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Research Article

EVALUATION OF ACID HYDROLYSED STARCH DERIVED FROM *DIGITARIA IBURUA* AS BINDER

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ABSTRACT

Objective: This research work was aimed at investigating the binding properties of Digitaria iburua starch (DS) and acid hydrolyzed starch or microcrystalline starch (MCS) in the formulation of metronidazole (MET) tablet comparing it with gelatin (GLT) as a standard binder.

Methods: DS was obtained from steeping the D. iburua grains in water. MCS was produced using 6 N HCl at 50°C for 24 hrs. The dilution potential test was conducted. MET granules of binder concentrations (2.5, 5.0, 7.5, 10.0 and 12.5% w/v) of DS and MCS was prepared by wet granulation method and compared with GLT. The granules flow properties were evaluated. The particle size distribution of the granules was determined. The quality of tablets was assessed by standard methods.

Results: A yield of 62.88% w/w DS was obtained whereas MCS was found to be 85.14% w/w. The MCS was unable to bind MET at all ratios. The granules had good flow and compressible properties and are uniformly distributed. The crushing strength (CS) of the binder types is ranked: GLT>MCS>DS. The friability (FR) values decreased with increase in binder concentration for all binder types. Only FR at 12.5% w/v of MCS and GLT was <1%. The disintegration time (DT) increased with increase in binder concentration. The (CS/FR)/DT values of DS and MCS obtained >2.

Conclusion: The Carr's index, Hausner's ratio and (CS/FR)/DT values suggests that DS and MCS are poor binders.

Keywords: Acid hydrolyzed starch, Excipients, Digitaria iburua, Metronidazole.

INTRODUCTION

Several starches obtained from different food crops have shown enough potential as excipients in tablet formulations [1]. A binder is a ductile material that is prone to undergo plastic (irreversible) deformation. An extensive knowledge of the significance of binding properties is necessary to determine the choice of a suitable binder for a tablet formation. Binders are either added as a solution or as a solid into a powder mix to ensure that granules and tablets can be formed with the required mechanical strength.

Starch is commonly used in an amount of 5-15% when it functions as a binder [2]. All percentages, unless specified are percentage by weight based on the total weight of the compressed solid dosage form. The role of tablet excipients is to ensure that the tablet operation can run satisfactorily and to ensure that tablets of specified quality are prepared [3]. Modification of starch involves altering the structure and affecting the hydrogen bonding in a controllable manner to enhance and extend their application.

This research work was aimed at investigating the binding properties of native and acid hydrolyzed starches derived from Digitaria iburua in formulation of metronidazole (MET) tablet comparing it with gelatin (GLT) as a standard binder.

METHODS

Materials

D. iburua grains were obtained from a village in Samaru, Zaria-Nigeria. Maize starch BP was sourced from BDH Chemicals Ltd., Poole-England. Chemicals used include-hydrochloric acid, talc, magnesium stearate and sodium hydroxide; all from BDH Chemicals Ltd., Poole-England. All other reagents and solvent used were of pharmaceutical or analytical grade.

Collection and identification of *D. iburua* grains

D. iburua grains were obtained from a commercial source in Samaru, Zaria-Nigeria. The grains were identified, authenticated and assigned a voucher number 1315 by the taxonomist in the herbarium unit of the Department of Biological Sciences, Ahmadu Bello University, Zaria, Nigeria.

Extraction of *D. iburua* starch (DS) and preparation of microcrystalline starch (MCS)

The DS was extracted from the grain [4]. The gelatinization temperature was determined [5] before production of MCS using 6 N HCl [5] at 24 hrs of hydrolysis.

Dilution potential

A binary mix of the drug and the hydrolyzed starch was carried out in the following ratios: 10:90, 20:80, 30:70, 40:60, 50:50, 60:40, 70:30, 80:20 and 90:10. It was then compressed at varying compression loads on a single punch tableting machine (T**ype** Eko, Erweka-Apparateu-G.m.b.H Heusenstamm, Germany). The crushing strength (CS) of each binary mix was determined and recorded.

Preparation of granules

The wet granulation method was used in the preparation of MET granules. 400 mg MET powder and 5.0% w/w maize starch BP were weighed appropriately and dry mixed for 5 minutes in a mortar with pestle until fine powder was obtained. An appropriate quantity of binder of concentration of 2.5, 5.0, 7.5, 10.0 and 12.5% w/v was prepared and added depending on the batch to produce a moist and cohesive mass. The wet mass was then passed through a 1.7 mm sieve mesh screen and then oven dried at 40°C for 30 minutes after which they were re-screened through a 1.6 mm mesh size and further dried for another 30 minutes. The granules were allowed to cool and stored in an airtight container.

