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Analysis of Activities of Some Starch Disintegrants in Paracetamol Tablets by Application of a Factorial Experimental Design

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Abstract
The effects of the nature of disintegrant (N), its concentration(C) and its type (T) on the disintegrant properties - crushing strength (C_s), friability (F_r) and disintegration time (D_t) - of paracetamol tablets formulated with starch disintegrants from white and yellow trifoliate yam varieties (*Dioscorea dumetorum* Pax) and rice (*Oryza sativa*, Linn) were studied comparatively with those containing official corn starch by the application of statistical principles based on a 23 experimental design. Generally, for all the starch disintegrants, the ranking for the individual effects on Cs, Fr and Dt were N>C>T, N>C>T and C>F>T, respectively. The general ranking for the interactions would appear to be N-C > C-T > N-T. From these, it may be inferred that the concentration of disintegrant, C which is apparently involved in the two largest groups of interaction is generally the most important in influencing the effects of the variables on the disintegration properties of the various starches since it would influence the effects of the two other variables considerably. These findings can be useful in manipulating the variables to obtain desired disintegration properties for formulated paracetamol tablets.

Keywords: disintegrant activities; starch disintegrants; *Dioscorea dumetorum*; *Oryza sativa*; crushing strength; friability; disintegration time;

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INTRODUCTION

For a compressed tablet to be worth its value, when exposed to fluid, it must undergo some sequential processes that ultimately lead to the bioavailability of the active component(s). For most conventional tablets, the first main step in the sequence is disintegration, followed by dissolution. Disintegration is the breakdown or rupture of the tablet into smaller particles or granules in water or gastric fluid [1]. This is made possible by incorporating a disintegrant into the formula and this can be done intragranularly (endo-disintegrants), extra-granularly (exo-disintegrants) or a combination of both (endo-exo-disintegrants) [2]. The position of disintegrants in the formulation determines their effectiveness [3]. Starch is one main class of substances often employed as disintegrants in tableting.

Starch, a polysaccharide found especially in plant roots, rhizomes, fruits and seeds is used in a variety of food and pharmaceutical industries [4]. Worldwide, it constitutes 70-80% of the calories consumed by humans and is generally deposited in the form of minute granules or cells ranging from 1-100µm or more in diameter depending on its botanical source and treatment [5,6,7]. Generally, it is tasteless and odourless solid, white, amorphous in nature and is insoluble in cold water [8,9].

In tablet formulations, starch is a multifunctional excipient, which can be employed not only as disintegrants, but also as binders, glidants, lubricants or fillers [10,11,12,13] owing to its relative inertness and suitable physicochemical characteristics [14,15].

Trifoliate yam or three-leafed yam is the tuber of *Dioscorea dumetorum* Pax (Family Dioscoreaceae) commonly found in West Africa. The flesh of the peeled tubers are of three types; white, yellow and pink. The first two are found in Western and Eastern Nigeria while the third type is found in Cameroun. The plant as a whole consists of steroids and alkaloids and other poisonous components. This yam is cultivated and sometimes found wild. Hence, sometimes called "Wild yam" [16]. The wild type is not edible and the consumption of even the edible type is constrained by a rapid post-harvest hardening phenomenon that occurs after 24hours of harvest [17]. Trifoliate yam starch has about the smallest grains of all starches (about 1-3µm). Upon heat treatment, it also produces a very thin paste of very low viscosity [18].

