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Original Research Article

Evaluation of super-disintegrant potential of acid-modified starch derived from *Borassus aethiopum* (Aracaceae) shoot in paracetamol tablet formulations

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Abstract

Purpose: *To evaluate the super-disintegrant potentials of acid modified Borassus aethiopum starch (AMS) in comparison with native starch (NS) and commercial disintegrant sodium starch glycolate (SSG).*
Methods: *Compatibility of AMS with paracetamol powder was evaluated using Fourier transform infra-red (FTIR) spectrophotometry. Seven batches of paracetamol granules and tablets were prepared by wet granulation. AMS and NS were employed as disintegrants at concentrations of 2.43, 4.86 and 9.72 %w/w, respectively while 4.86 %w/w SSG was used as standard disintegrant. All the batches of the granules were compressed under the same compression settings. The properties of the granules as well as those of the tablets were assessed.*
Results: *AMS was compatible with paracetamol powder as no noticeable interaction was observed in FTIR study. The paracetamol tablets formulated using AMS as disintegrant demonstrated satisfactory friability, weight uniformity, hardness, and superior disintegration characteristics to the formulations containing NS and SSG as disintegrant. Even at a lower concentration (2.43 %w/w), AMS possessed better disintegrant property than NS and SSG. AMS and NS had dimensionless disintegrant quantity of 1.447 and 0.005, respectively. As expected, increase in AMS concentration showed a decrease in disintegration time.*
Conclusion: *AMS could be a potential low-cost super-disintegrant in formulation of paracetamol tablets.*

Keywords: *Acid modified starch, Borassus aethiopum, Disintegrant, Compatibility*

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INTRODUCTION

Disintegrants are added to solid dosage formulations to promote the break-up of the compacted mass into smaller fragments hence increasing the available surface area and promoting a more rapid release of the active ingredient [1]. Orodispersible dosage form; a product of novel technologies that involves fast disintegration and dissolution of the dosage form

is receiving more attention in recent times [2-4]. This type of property in dosage form can be attained by addition of super-disintegrant. Super-disintegrants are generally used at low concentrations (1 - 10 %w/w) in the dosage forms [5].

Among other industrial applications, starch, the second most abundant biomass material in nature is one of the oldest disintegrant, however, in recent times, modified starches like sodium starch glycolate offer more improvements over native starch as super-disintegrants. Modification techniques alter the starch polymer, making it highly flexible and changing its physicochemical properties and structural attributes to increase its value for biopolymer industries [6-8]. Acid hydrolysis is a chemical modification which introduce functional groups into the starch molecule using derivatization or involve breakdown reactions. Studies have shown that acid hydrolysis leads to changes in physical and chemical properties without destroying its granular nature. It also leads to increase crystallinity, increase solubility and gel strength, decrease viscosity and slight increase in flow properties [9-11,].

Recently, *Borassus aethiopum* starch has been modified by acid hydrolysis using 6 % w/v HCl at 37 ± 2 ºC for 192 h [11]. The physicochemical properties and microbiological quality of the Borassus *aethiopum* shoot acid-modified starch (AMS) were evaluated for its potential pharmaceutical applications. The study revealed that AMS met United States Pharmacopoeia microbiological quality requirements and there was increased aqueous solubility, increased crystallinity and slight increase in flow properties. Furthermore, there was a reduction in viscosity, hydration and swelling capacities as well as amylose content upon modification. So far, pharmaceutical application of AMS as a pharmaceutical excipient has not been studied. Thus, in this present study, AMS has been evaluated as super-disintegrant in paracetamol tablet formulations. The disintegrant potential was compared with that of the unmodified starch and a commercial paracetamol tablet formulation containing sodium starch glycolate as disintegrant. The disintegration efficiency ratio (DER) and dimensionless disintegrant quantity (DER_C) were also reported.

EXPERIMENTAL

Materials

Paracetamol powder, polyvinylpovidone 30 (PVPK30), sodium starch glycolate, magnesium stearate and pregelatinised starch were gift samples from Phamatex Industry Limited, Lagos Nigeria. All other chemicals used were of analytical grade. Acid modified *Borassus aethiopum* shoot starch (AMS) was prepared in the Pharmaceutical Technology Laboratory of Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, University of Lagos, Nigeria. The isolation procedure as well as the physicochemical properties of AMS have been reported in a previous study [11].