Analysis of MET granules

The granules were subjected to the following tests: Sieve analysis, angle of repose, bulk and tapped densities Carr's index (CI) and Hausner's ratio (HR).

Particle size analysis

The particle size analysis of MET granules was determined [6] at 7.5% w/v binder concentration.

Angle of repose
A glass funnel of orifice diameter 0.8 cm was plugged and clamped at a height of 10 cm on a flat laboratory bench. A 20 g granule sample was weighed and placed in the funnel and then allowed to flow freely. The angle of repose was calculated from the equation: –

$$\theta = \mathrm{Tan}^{-1}\left(\frac{2h}{D}\right) \quad (1)$$

Where,
h=height of heap and D is the diameter. It was repeated thrice and the average were calculated.

Flow rate
The flow rate of MET granules was determined [6]. The flow rate was estimated as the ratio of mass (g) to time (seconds). The mean of three determinations was recorded.

$$\text{Flow rate} = \frac{\text{Weight of powder (g)}}{\text{Time of flow (seconds)}} \quad (2)$$

Bulk and tapped densities
A 50 g granule sample was weighed and poured into a 100 ml glass measuring cylinder. The cylinder was dropped on a wooden platform from a height of 2.5 cm 3 times at 2 seconds intervals. The bulk volume was recorded as the volume occupied by the starch. The bulk density was calculated as the ratio of the weight of starch sample to the volume occupied in the cylinder. The cylinder was then tapped uniformly on the wooden platform until the volume occupied by the powder became constant. The tapped density was calculated as the ratio of weight to volume. The values obtained used in calculating the CI and HR using the equations below:

$$\text{Carr's Index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density} \times 100\%} \quad (3)$$

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Bulk density}} \quad (4)$$

Compaction of granules to tablets
The granules were mixed in a tumble mixer for 5 minutes with 2.0% w/w dried talc, 0.2% w/w magnesium stearate and 7.8% w/w maize starch BP. The granules were compressed at 7.0 metric tones using 12.5 mm normal concave-faced punches on a single punch tablet machine (Type Eko Erweka Apparatebau. G.m.b.H Heusentamm, Germany). 15 batches each containing 400 mg MET tablets were prepared using the tablet batch formula in Table 1. Each batch consisted of 100 tablets.

Quality control tests
Quality control tests were conducted for all batches of tablets produced after 48 hrs of production.

Weight uniformity test
Twenty tablets from each batch were randomly selected and weighed together and then individually using an analytical balance (Mettler Analytical Balance Philip Harris Ltd., England). Their mean weight was determined based on the official book [7].

Thickness and diameter measurement
The thickness and diameter of five tablets from each batch were measured using a digital caliper. A mean of five determinations was obtained and recorded.

CS test
Five tablets were randomly selected from each batch, and the CS was determined using Monsanto hardness tester (Monsanto Chemical Corp., USA). The unit of measurement is kilogram force (Kgf).

Friability (FR) test
Ten tablets randomly selected from each batch were dusted, weighed and then subjected to abrasion shock in an Erweka Friabilator operated at 25 revolutions per minute for 4 minutes. The tablets were then dusted again and reweighed. The percentage loss in weight was determined for each batch of tablets.

Disintegration time (DT) test
The DT for each batch of tablets was determined in distilled water at 37±0.5°C using the Erweka distintegration test apparatus (Type ZT3, Erweka-Apparatebau-G.m.b.H Heusenstamm, Germany). Six tablets were tested, and the time taken for each tablet to break into small particles and pass through the mesh was recorded as the DT.

Data analysis
Statistical analysis was carried out to compare the tableting properties of DS/MCS/GLT at 2.5-12.5% w/v binder concentration in the formulation of MET tablets using correlation analysis as a statistical tool. Correlations were considered significant at the 0.01 level.

RESULTS AND DISCUSSION

Extraction of DS and preparation of MCS
Table 2 shows that a greater percentage yield of MCS (85.14%) was obtained when compared to DS (62.88%). The gelatinization temperature was 56°C.

Dilution potential
The results for dilution potential are displayed on Table 3 and the results show that MCS was unable to bind MET thus compressibility was not achieved at all ratios. The result obtained from the dilution potential test

Table 1: The tablet formula for studying the binding properties of DS and MCS

Ingredient	Percentage
Metronidazole	57.14 w/w
Maize starch BP	5.0 w/w
*Binder (DS/MCS/GLT)	(2.5, 5.0, 7.5, 10.0, 12.5) w/v
Dried talc	2.0 w/w
Magnesium stearate	0.2 w/w
Maize starch BP	7.8 w/w
Lactose	q.s
Total weight	700 mg

*: Binder concentrartion, DS: Digitaria iburua starch, MCS: Microcrystalline starch, GLT: Gelatin