Rice is obtained from the plant *Oryza sativa* Linn. (Family, Gramineae). There are two types cultivated in Nigeria-the irrigated lowland/swamp rice and the non-irrigated upland type. The lowland types are usually grown in swampy areas all year round. They, however, need to be irrigated in dry season. The upland rice varieties are cultivated on non-swampy land only in rainy season. Natural rice starch has granule size of about 2-6µm [9,18]. Rice starch amylose and its amylopectin have more branches than those of other starches. Also, rice starches are much more stable overtime (very slow retrogadation), and yield smooth gels. Rice starches are of various forms; non-waxy rice starch, waxy rice starch, Organic rice starch and modified rice starch. Modified rice starch has been formed to replace gelatin in wide range of applications. Although, rice starch is more than twice as expensive as wheat and corn it is often used by the food industry for its gel strength, gelling temperature and starch granule rigidity [19]. Rice starch has been listed as one of the pharmaceutically used starches of biological origin [9]. Factorial experimental design had been applied and found to be useful by quite a number of workers [14,20,21,22,23] in the assessment of pharmaceutical systems. Meanwhile, the influence of nature of disintegrant (N), its concentration(C) and its type (T) on the disintegrant properties - crushing strength (C_s), friability (F_r) and disintegration time (D_t) - of paracetamol tablets formulated with starch disintegrants from white and yellow trifoliate yam varieties (*Dioscorea dumetorum* Pax) and rice (*Oryza sativa*, Linn which appears not to have been investigated, is the focus of this work.

MATERIALS AND METHODS

Materials:

The materials used were 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 Tubers of white and yellow varieties of trifoliate yam (*Dioscorea dumetorum* Pax), purchased from a local farm near Oyo town in Oyo state, Nigeria and grains of unmilled rice (*Oryza sativa*; Linn; ITA 150) obtained from the International Institute for Tropical Agriculture (IITA), Ibadan, Nigeria.

Methods:

Preparation of natural starches:

Weighed quantities of tubers of white and yellow trifoliate yams were peeled, washed and chopped into small pieces. A weighed quantity of rice (ITA 150) was also milled using the local wooden mortar and pestle, and then washed. Each of these materials was separately soaked overnight in de-ionised water containing 0.1% sodium metabisulphite. Each material was then wet milled using an industrial milling machine (Manesty Machines, Poole, UK). The fine pulp was then strained through a piece of calico cloth. The resultant milky liquid was allowed to stand for 12 hours after which the supernatant was decanted. The sediment was then mixed with deionised water of

about three times its volume and allowed to stand again for 12 hours before the supernatant was decanted. This process of washing was repeated after every 12 hours for 3 days, and then after every 24 hours for 7 days. The resultant starch slurry was centrifuged (Optima Centrifuge, Type BGH 500, Germany) at 4000 rpm for about 30 minutes and dried at 60^0C for 6hours [24].

Different starches, after drying, were each pulverized using a laboratory mill (Christy and Norris Ltd, U.K), passed through a 120 mesh sieve (125µm), weighed and stored in airtight amber-coloured bottles.

Heat-modification of the starches:

All the four starches – white and yellow trifoliate yams, rice and corn – were heat-modified using the method described by some researchers and in The Pharmaceutical Codex [14,15,25,26]. A weighed quantity (100g) of each of the natural starches was dispersed in 100ml of distilled water and then heated at 55^0C with constant stirring for 10 minutes to form a paste, which was then crisp-dried in an oven at 60^0C for 48 hours. The resultant mass was pulverized in a laboratory mill (Christy and Norris Ltd, U.K). Each sample was passed through a number 120 mesh sieve (125µm) and then stored in an airtight amber-coloured bottle.

Granulation:

A 280 g quantity of a paracetamol formulation containing either 3.0 %w/w, 6.0 %w/w, 9.0 %w/w or 12.0 %w/w of natural or heat-modified starch incorporated as endo- (A), or exo- (B) or 50 % endo- + 50 % exo- (C) disintegrants.

To prepare type A 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 600C for 6 hours in a hot air oven and then dry-screened using a number 16 mesh sieve (1000µm). For type B 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 done for type A. The required quantity of starch was then added as exo-disintegrant and mixed with the granules in a bottle.

The type C granules were prepared by dry-mixing the required quantity of paracetamol with 50% of the starch, moistened with PVP solution as before for types A and B 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 formulation containing no starch disintegrant was also prepared.