Compatibility studies

FTIR technique was employed for paracetamol-AMS compatibility studies. FTIR analysis was carried out using FTIR spectrophotometer (Bruker, South Africa). Five milligrams of AMS and paracetamol powder were individually blended with solid potassium bromide (KBr) (≈ 50 mg) and compressed into discs. Also physical mixtures (1:1) of AMS and paracetamol powder (≈ 5 mg) were blended with solid KBr (≈ 50 mg) and compressed into disc. The spectra were obtained over a wavelength range of 500 - 4000 cm^{-1} under dry air at room temperature.

Preparation of paracetamol granules and tablets

Seven batches of paracetamol granules were prepared (Table 1). Appropriate quantities of paracetamol, pregelatinised starch and test starch (intra-granular disintegrant) were loaded into a rapid mixer granulator (Lab/Betochem, Gujarat 393002, India) and mixed for 30 min. PVPK30 was sifted through a sieve (420 µm) and collected separately in a plain transparent polythene. Distilled water was heated to 90 ºC and the PVPK30 was added to it under stirring till it dissolved. The resulting contents were added into the rapid mixer granulator and mixed intermittently in order to get uniform distribution of the paste throughout the dry mix for 5 min. The sides were scraped and the mixing continued for another 3 min. The high-speed mixer was unloaded and the content transferred into the fluidized bed dryer (Lab/Betochem Gujarat 393002, India) bowl to dry with the inlet temperature of 65 ± 2 ºC for 60 min. The dried granules were passed through #20 sieve (841 µm) on a vibratory sieve shaker (Lab/Betochem Gujarat 393002, India) and the sifted granules was collected separately in a plain transparent polythene. Test starch (extra-granular disintegrant) was then mixed with the granules in a cage blender for 15 min before adding magnesium stearate.

Pre-compression evaluations were carried out on the granules after which they were compressed in a single rotary compression machine (/BB/D/B/ ADEPT Mumbai, India) fitted with 12.5 mm round flat lever press punches with a compression pressure of 7 KN. All the batches of the granules were compressed under the same compression settings.

Pre-compression studies

The pre-compression studies were carried out for the seven batches of the granules. The moisture content of each batch of the granules was determined using a Sigmum test AG moisture balance (Sartorius AG, Germany) in triplicates. Three milligrams of the granule was placed in the pan of the moisture balance and the machine was then set to determine the moisture content. The readings were taken when the machine automatically stopped after 15 min.

The bulk and tapped densities were determined as reported in a previous study while the Carr's index and Hausner's ratio were derived from the values of bulk and tapped densities [12].

Post-compression studies

Physicochemical characteristics

The post-compression studies were carried out for the seven batches of the paracetamol tablet formulations. Tablet thickness, uniformity of weight, crushing strength and friability were carried out using standard procedures [12]. The means and standard deviations of each parameter were determined.

Briefly, the thickness of each of ten randomly selected tablets per batch was measured using Vernier caliper (Digital/ Whitworth Hardinsburg, KY, 40143). For uniformity of weight, the weight of twenty tablets from each batch was determined using weighing balance (Ana ML-204/ Mettler Toledo Royston SG8 5HN, UK). The crushing strength of twenty tablets randomly selected from each batch was determined using an auto hardness tester (Digital automato/ Erweka 63150 Heusenstamm, Germany) while friability test was determined using friabilator (Ef-2w/ Electrolab Navi Mumbai- 400710, India).

Disintegration studies

The disintegration time for six tablets per batch was determined according to B.P method [13] using disintegration tester (USD ED 2L/ Electrolab Navi Mumbai- 400710, India). The disintegration efficiency ratio (DER) and dimensionless disintegrant quantity (DER_C) were calculated using equations 1 and 2 [14].

$$DER = (C_a/F_r)/D_T \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(1)$$

$$DER_C = DER_{sample}/DER_{standard} \quad \ldots\ldots\ldots\ldots\ldots(2)$$

where C_a is crushing strength, F_r is friability and D_T is disintegration time.

Dissolution studies

Dissolution rate was carried out using the paddle type dissolution tester (TDT 08L, Dissolution tester, Electrolab, Mumbai, India) following B.P specifications [13].

The dissolution medium used was 900 mL of phosphate buffer pH 5.80, thermostatically maintained at 37 ± 0.5 °C at 50 rpm paddle speed. One tablet was placed into each glass jar.

