C_s/F_r)/D_t$	D_t	$-0.129D_t + 6.485$	-0.982	<0.05
	Pregel			$-2.347D_t + 19.695$	-0.918	<0.001
	Natural	C_s	D_t	$2.555D_t + 32.099$	0.983	<0.001
	Pregel			$3.843D_t + 30.666$	0.994	<0.05
	Natural	$(C_s/F_r)/D_t$	C_s	$-0.050C_s + 8.056$	-0.982	<0.01
	Pregel			$-0.584C_s + 37.281$	-0.883	<0.005
Yellow T. yam starch	Natural	D_t	C_s/F_r	$0.304C_s/F_r - 4.134$	0.970	<0.005
	Pregel			$0.359C_s/F_r - 8.895$	0.930	<0.005
	Natural	$(C_s/F_r)/D_t$	C_s/F_r	$-0.085C_s/F_r +9.433$	-0.575	<0.05
	Pregel			$-0.663C_s/F_r+34.481$	-0.905	<0.01
	Natural	$(C_s/F_r)/D_t$	D_t	$-0.359 D_t + 9.026$	-0.756	>0.001
	Pregel			$-1.822 D_t + 17.949$	-0.917	<0.01
	Natural	C_s	D_t	$2.364 D_t + 29.146$	0.975	<0.001
	Pregel			$2.835 D_t + 37.427$	0.967	<0.01
	Natural	$(C_s/F_r)/D_t$	C_s	$-0.119C_s + 11.719$	-0.606	>0.05
	Pregel			$-0.602C_s + 40.025$	-0.889	<0.05
Rice starch	Natural	D_t	C_s/F_r	$0.491C_s/F_r - 5.426$	0.990	<0.01
	Pregel			$0.584C_s/F_r - 7.847$	0.987	<0.05
	Natural	$(C_s/F_r)/D_t$	C_s/F_r	$-0.072C_s/F_r + 5.783$	-0.805	>0.05
	Pregel			$-0.452C_s/F_r+15.765$	-0.843	<0.05
	Natural	$(C_s/F_r)/D_t$	D_t	$-0.156 D_t + 5.089$	-0.860	<0.005
	Pregel			$-0.822 D_t + 9.961$	-0.907	<0.05
	Natural	C_s	D_t	$2.475 D_t + 18.032$	0.996	<0.01
	Pregel			$1.988 D_t + 20.521$	0.980	<0.05
	Natural	$(C_s/F_r)/D_t$	C_s	$-0.059C_s + 6.065$	-0.816	>0.05
	Pregel			$-0.366C_s + 16.964$	-0.820	>0.05
Corn starch	Natural	D_t	C_s/F_r	$0.359C_s/F_r - 8.700$	0.988	<0.05
	Pregel			$0.217C_s/F_r - 2.464$	0.996	<0.005
	Natural	$(C_s/F_r)/D_t$	C_s/F_r	$-0.072C_s/F_r + 5.783$	-0.805	>0.05
	Pregel			$-0.452C_s/F_r+15.765$	-0.843	<0.05
	Natural	$(C_s/F_r)/D_t$	D_t	$-0.156 D_t + 5.089$	-0.860	<0.005
	Pregel			$-0.822 D_t + 9.961$	-0.907	<0.05
	Natural	C_s	D_t	$2.475 D_t + 18.032$	0.996	<0.01
	Pregel			$1.988 D_t + 20.521$	0.980	<0.05
	Natural	$(C_s/F_r)/D_t$	C_s	$-0.059C_s + 6.065$	-0.816	>0.05
	Pregel			$-0.366C_s + 16.964$	-0.820	>0.05

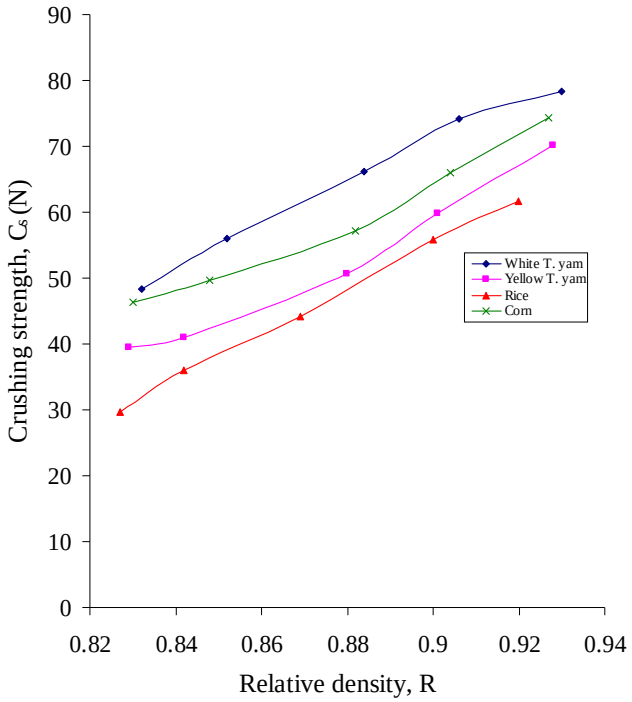

Fig.1: Plots of crushing strength (C_s) versus relative density (R) for paracetamol tablets formulated with 6% w/w natural starch exo-disintegrants.