Evaluation of the starches as disintegrants in paracetamol tablets:

Granule size distribution:

The size distribution of each granule formulation was determined by sieve analysis (British Standard 1460). A stack of sieves of the following sizes: 12 mesh (1400µm), 16 mesh (1000µm), 22 mesh (710µm) 30 mesh (500µm) 44 mesh (355µm), 60 mesh (250µm), 120 mesh (125µm) and the receiver, was arranged in descending order of aperture size with the receiver at the bottom. 100g of granules was put on the uppermost sieve, firmly covered and the stack of sieves was shaken for 10minutes on a sieve shaker (Pascal Engineering, Essex, England). The quantity of granules retained on each sieve was weighed and the cumulative weight percentage oversize curve was plotted and the mean granule size , which corresponds to the sieve size (µm) at 50% cumulative weight percentage oversize, was calculated. For each sample, the granules of size 500-1000µm were collected and stored in an airtight container for subsequent experiments.

Crushing strength test:

The crushing strength of the tablets was determined using the Monsanto hardness tester The load, F (MN) required to break each starch tablet diametrically into two halves was measured using a Monsanto hardness tester [27]. Each tablet was placed between the platens of the tester and the knob was screwed until contact was made and then further screwed until there was just enough pressure to cause fracture. The value displayed on the scale of the tester was recorded as the crushing strength. Results were taken only from tablets that split cleanly into two halves without any sign of lamination. All 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 + 0.5^0C 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.

Factorial experimental design for starch disintegrants:

The effects of the nature of disintegrant (denoted by N), concentration of disintegrant (denoted by C) and the type of disintegrant (denoted by T) on the friability, crushing strength and disintegration time of tablets made from starch disintegrant formulations was studied by the application of statistical principles [28]. The experimental design was based on 2^n, where n is the number of variables (that is, 2^3 or 8; since three variables were used). This was carried out by using each of the variables at a "high" level (denoted by subscript, H) and a "low" level (denoted by subscript, L).Applying the above numenclature, the various combinations between the variables used in the design were:

$N_LC_LT_L$, $N_LC_HT_L$, $N_LC_HT_H$, $N_LC_LT_H$, $N_HC_LT_L$, $N_HC_HT_L$, $N_HC_HT_H$, $N_HC_LT_H$

Nature of disintegrant (heat-modified starches)

N_H = Nature of disintegrant (natural starches)

C_L = Concentration of disintegrant (3%w/w)

C_H = Concentration of disintegrant (12%w/w)

T_L = Type of disintegrant (endo-disintegrant)

T_H = Type of disintegrant (exo-disintegrant)

Grouping the results into a number of sets made it possible to assess the effects that each of the three variables had separately on the friability, crushing strength and disintegration time, and also to determine whether the variables were interacting or acting independently of each other.

The effects of increasing say nature of disintegrant F, from its 'low' level to its 'high' level on the friability, crushing strength or disintegration time were determined by summing all the values of friability, crushing strength or disintegration time of samples containing 'high' level of F and subtracting the sum of the values containing 'low' level of F, and since there were four pairs, the net value was divided by 4. Thus:

$1/4\ [(N_HC_LT_L + N_HC_HT_L + N_HC_HT_H + N_HC_LT_H) - (N_LC_LT_L + N_LC_HT_L + N_LC_HT_H + N_LC_LT_H)]$

In the same way, the effect of increasing C and T were calculated:

For concentration of disintegrant, C:

$1/4\ [(N_HC_HT_L + N_HC_HT_H + N_LC_HT_L + N_LC_HT_H) - (N_HC_LT_L + N_HC_LT_H + N_LC_LT_L + N_LC_LT_H)]$

For type of disintegrant, T:

$1/4\ [(N_HC_HT_H + N_HC_LT_H + N_LC_HT_H + N_LC_LT_H) - (N_HC_LT_L + N_HC_HT_L + N_LC_LT_L + N_LC_HT_L)]$

Whether or not interaction exists between two variables was determined by summing the results of the combinations in which they appeared together at either "low" or "high" levels and then subtracting the sum of other combinations from this to obtain the interaction coefficient. Thus:

For nature and concentration of disintegrant (N and C):

$1/4\ [(N_HC_HT_L + N_HC_HT_H + N_LC_LT_L + N_LC_LT_H) - (N_HC_LT_L + N_HC_LT_H + N_LC_HT_L + N_LC_HT_H)]$

For nature and type of disintegrant (N and T):

$1/4\ [(N_HC_HT_H + N_HC_LT_H + N_LC_LT_L + N_LC_HT_L) - (N_HC_LT_L + N_HC_HT_L + N_LC_HT_H + N_LC_LT_H)]$

And for concentration and type of disintegrant (C and T):

$1/4\ [(N_HC_LT_L + N_HC_HT_H + N_LC_LT_L + N_LC_HT_H) - (N_HC_HT_L + N_HC_LT_H + N_LC_HT_L + N_LC_LT_H)]$

The individual and interaction coefficients obtained provide an indication of the quantitative effects of the three variables studied on the friability, crushing strength and disintegration time of the paracetamol tablets.

A numerically small result of this treatment is an indication that the effect of the variable on the friability (or crushing strength or disintegration time) was small and vice versa for a large value. If the interaction coefficient value so obtained was zero, then there was no interaction between the variables, but if the value was significantly removed from zero, then the two variables were interacting with each other. The higher the degree of the removal from zero, regardless of whether positive or negative, the higher was the magnitude of interaction. A positive sign indicates that the value of the parameter has increased with the opposite being the case for a negative sign [28].

RESULTS

Representative plots of cumulative weight percentage oversize for the paracetamol formulations containing 0%w/w and 6%w/w of natural exo-disintegrants are shown in Figure 1. The values of mean granule size, derived from plots of cumulative weight percentage oversize for all the batches are listed in Tables 1(a) and (b). From the results, values appeared not to be materially affected by the concentration of the disintegrants. Figures 2 and 3 show typical plots of crushing strength (C_s), and friability (F_r) against relative density for the tablets formulated with 6% w/w natural starch exo-disintegrants. It can be seen that crushing strength is a direct function of relative density while an inverse relationship was observed between relative density and Fr. The values of Cs, Fr and disintegration time (D_t) for the factorial experimental design are presented in Tables 2(a) – (d). Individual and interaction coefficients for the variables as explained earlier are presented in Tables 3 and 4.

The individual variables – nature (N), concentration (C) and type (T) of disintegrant produced different effects on C_s, F_r and D_t. (Table 3). When white T. yam starch disintegrant was employed, the individual effects of the variables on C_s and F_r was of the rank order N > C > T, and on D_t was C > N > T. When yellow T. yam starch disintegrant was used, the rank order of the effects of the individual variables on C_s was T > C > N, on F_r was N > C > T, and on D_t, was C > N > T. For rice starch disintegrant, the effect on C_s was of the rank order N> C > T, and on both F_r and D_t was C > N > T. On employing corn starch disintegrant, the rank order of the individual effect on Cs was N > T > C, and on F_r and D_t, was C > T > N.

The values of interaction coefficients for the variables are presented in Table 4. The combinations of variables considered were: nature and concentration of starch disintegrant (N-C), concentration and type of starch disintegrant (C-T), and nature and type of disintegrant (N-T). When white T. yam starch was employed as disintegrant, the rank order of the interaction effects of the variables on C_s was N-C > N-T > C-T, on F_r was N-C = N-T > C-T, while on D_t was N-C > C-T > N-T. For yellow T. yam starch disintegrant, the effect on C_s followed the order of N-T > N-C > C-T, on F_r, was N-C > C-T > N-T and on D_t was N-C > N-T > C-T. On employing rice starch disintegrant, the combined effect of the variables on C_s was of the rank order: N-T > C-T > N-C, while on both F_r and D_t was N-C > N-T > C-T. When corn starch disintegrant was employed, the effect of the variables in combination on C_s was N-T > C-T > N-C, on F_r, was C-T > N-C = N-T and on D_t, was N-C > N-T > C-T.