Table 1: Composition of the seven batches of the paracetamol granules/tablet formulations

Ingredient	A (%)	B (%)	C (%)	D (%)	E (%)	F (%)	G (%)	Function
Paracetamol	89.29	89.29	89.29	89.29	89.29	89.29	89.29	Active
PGS	5.97	3.54	0.00	5.97	3.54	0.00	3.54	Diluent
SSG (I)	0.00	0.00	0.00	0.00	0.00	0.00	1.28	Disintegrant
AMS (I)	0.64	1.28	2.71	0.00	0.00	0.00	0.00	Disintegrant
NS (I)	0.00	0.00	0.00	0.64	1.28	2.71	0.00	Disintegrant
PVPK30	1.78	1.78	1.78	1.78	1.78	1.78	1.78	Binder
SSG (E)	0.00	0.00	0.00	0.00	0.00	0.00	3.58	Disintegrant
AMS (E)	1.79	3.58	7.05	0.00	0.00	0.00	0.00	Disintegrant
NS (E)	0.00	0.00	0.00	1.79	3.58	7.05	0.00	Disintegrant
Magnesium stearate	0.53	0.53	0.53	0.53	0.53	0.53	0.53	Lubricant

PGS is pregelatinised starch, SSG (I) is sodium starch glycolate granules mixed intra-granularly, SSG (E) is sodium starch glycolate granules mixed extra-granularly, AMS (I) is acid modified starch granules mixed intra-granularly, AMS (E) is acid modified starch granules mixed extra-granularly. NS (I) is native starch granules mixed intra-granularly, NS (E) is native starch granules mixed extra-granularly PVPK30 is polyvinylpovidone 30, Batches A to C containing different concentrations of AMS, Batches D to F containing different concentrations of NS while G is the standard containing SSG as disintegrant

Samples of the dissolution medium (5 mL) was withdrawn at 30 min interval and diluted to 100 mL spectrophotometrically analysed for paracetamol at 257 nm wavelength. The medium was replenished with 5 mL of the buffer solution after each sample collection.

Statistical analysis

OriginPro 2016 (64-bit) Software OriginLab Corporation Northampton, MA 01060 USA was used for descriptive and inferential statistics. Comparison with the standard was evaluated using one-way analysis of variance. P value (< 0.05) was considered statistically significant.

RESULTS

Compatibility of modified starch

The FTIR spectra of AMS, paracetamol powder (PCM) and physical mixtures (1:1) of AMS and paracetamol (AMS + PCM) are presented in Figure 1. FTIR spectrum of pure paracetamol displayed a characteristic vibrational broad peak at about 3336.68 cm^{-1} for O-H and that for CH_3 stretching at 3151.34 cm^{-1}. Vibrational peaks of carbonyl group C=O was shown by 1673.49 cm^{-1} stretching. At 691.19 cm^{-1} a para-disubstituted aromatic ring was observed.

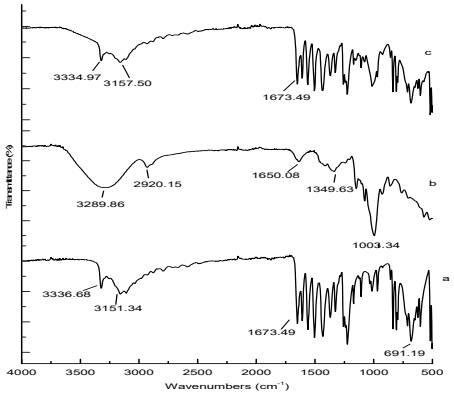

Figure 1: FTIR spectra of (a) Paracetamol, (b) Borassus acid modified starch (AMS), and (c) mixture of Paracetamol and AMS

Properties of paracetamol granules

Table 2 shows some of the physicochemical parameters of the granules. The bulk density (g/mL) of the granules varied from 0.53 to 0.67 while that of the tapped density varied from 0.59 to 0.82 g/mL. The moisture content of the granules fell within 1.03 and 3.04 %. The Carr's index (%) of the granules formulated varied from 10.52 to 23.78 % while the Hausner's ratio varied from 1.11 to 1.32.