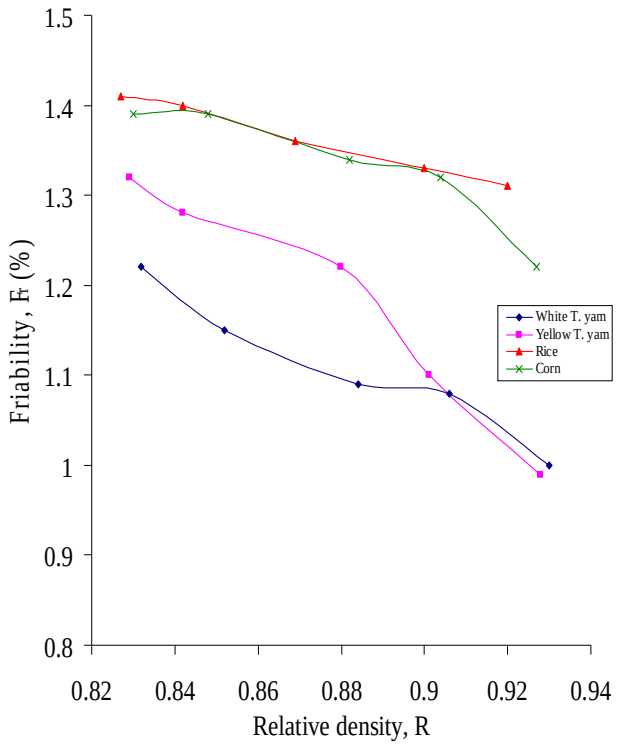

Fig. 2: Plots of Friability (F_r) versus relative density (R) for paracetamol tablets formulated with 6% w/w natural starch exo-disintegrants.

Also, as the disintegrant concentration increased, the crushing strength values increased. This relationship could be due to the fact that as more starch disintegrants are added, more particles become available for closer contact, thus enhancing interparticulate bonding forces. This can be important in formulation studies and suggests that low concentration of disintegrant may be sufficient to achieve the desired effect in particular tablet formulations.

The values of the crushing strength of the tablets followed the ranking: exo-disintegrant > endo-exo-disintegrant > endo-disintegrant, probably because, in agreement with previous findings (Bi, *et al.*, 1999), starch exo-disintegrants would produce more interparticulate contact points between starch particles and those of other components of the tablet, thus, creating more solid bonds, and hence, higher values of crushing strength.

Paracetamol tablets formulated with natural starch disintegrants exhibited higher values of crushing strength than those formulated with pregelatinized starch disintegrants, regardless of their modes of incorporation. This may be due to the higher tensile strength values exhibited by the natural starches.

A direct relationship between the concentration of starch disintegrant and the crushing strength of the paracetamol tablets was also observed. However, there is a minimum value at 3% concentration of starch when values are compared with the formulation containing no starch disintegrant (that is, 0%). Paracetamol tablets formulated with natural starch disintegrants exhibited higher values of crushing strength than those formulated with pregelatinized starch disintegrants, for the three modes of starch disintegrant incorporation. The rankings of crushing strength for paracetamol tablets formulated with natural starches and with pregelatinized starches were: white T. yam > corn > rice > yellow T. yam, and, yellow T. yam > white T. yam > corn > rice, respectively.

Fig. 2 shows representative plots of friability against relative density for paracetamol tablets formulated with 6% w/w natural starch exo-disintegrants. As the disintegrant concentration increased, the values of friability of the tablets decreased. This could be as a result of the existence of more interparticulate contact points with increased disintegrant concentration which would lead to formation of more solid bonds and hence less friable tablets. Also, the inverse relationship between the relative density and friability observed could be as a result of greater number of solid bonds formed due to increase in contact points with increase in relative density which would lead to stronger tablets with less friability. Tablets formulated with natural disintegrants exhibited lower friability than those formulated with pregelatinized starch disintegrants. The rankings of friability for the paracetamol tablets containing natural starch disintegrants, and for those containing pregelatinized starch disintegrants, were: white T. yam > yellow T. yam > corn > rice and, corn > white T. yam > yellow T. yam > rice, respectively. Also, the ranking of friability for the different modes of starch incorporation was: endo-disintegrant < endo-exo-