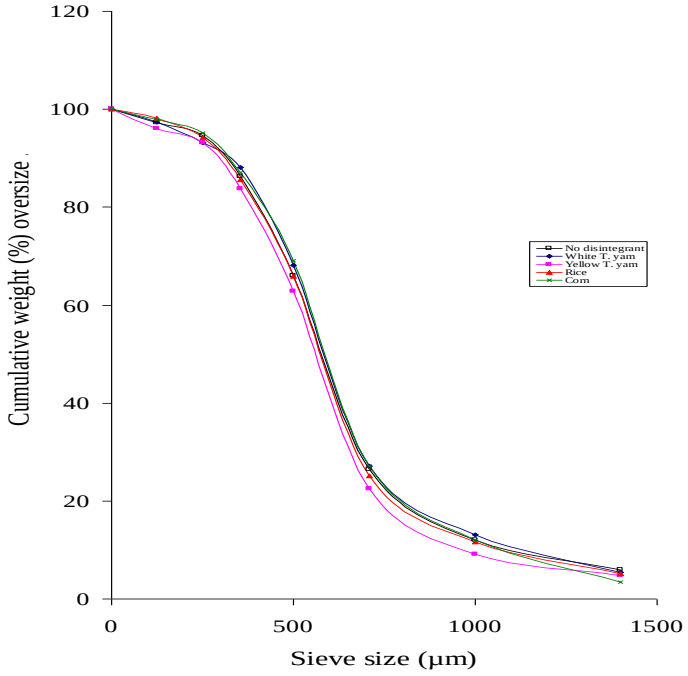

Figure 1: Plots of cumulative weight percentage oversize for paracetamol formulations containing 0% w/w and 6% w/w natural starch exo-disintegrants

Type of starch disintegrant	Concentration (% w/w)	Mean granule size $(\bar{g})$ (μm)		
		Endo-	Exo-	Endo-exo-
None	0.0	580	–	–
White T. yam	3.0	573	560	575
	6.0	578	586	589
	9.0	570	560	574
	12.0	579	563	585
Yellow T. yam	3.0	560	558	563
	6.0	569	564	571
	9.0	566	555	568
	12.0	587	575	588
Rice	3.0	562	558	569
	6.0	574	572	575
	9.0	577	570	571
	12.0	585	582	570
Corn	3.0	573	563	560
	6.0	578	591	593
	9.0	572	568	579
	12.0	570	560	572

Table 1(a): Values of mean granule size for formulations containing natural starch disintegrants

Type of starch disintegrant	Concentration (% w/w)	Mean granule size $(\bar{g})$ (μm)		
		Endo-	Exo-	Endo-exo-
None	0.0	580	–	–
White T. yam	3.0	556	552	580
	6.0	560	578	577
	9.0	566	560	578
	12.0	572	561	580
Yellow T. yam	3.0	560	545	564
	6.0	562	557	571
	9.0	561	550	574
	12.0	560	552	578
Rice	3.0	549	542	551
	6.0	566	568	571
	9.0	565	564	570
	12.0	569	558	572
Corn	3.0	572	568	571
	6.0	570	582	583
	9.0	569	560	565
	12.0	570	565	570

Table 1(b): Values of mean granule size for formulations containing heat-modified starch disintegrants

Starch disintegrant employed	Variables and combination codes	C_s	F_r	D_t
White T. yam	$N_LC_LT_L$	34.05	1.36	9.09
	$N_LC_HT_L$	52.49	1.21	3.69
	$N_LC_HT_H$	61.80	1.20	1.85
	$N_LC_LT_H$	45.77	1.34	5.72
	$N_HC_LT_L$	56.33	1.11	21.86
	$N_HC_HT_L$	77.42	0.83	8.36
	$N_HC_HT_H$	86.95	0.95	5.67
	$N_HC_LT_H$	59.45	1.11	17.81