Post-compression characteristics of paracetamol granules

The results of the post-compression parameters of the tablets are presented in Table 3. Tablet thickness varied from 4.12 to 4.20 mm while uniformity of weight ranged from 5.57 to 5.61 g. The friability of tablets formulated with AMS and NS varied with increasing disintegrant concentration though there was significant variation ($p < 0.05$) compared to standard in both cases.

The disintegration time for tablets containing AMS and NS decreased as the concentration of disintegrant was increased and crushing strength varied with increase in the disintegrant concentration. The disintegration efficiency ratio (DER) and dimensionless disintegrant quantity are presented in Table 3. The DER and DERc values calculated increased with an increase in disintegrant concentration for tablets containg AMS while those containing NS were aproximately. All the batches released over 97.00 % of the active drug within 30 min.

DISCUSSION

Similar peaks were observed for the sample containing pure paracetamol and that containing mixture of paracetamol and AMS. Since the two spectra had no significant difference in both transmittance and wavenumbers, it could be concluded that paracetamol is compatible with AMS. Comparison of the bulk and tapped densities gives an idea of inter-particulate interactions influencing the bulking properties of a powder as well as its flow characteristics. Carr's index and Hausner's ratio derived from bulk and tapped densities are measures of the propensity of a powder to be compressed as well as its flow characteristics [15]. Based on the Carr's index and Hausner's ratio values for the granules, batches A, B, C, E and F had good flow properties while batches E and D had fair to passable flow [16]. The higher values of the Carr's index and Hausner's ratio of the granules containing SSG as disintegrant might be attributed to the higher moisture content (Table 2) observed for the granules containing SSG as the disintegrant.

The granules contain 2 % moisture which is required for binding of the granules during compression in the die cavity. Upon granulation, there were remarkable improvement in the flow properties of the granules containing AMS as

Table 2: Physicochemical properties of granules prepared with different concentration of disintegrants

Batch	Bulk Density (g/mL)±SD	Tapped Density (g/mL) ± SD	Moisture Content (%) ± SD	Carr's Index (%)	Hausner's Ratio
A	0.53 ± 0.00	0.59 ± 0.00	1.30 ± 0.28	10.52	1.12
B	0.53 ± 0.00	0.63 ± 0.00	1.03 ± 0.37	15.79	1.19
C	0.59 ± 0.05	0.69 ± 0.03	1.11 ± 0.21	14.51	1.17
D	0.65± 0.08	0.79± 0.14	2.03± 0.31	21.54	1.26
E	0.67± 0.13	0.82± 0.14	2.52± 0.25	18.29	1.22
F	0.64± 0.09	0.81± 0.24	3.04± 0.65	17.28	1.27
G	0.63 ± 0.02	0.82 ± 0.01	2.01 ± 0.15	23.78	1.32

**SD is the standard deviation and n = 3. Batches A to C containing different concentrations of AMS, Batches D to F containing different concentrations of NS while G is the standard containing SSG as disintegrant*

Table 3: Properties of paracetamol tablets formulated with different concentrations of disintegrants

Parameter	A	B	C	D	E	F	G
Crushing strength[a] (kgf) ± SD	9.76 ± 0.72	9.42 ± 0.69	7.35 ± 0.57	6.25 ± 0.44	5.95 ± 0.67	5.45 ± 0.19	5.85 ± 0.41
Friability test[b] (%)	0.63 ± 0.08	0.71 ± 0.08	0.65 ± 0.09	0.70 ± 0.07	0.68 ± 0.06	0.69 ± 0.05	0.24 ± 0.02
Disintegration time[c] (Secs)±SD	56.92± 2.23	45.58± 3.23	21.83±2.21	630.66±46.24	610.98±50.24	600.86±45.29	130.04±56.24
Weight[d] (mg) ± SD	561.1±3.47	561.1±3.98	559.0±2.58	562.12±2.53	563.12±1.89	562.12±0.99	566.92±1.62
Thickness[e] (mm) ± SD	4.10± 0.03	4.10± 0.03	4.12± 0.03	4.12± 0.04	4.12± 0.05	4.13± 0.05	4.04± 0.02
Disintegration efficiency ratio	2.72	2.91	5.18	0.01	0.01	0.01	1.88
Dimensionless disintegrant quantity	1.447	1.548	2.755	0.005	0.005	0.005	-
% Dissolved[f] at 30 min	101.37±1.25	101.29±1.27	98.29±2.21	97.29±3.17	99.29±1.47	99.29±2.37	97.97±0.97