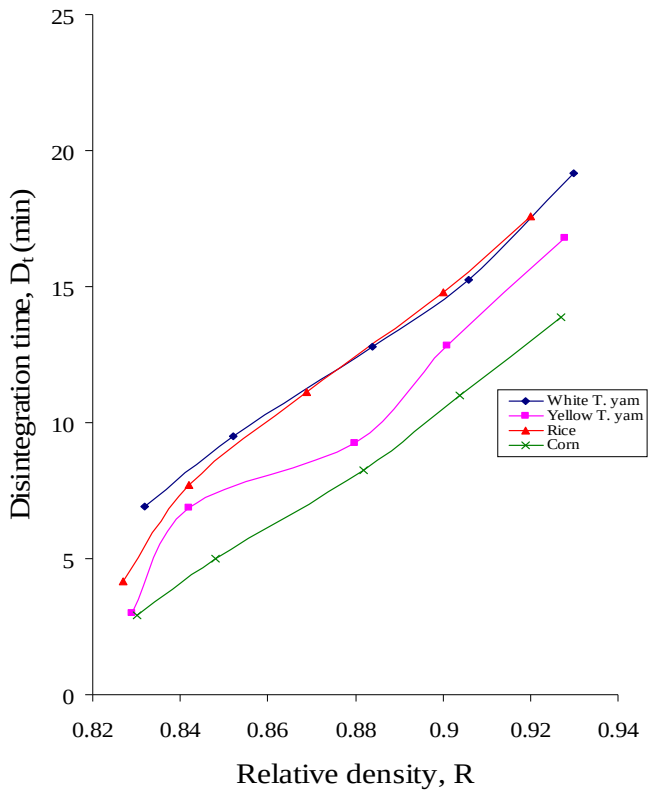

Fig. 3: Plots of disintegration time (D_t) versus relative density (R) for paracetamol tablets formulated with 6% w/w natural starch exo-disintegrants.

disintegrant < exo-disintegrint, for both natural and pregelatinized starches, respectively.

Typical plots of disintegration time against relative density for paracetamol tablets containing 6% w/w natural starch exo-disintegrant are shown in Fig. 3. The values of the disintegration time increased as the relative density increased. This could be due to the reduction in porosity (that is, capillary microstructure) of tablets as the relative density increased (Pilpel, *et al.*, 1978; Itiola and Pilpel, 1996). According to Bi *et al.* (1999), decrease in porosity leads to formation of more solid bridge, thus making annihilation of interparticulate bonds more difficult. The reduction in porosity would lead to slower water penetration into tablets, and, consequently, swelling would be reduced and, eventually, development of active mechanism of disintegration would be reduced. Paracetamol tablets formulated with pregelatinized starch disintegrants exhibited lower D_t values than those formulated with natural starch disintegrants, probably due to the higher swelling power of the pregelatinized starches than the natural ones, thereby promoting active disintegration mechanism in the tablets caused by the generation of swelling force of the starch disintegrants (Adedokun and Itiola, 2010). Also, for all the starches, as the concentration of disintegrant increased, D_t values of tablets decreased. This effect of increase in disintegrant concentration was less pronounced with pregelatinized starch disintegrants than with natural starch disintegrants. This is because the reduction in D_t of tablets between two concentrations of pregelatinized starch disintegrants was lower than the rate for two similar concentrations of natural starch disintegrants. This could be due to very high swelling ability of the pregelatinized starches (Alebiowu and Itiola, 2002), which, as the concentration increases, causes the blockage of the pores and subsequently reduces the water absorption into the core of the tablets (Lowenthal, 1973). As the concentration of pregelatinized starch disintegrant increased, the expected fast rate of reduction of D_t of the tablets (Balamuralidhara, *et al.*, 2009) would be impeded by the reduced water absorption.

The mode of incorporation of disintegrants has been observed to affect the disintegration time. Thus, the ranking of D_t was exo-disintegrant < endo-exo-disintegrant < endo-disintegrant. This is, possibly, as a result of the varying relative proportion of starch (disintegrant) initially exposed to the disintegrating medium (distilled water). In tablets formulated with starch exo-disintegrants, a large quantity of starch is initially exposed to the medium, leading to absorption of large amounts of water, generation of high swelling force and eventual initiation of active disintegration process. Expectedly, this action would be less in endo-exo-disintegrant, and least in endo-disintegrant formulations since the quantities of starch initially exposed to the disintegrating medium reduced in that order.