Table 2(a): Values of crushing strength (Cs), friability (Fr) and disintegration time (Dt) for paracetamol tablets for factorial experimental design for paracetamol tablets formulated with white T. yam starch binder

Starch disintegrant employed	Variables and combination codes	C_s	F_r	D_t
Yellow T. yam	$N_LC_LT_L$	34.08	1.34	8.82
	$N_LC_HT_L$	40.68	1.21	7.19
	$N_LC_HT_H$	64.15	1.23	3.22
	$N_LC_LT_H$	51.54	1.35	6.93
	$N_HC_LT_L$	35.75	1.16	14.30
	$N_HC_HT_L$	51.68	0.92	7.80
	$N_HC_HT_H$	64.61	0.94	6.13
	$N_HC_LT_H$	53.61	1.17	14.32

Table 2(b): Values of crushing strength (C_s), friability (F_r) and disintegration time (D_t) for paracetamol tablets for factorial experimental design for paracetamol tablets formulated with yellow T. yam starch binder

Starch disintegrant employed	Variables and combination codes	C_s	F_r	D_t
Rice	$N_LC_LT_L$	19.75	1.48	10.53
	$N_LC_HT_L$	34.42	1.21	8.92
	$N_LC_HT_H$	43.73	1.22	5.85
	$N_LC_LT_H$	33.73	1.41	9.35
	$N_HC_LT_L$	46.71	1.35	19.76
	$N_HC_HT_L$	59.62	1.24	8.37
	$N_HC_HT_H$	65.34	1.21	6.92
	$N_HC_LT_H$	52.59	1.38	15.85

Table 2(c): Values of crushing strength (C_s), friability (F_r) and disintegration time (D_t) for paracetamol tablets for factorial experimental design for paracetamol tablets formulated with rice starch binder

Starch disintegrant employed	Variables and combination codes	C_s	F_r	D_t
Corn	$N_LC_LT_L$	26.42	1.22	10.31
	$N_LC_HT_L$	34.87	1.00	8.34
	$N_LC_HT_H$	53.42	1.05	3.74
	$N_LC_LT_H$	38.86	1.23	6.72
	$N_HC_LT_L$	46.13	1.22	14.24
	$N_HC_HT_L$	60.30	0.99	7.08
	$N_HC_HT_H$	70.34	1.06	5.02
	$N_HC_LT_H$	61.72	1.26	13.48

Table 2(d): Values of crushing strength (C_s), friability (F_r) and disintegration time (D_t) for paracetamol tablets for factorial experimental design for paracetamol tablets formulated with corn starch binder

Starch disintegrant employed	Variable	Independent coefficient		
		C_s	F_r	D_t
White T. yam	N	21.51	-0.28	8.34
	C	20.77	-0.18	-8.73
	T	8.42	0.02	-2.99
Yellow T. yam	N	3.80	-0.24	4.10
	C	11.54	-0.18	-5.10
	T	17.93	0.02	-1.88
Rice	N	23.16	-0.04	4.06
	C	12.58	-0.19	-6.36
	T	8.72	-0.02	-2.40
Corn	N	21.23	0.01	2.68
	C	11.45	-0.21	-5.14
	T	14.16	0.04	-2.75

Table 3: Individual effects of nature (N), concentration (C) and type (T) of starch disintegrant on crushing strength (C_s), friability (F_r) and disintegration time (D_t) of paracetamol tablets