** SD is the standard deviation. For superscripts: a, n = 20; b, n = 20; c, n = 6; d, n = 30; e, n = 10; f, n = 3. Batches A to C containing different concentrations of AMS, Batches D to F containing different concentrations of NS while G is the standard containing SSG as disintegrant*

disintegrant compared to AMS primary powders [11]. The mean weight of all the batches passed the uniformity of weight specifications since the ranges of deviation of the tablets weight for the whole batches produced were within the specified limit [13]. British Pharmacopoeia stipulates that no individual weight should deviate by more than 10 % and that not more than two of the individual weights should deviate from the mean weights by more than ± 5 % [13].

Tablet thickness is important in producing tablets identical in appearance and to ensure that every production lot will be usable with selected packaging components. The variation in the thickness of the tablets was insignificant since the values of their standard deviation was low. Also, when compared with the standard, the difference observed was insignificant for the tablets prepared using different concentrations of the test disintegrant. The data for tablet thickness also conformed to the report of Troy, which states that the range of tablet thickness should be within ± 5 % [17].

The crushing strength values of all the batches were within acceptable range. Crushing strength above 4 kgf is considered satisfactory for compressed tablets [18]. Generally, the crushing strengths of tablets containing AMS as disintegrant were higher. This is likely due to low moisture content of the granules containing AMS (Table 2) and decrease in the amylose content of the acid modified starch (11). The crushing strength of the granules decreased with increase in the test disintegrant concentrations. All the seven batches of the granules had acceptable friability values according to official specifications. BP [13] specifies values below 0.8 % loss in weight of the tested tablets without lamination, capping or breaking while USP [16] specifies values below 1 % to be acceptable. The friability of the batches varied and was higher for the batches containing the test disintegrants compared to the standard which explains that the

tablets produced were more friable than the standard.

According to the BP [13], the disintegration time should be in less than 15 min for uncoated tablets. All the batches passed this test as they all disintegrated in less than 15 min. With respect to fast disintegrating tablets, the three batches containing AMS and the batch containing SSG met the requirement for super-disintegrants as they disintegrated within 3 min [19]. However, the three batches containing different concentrations of the AMS disintegrated within 1 min while the standard formulation had disintegration time of above 2 min. It was observed that an increase in concentration of the AMS disintegrant showed a decrease in disintegration time.

Disintegration efficiency ratio (DER) is a measure of the balance between mechanical and disintegrant property of tablets [14]. The DER values increased with increase in the concentration of AMS disintegrant. At the same disintegrant concentration, there was over 250 % difference between the DER values of the test formulation and the standard, the AMS showed better disintegration efficiency. However, formulations containing NS disintegrant did not meet the requirement for super- disintegrants. The dimensionless disintegration quantity, DERc, is a measure that compare the efficiency of the test and standard tablet disintegrants.

A value of DERc greater than 1 indicates that the DER of the experimental starch is better than that of the standard disintegrant [14]. Even at lower concentration of AMS, the DERc value was 1.45, thus confirming that the experimental starch (acid modified *B. aethiopum* shoots) possessed a better disintegrant property than the standard (sodium starch glycolate). In the case of formulation containing NS, the DERc value was 0.005, thus confirming that SSG possessed a better disintegrant property than NS. The excellent disintegration potential of AMS might be attributed to those desirable physicochemical parameters of AMS with respect to tablet disintegration reported in the previous study [11].

All the seven batches had acceptable dissolution rate [13]. It can be observed from the results obtained that the dissolution of paracetamol tablets corresponded with the disintegration – dissolution theory which proves that disintegration usually play a vital role in dissolution process since it determines to a large extent the area of contact between the solid and the liquid media [20].

CONCLUSION

The results show that the low-cost acid-modified starch (AMS) obtained by acid hydrolysis of *Borassus aethiopum* shoot native starch has superior disintegrant property to a commercial brand of sodium starch glycolate at the same concentration in paracetamol tablet formulations. Thus, acid modified *Borassus aethiopum* starch is a potential low-cost super-disintegrant for the manufacture of solid dosage forms.

DECLARATIONS

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Conflict of interest

No conflict of interest is associated with this study.

Contribution of authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. CPA and UCU conceived and designed the study, ARA collected and analysed the data, CPA and IMC wrote the manuscript. All authors read and approved the manuscript for publication.

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