Some of the tablets formulated with natural starch disintegrants did not meet the official D_t specifications of not more than 15 minutes for uncoated tablets (British Pharmacopoeia, 1998) while all the tablets formulated with pregelatinized starch disintegrants did. It is important to note, however, that these disintegrant formulations are not ideal as they contain paracetamol, PVP and the experimental starch disintegrants only, just to assess the relative disintegrant activity of the starches against the bonding potential of PVP.

For paracetamol tablets containing natural starch disintegrants, the ranking of D_t was: corn < yellow T. yam < rice < white T. yam, and for those containing pregelatinized starch disintegrants, the ranking was corn < yellow T. yam < white T. yam < rice. The rankings were not the same, possibly, because of the different properties of the starches as has been detailed earlier on.

The values of (Crushing strength / friability) / disintegration time ratio $\{(C_\delta/F_\gamma)\ /D_t\}$ of paracetamol tablets formulated with different starches as endo-, exo-, and endo-exo-disintegrants, at relative density of 0.90, are presented in Table II. The (crushing strength/friability)/disintegration time ratio $\{(C_\delta/F_\gamma)\ /D_t\}$ has been suggested as a better index of assessing tablet quality, especially when compared with the crushing strength: friability ratio (C_s/F_r). This is because, in addition to measuring tablet strength (crushing strength) and weakness (friability), it simultaneously assesses the net effect of these parameters on disintegration time (Upadrashta, *et al.*, 1992). Generally, the higher the value of $\{(C_\delta/F_\gamma)/D_t\}$ the better the combined effects of binding and disintegrant activities in a tablet. Incorporation of the starches as endo-, exo-, and endo-exo-disintegrants in paracetamol formulations reduced C_s and D_t and increased F_r and the combined

$\{(C_\delta/F_\gamma)/D_t\}$ of the tablets. The starches showed the best balance as exo-disintegrants (exhibiting the highest values of $\{(C_\delta/F_\gamma)/D_t\}$ and least balance as endo-disintegrants.

Tablets formulated with pregelatinized starch disintegrants had higher values of $\{(C_\delta/F_\gamma)/D_t\}$ than those formulated with natural starch disintegrants implying that there was a better balance between binding and disintegration for the tablets formulated with pregelatinized starch disintegrants. The rankings of $\{(C_\delta/F_\gamma)/D_t\}$ for the natural and pregelatinized starch disintegrants were white T. yam > corn > yellow T. yam > rice; and white T. yam > yellow T. yam > corn > rice, respectively. Different rankings were observed for the two forms of the disintegrants, probably due to their different properties especially swelling ability. In both forms, white T. yam starch had the highest $\{(C_\delta/F_\gamma)/D_t\}$ and rice starch had the least, suggesting that the latter starch would show the least balance while the former would show the best balance.

Disintegrant activity of starch has been affirmed to be by swelling and by capillarity (Ibezim, *et al.*, 2008). Hence the importance of such parameters as swelling capacity, water absorption capacity, moisture content as well as solubility determined for these materials, on their efficiency as disintegrants. Expectedly, pregelatinized starches exhibited higher disintegrant activity as they had higher swelling power and water absorption capacity. Also, corn starch, which generally produced the highest values of these parameters, yielded tablets with the least D_t values.

Incorporation of the starches as endo-, exo- and endo-exo-disintegrants in paracetamol tablet formulations reduced the values of crushing strength, C_s and disintegration time, D_t, and increased the values of friability, F_r and the combined $(C_s/F_r)/D_t$ of the tablets. This suggests that the starch disintegrants yielded better balance between binding and disintegration forces. Similarly, pregelatinized starch disintegrants yielded tablets with higher $(C_s/F_r)/D_t$ values. The disintegrant activity was also seen to be affected by the mode of incorporation. The starch disintegrants were most effective as exo-disintegrants, followed by endo-exo-disintegrants, and least effective as endo-disintegrants. This was probably because out of these three modes of incorporation, exo-disintegrant formulations would provide the largest quantity of starch initially exposed to water (disintegrating medium), leading to the absorption of the largest amount of water and eventual generation of the highest swelling force. The latter force would generate the fastest rate of active disintegration mechanism in exo-disintegrant formulations, followed by endo-exo, and lastly, endo-disintegrant formulations

CONCLUSIONS

The disintegrant activity of starches is determined by their nature, form, mode of incorporation and their concentration. Physicochemical parameters as water solubility, swelling capacity as well as water absorption capacity exhibit some direct effect on disintegrant activity of the starches. Pregelatinized starches produced better combined disintegrant properties of $(C_s/F_r)/D_t$ than natural starches. White T. yam starch gave the best $(C_s/F_r)/D_t$ ratio of all the starches. Tablets formulated with official corn starch disintegrant exhibited the lowest disintegration time values, but generally all the tablets containing the experimental starches also passed the official disintegration time test.

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