Starch disintegrant employed	Combination of variable	Interaction coefficient		
		C_s	F_r	D_t
White T. yam	N-C	3.53	-0.04	-4.09
	C-T	1.00	0.03	0.72
	N-T	-2.10	0.04	-0.38
Yellow T. yam	N-C	1.93	-0.06	-2.34
	C-T	0.27	-0.01	-0.94
	N-T	-2.54	0.00	1.05
Rice	N-C	0.25	0.05	-3.80
	C-T	-1.21	0.01	0.14
	N-T	-2.92	0.02	-0.28
Corn	N-C	-0.06	-0.01	2.67
	C-T	0.14	0.02	-0.58
	N-T	-1.34	0.01	1.34

Table 4: Interaction effects of nature (N), concentration (C) and Type (T) of starch disintegrant on crushing strength (Cs), friability (F_r) and disintegration time (D_t) of paracetamol tablets

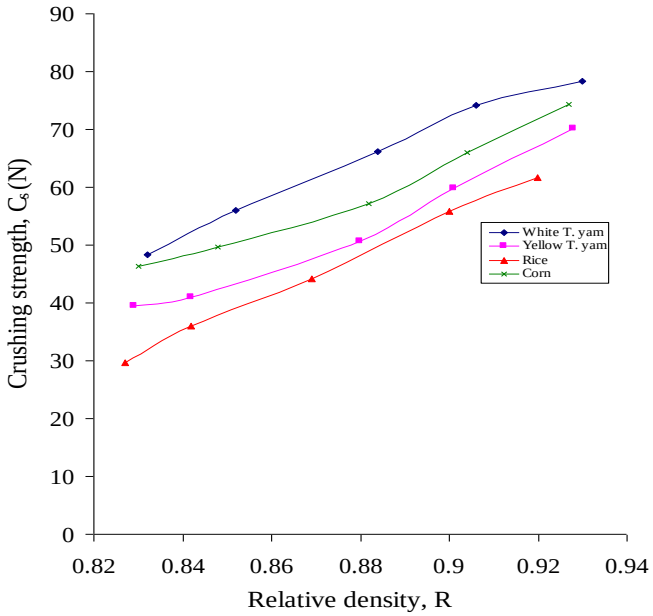

Figure 2: Plots of crushing strength (C_s) versus relative density (R) for paracetamol tablets formulated with 6% w/w natural starch exo-disintegrants.

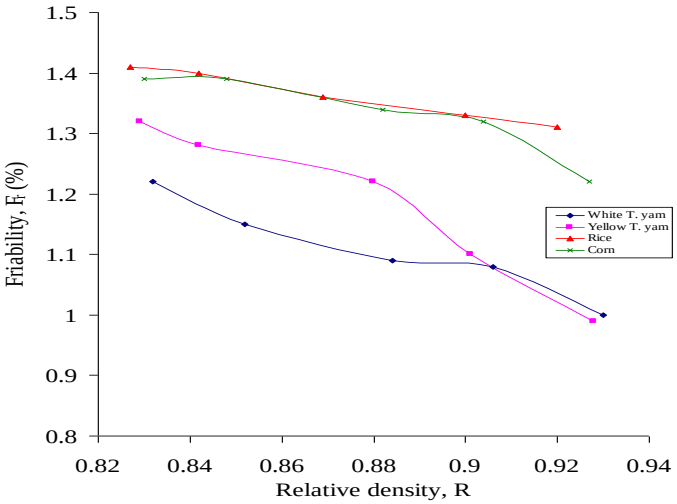

Figure 3: Plots of Friability (F_r) versus relative density (R) for paracetamol tablets formulated with 6% w/w natural starch exo-disintegrants.

DISCUSSION

Individual variables – nature (N), concentration (C) and type (T) of disintegrant– employed in the factorial experimental design, produced varying effects on the C_s, F_r and D_t. For all the starch disintegrants, nature of disintegrant generally exhibited the highest and positive effect on C_s. This implies that employing a heat-modified starch as a disintegrant instead of a natural one would increase the development of active disintegration mechanism within the tablets, possibly due to the higher swelling ability exhibited by heat-modified starches. Both the form and concentration of disintegrant had some negative effect on F_r. This means that, changing the disintegrant from natural to heat-modified and/or increasing the concentration from 3%w/w to 12%w/w, would reduce friability. On Dt, the form and concentration of disintegrant had positive and negative effects, respectively. That means that, changing the nature of disintegrant from heat-modified to natural starch would increase D_t while, increasing concentration from 3%w/w to 12%w/w would reduce it.