Table 2: Data of production of DS and MCS

Properties	Result
Percentage yield (% w/w)	62.88
Gelatinisation temperature	56°C
Percentage yield after hydrolysis at 24 hrs (% w/w)	85.14

DS: Digitaria iburua starch, MCS: Microcrystalline starch

Table 3: Dilution potential for MET:MCS

Binary mix (MET:MCS)	Crushing strength (Kgf)	Compressibility description
10:90	3.5	Fair
20:80	3.0	Fair
30:70	3.0	Fair
40:60	2.5	Poor
50:50	2.0	Poor
60:40	2.0	Poor
70:30	1.5	Poor
80:20	1.5	Poor
90:10	1.0	Poor

MET: Metronidazole, MCS: Microcrystalline starch

showed that the hydrolyzed starch is a poor direct compressible material because compressibility was not achieved at all ratios. Thus, the wet granulation method of tablet production was adopted for further study.

Analysis of granules

The result of the particle size distribution of granules at 7.5% w/v formulated with DS and MCS is displayed in Fig. 1. The result showed that granules sizes are uniformly distributed.

The angle of repose and flow rate were the indices used to assess the flow rate while CI and HR are used to assess compressibility of the granules as presented in Table 4. The values of angle of repose obtained was <50° which reflects satisfactory flow properties [8]. The CI and HR values obtained were <28% and 1.20 respectively thus have satisfactory compressible property [9]. The CI and HR for the materials are ranked in the order; GLT<MCS<DS. The percentage compressibility (CI) and ultimately the HR express the difference between the bulk and tapped densities and the ratio of tapped to bulk density. These indices give a measure of the ability of a material to be reduced in volume under

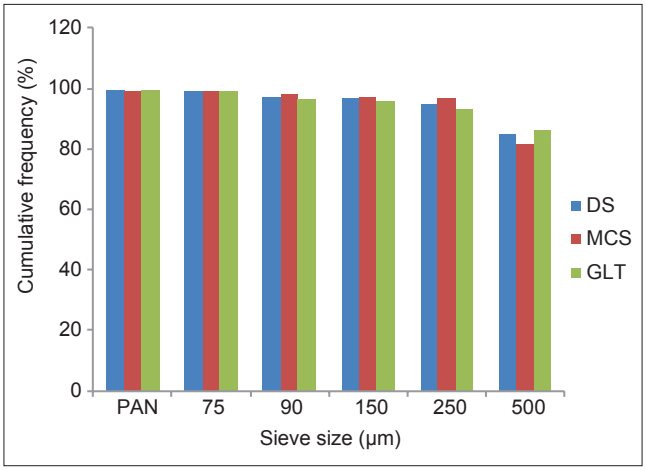

Fig. 1: Graph of cumulative oversize distribution of granules

Table 4: The effects of binder concentration (% w/v) on the physical properties of granules

Binder concentration (% w/v)	Angle of repose (°)	Flow rate (g/second)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	CI (%)	Hausner's ratio
2.5%						
DS	33.33	4.27	0.05	0.56	10.71	1.12
MCS	30.07	4.32	0.54	0.59	8.47	1.09
GLT	35.29	3.20	0.42	0.45	7.10	1.07
5.0%						
DS	34.52	2.97	0.45	0.51	11.76	1.13
MCS	30.07	4.03	0.54	0.61	11.48	1.13
GLT	36.03	2.89	0.42	0.44	4.50	1.05
7.5%						
DS	33.34	3.31	0.46	0.53	13.21	1.15
MCS	32.62	4.26	0.53	0.59	10.17	1.11
GLT	31.19	2.79	0.43	0.48	10.41	1.12
10.0%						
DS	34.03	3.36	0.46	0.51	9.80	1.11
MCS	32.28	4.29	0.51	0.59	13.56	1.16
GLT	28.70	2.86	0.46	0.51	9.80	1.11
12.5%						
DS	32.33	3.68	0.46	0.53	13.21	1.15
MCS	31.76	4.30	0.51	0.59	13.56	1.16
GLT	31.20	2.90	0.46	0.54	10.42	1.16

DS: Digitaria iburua starch, MCS: Microcrystalline starch, GLT: Gelatin, CI: Carr's index