The type (that is, the mode of incorporation) of disintegrant exhibited the least individual effect on virtually all the parameters. This suggests that the type of disintegrant (T) is not as important as the nature of starch (N) and the concentration of starch (C) employed. It would appear therefore that N and C have to be selected before consideration is given to the mode of incorporation of the starch disintegrant. The variable, T remains important however as relatively small changes in value of disintegration parameters which can be brought about by the mode of disintegrant incorporation (T) selected can be crucial to the success or otherwise of tablet formulations developed. The mode of incorporation will of course have important interactions with other variables thus making it unwise to relegate it to minor consideration because of relatively low individual effects on parameters. The effect of T on Cs was considerable and positive, probably because, there were more interparticular contact points between the corn starch particles and the particles of other constituents of the tablets, which could have created more solid bonds and consequently, the higher Cs [29]. This could also account for some negative effects that T had on friability. Also, T had considerable but negative effects on D_t. This is probably so because for exo-disintegrants (as opposed to endo-disintegrants), a larger amount of starch disintegrant is initially exposed to the disintegrating medium, which would lead to the absorption of large quantity of water and subsequent production of higher swelling force. The results obtained showed that there were varying degrees of interaction effects of the variables– nature and concentration of starch disintegrant (N-C), concentration and type of starch disintegrant (C-T), and nature and type of disintegrant (N-T) – on the disintegrant activity of the starch disintegrants. The interactions between nature and concentration of disintegrant (N-C) were generally the highest and those between nature and type of the disintegrant (N-T) were generally the least. The implication is that C-T generally had the intermediate interactions. Thus the general ranking for the interactions would appear to be N-C > C-T > N-T. From these, it may be inferred that the concentration of disintegrant, C which is apparently involved in the two largest groups of interaction is generally the most important in influencing the effects of the variables on the disintegration properties of the various starches since it would influence the effects of the two other variables considerably. On the other hand, the type of disintegrant, T which appears to generally have the least interactions with the other variables coupled with its generally have the least individual effects, is the least influential variable. These findings can be useful in manipulating the variables to obtain desired disintegration properties for formulated paracetamol tablets. It should be remembered however that the foregoing evaluation is solely on determining the disintegrant properties of the different starches. The performance of the starches in real formulations containing other excipients will need to be taken into account.

Factorial experimental design was employed to assess the individual and interaction effects of some variables on disintegrant parameters, and on tensile strength, disintegration and dissolution times of formulated paracetamol tablets. The results indicate that these variables would have individual and interaction effects on all the parameters. The two effects are very important. While the individual effect can quickly show the magnitude of the effect of a variable on a parameter, the interaction effect is important in showing whether the particular individual effect is independent of the effects of other variables in the formulation or whether it is dependent on these other variables. The fact that an individual effect is largely independent can be very important in a practical way especially when the magnitude is large, because it can be used to solve particular problems. When an individual effect of a variable is dependent on the effects of other variables in the system, it cannot be considered in isolation regardless of its magnitude, because its effect will be influenced by the effects of the other variables. Thus, if any of these variables is changed or its concentration is altered, it will materially influence the effect of the particular individual effect in question, thus potentially reducing the significance of that individual effect.

CONCLUSION

The disintegrant activity of starches is determined by their nature, mode of incorporation and their concentration. 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. From factorial experimentation, the concentration of disintegrant seems to generally have the highest influence on the disintegrant activity of the tablets. Hence, care has to be taken when choices are to be made from the disintegrants studied in the present work in tablet formulation.

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