Table 5: QC tests conducted on tablets produced by wet granulation

Binder concentration (% w/v)	Mean weight (mg)	Thickness (mm)	Diameter (mm)	CS (kgf)	FR (%)	DT (minutes)	CS/FR	(CS/FR)/ DT
2.5%								
DS	705±6.42	5.49±0.07	12.10±0.004	9.77±0.145	1.44±0.012	0.19±0.006	6.78	33.68
MCS	714±5.54	5.52±0.09	12.10±0.008	11.17±0.167	1.39±0.007	0.55±0.020	8.04	14.62
GLT	723±4.17	5.67±0.04	12.09±0.003	10.17±0.167	1.61±0.003	2.42±0.015	6.32	2.61
5.0%								
DS	693±5.54	5.33±0.03	12.09±0.003	10.17±0.333	1.43±0.006	0.27±0.012	7.11	26.34
MCS	681±6.30	5.21±0.03	12.10±0.010	11.50±0.289	1.80±0.104	2.50±0.006	6.39	2.56
GLT	697±6.85	5.55±0.02	12.09±0.003	11.17±0.167	1.30±0.006	4.30±0.029	8.59	2.00
7.5%								
DS	700±6.53	5.45±0.03	12.10±0.004	10.73±0.145	1.42±0.017	0.34±0.015	7.55	22.22
MCS	721±3.94	5.37±0.07	12.09±0.005	12.16±0.167	1.25±0.009	3.41±0.015	9.73	2.85
GLT	705±4.44	5.61±0.06	12.10±0.004	11.50±0.000	1.08±0.012	11.57±0.059	10.65	0.92
10.0%								
DS	712±5.63	5.47±0.09	12.10±0.004	11.00±0.000	1.11±0.018	0.36±0.006	9.91	27.52
MCS	724±4.55	5.49±0.04	12.10±0.012	12.33±0.167	1.02±0.035	4.10±0.009	12.09	2.95
GLT	713±6.48	5.49±0.11	12.09±0.005	12.50±0.289	1.05±0.006	15.18±0.040	11.90	0.78
12.5%								
DS	707±6.58	5.42±0.06	12.09±0.003	11.67±0.167	1.04±0.038	0.49±0.006	11.22	22.90
MCS	719±6.07	5.56±0.12	12.09±0.003	12.50±0.000	0.97±0.003	4.12±0.006	12.89	3.12
GLT	696±4.61	5.51±0.05	12.09±0.005	12.50±0.289	0.87±0.012	23.41±0.318	14.37	0.61

DS: Digitaria iburua starch, MCS: Microcrystalline starch, GLT: Gelatin

pressure and the indication of the likely flow behavior of granules when subjected to compression forces to form a compact mass. Granules with a low CI value have a predicted good flow property [10]. GLT had the lowest CI.

At all binder concentrations, a strong positive correlation is noticed when GLT is compared with DS and MCS (>0.990) except at 5% w/v concentration (0.975 and 0.966). A much stronger correlation is noticed when MCS is compared with DS (>0.990). Thus, the correlation is significant at the 0.01 levels.

Quality control tests

Table 5 shows the result for tablet parameters. The values of the uniformity in weight for MET tablets produced ranged from 693 to 723 mg. The values are within the acceptable limits [7], for the respective weights of the tablets. Any variation in the weight of individual tablets is a valid indication of the corresponding variation in the drug content [11]. There is no official requirement for CS and FR [7]. The CS is the measure of the structural strength of the tablets [12]. The CS is the applied load that when applied diametrically to a tablet causes it to fracture. The CS values obtained increased as the binder concentration increased as shown and it is ranked in the order: GLT>MCS>DS. FR is a measure of the weakness of the tablets. It gives an indication of the likely edge damage that would occur when the tablets are handled during packing and dispensing. The FR test values obtained exceeded 1% except for tablets produced at 12.5% w/v binder concentration. The FR of tablets containing DS and MCS as binder far exceeded the limit of 1%. The time taken for a tablet to disintegrate when immersed in some test fluid should not exceed 15 minutes for uncoated tablets [7]. DS and MCS passed DT test at all binder concentration. GLT failed DT test at 10.0% w/v and 12.5% w/v. The DT test order for the materials was: GLT>MCS>DS. The CS/FR index increased with increase in binder concentration with GLT giving the highest CS/FR index and DS giving the least. (CS/FR)/DT is a better index of measuring the quality of tablets; it gives a balance between the binding and disintegration property of tablets [12]. It measures tablet strength and weakness and evaluates all negative effects of these parameters on the DT [13]. The (CS/FR)/DT values ranked in this order; GLT<MCS<DS.

There were slight variations in the mean weight and (CS/FR)/DT values of the tablets produced. The results were subjected to statistical analysis. The difference in the properties presented in Tables 5 when GLT is compared with DS/MCS was significant at $p \leq 0.05$ at the 95% confidence interval. There is a strong positive correlation when DS is compared with MCS.

CONCLUSION

Modification of DS by acid hydrolysis did not significantly improve the compressibility profile of the starch. The acid hydrolyzed starch is not a good direct compressible excipient because it failed the dilution potential test. The CI, HR and (CS/FR)/DT values suggest that DS and MCS are poor binders.

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