

Evaluation of the Disintegrant and Binding Properties of Avocado Seed Starch in Paracetamol Tablet FormulationsOsaretin D. Enadeghe^{1*}, Sylvester O. Eraga², Johnbull A. Obarisiagbon¹¹Department of Pharmaceutics and Pharmaceutical Technology, College of Pharmacy, Igbinedion University, Okada, Edo State, Nigeria.²Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, University of Benin, Benin City, Nigeria**ABSTRACT**

Starch is one of the most commonly used excipient as binder and disintegrant in tablet formulation. This study aims to investigate the disintegrant and binding properties of starch isolated from avocado (*Persea americana*) seeds in paracetamol tablet formulations. Starch extracted from avocado seed was used to prepare batches of paracetamol granules in varying amounts as disintegrant (2.5 - 15% w/w) and binder (5.0-15% w/v) using the wet granulation method. Granules formulated were assessed for their flow properties and drug-excipient interaction studies using differential scanning calorimetry (DSC) and Fourier transform infrared (FTIR) spectroscopy before compression into tablets. The formulated tablets were assessed for their tablet properties. All the batches of granules exhibited fair to good flow properties with Carr's indices $\leq 31.80\%$, Hausner's ratios ≤ 1.47 and angles of repose $\leq 30.26^\circ$. The formulated tablets were uniform in weights with hardness values ≥ 6.0 kp, friability values ranging from 0.14 - 1.56% and disintegration times from 0.25 - 1.66 min as well as variable drug release (72.78 - 90.67%) in 1.0 h of dissolution testing. Drug-excipient studies showed the absence of interaction between paracetamol and test starch. Tablets formulated with avocado (*Persea americana*) seed starch met pharmacopoeial specifications in their tablet properties and were also fast disintegrating. The starch may be a viable local source of a super-disintegrant.

Keywords: *Persea Americana*, starch, disintegration, dissolution, tablet properties

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Starch is a natural polysaccharide found in various parts of a plant such as seeds roots, bulbs, nuts etc, where they are stored as sources of energy.¹ It is usually extracted from these parts of plants and used in its native or modified form.² It has many uses in the agro-industry especially in the foods and pharmaceutical industries where it serves as a major ingredient or excipient. These numerous uses of starch are as a result of its availability, biodegradability, safety and cost-effectiveness.^{2,3}

Starch molecules have some unique physicochemical properties such as a gel former, hence their use as gel forming or thickening material in the pharmaceutical industry and as a stabilizer in the food or beverage industries.⁴⁻⁶ Starch has also been used in the formulation of immediate-release tablets, with the advantage of immediate drug release in the vicinity where the drug is absorbed.⁷

Maize is the most common source of starch, accounting for about 82% of total global production, followed by wheat, potatoes and cassava with individual amounts of about 5 - 8%. The estimated global starch market stands at 48.5 million tonnes and will have a yearly output of €15 billion by the year 2000.⁸ In Nigeria, the potential for national or local production of cheap medicines, as well as the development of less-costly excipients to meet the needs of local manufacturer, have been discussed and debated for many years.⁹

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The easy accessibility and availability of starches and their applications as food and pharmaceutical excipients make viable the search for other sources.

Avocado (*Persea americana* Miller) seeds are considered high in starch content (7.8-29.3%), depending on their variety.¹⁰⁻¹² This fact makes avocado seeds a promising alternative source of native starch. Also, the use of their seeds offers a solution to the problem of waste disposal since it is usually considered as waste in the processing of avocado fruits.

Though avocado starch is extensively employed in a variety of industrial applications especially in the food industry, it has received little attention as an excipient in the pharmaceutical industry, hence this study aimed at evaluating the disintegrant and binding potentials of starch extracted from avocado seeds in paracetamol tablet formulations.

Materials and methods**Materials**

The following materials were procured from local suppliers; paracetamol powder, lactose, maize starch BP, talc and magnesium stearate (Qualikens Chemical Industries, New Delhi, India). Avocado fruits harvested in February 2022, within the gardens of Edo State Medical Stores Complex, Benin City, Nigeria (6.3350° N, 5.6037° E) were sliced open and their seeds collected. The seeds were identified in the Department of Plant Biology and Biotechnology, Faculty of Life Sciences, University of Benin, Nigeria and a voucher (UBH-P408) specimen was deposited in their Herbarium Unit

Extraction and characterization of starch

The extraction of starch from avocado seeds as well as the physicochemical, powder and high-resolution characterization of the extracted starch have been previously reported.¹³

Preparation of paracetamol granules

Various batches of granules were prepared with the formula shown in Tables 1a and b. Fifteen (15) batches of paracetamol granules were prepared with varying amounts of the starch powder as disintegrant (2.5-15% w/w) and the starch mucilage as binder (5.0-15% w/v) using the wet granulation method.

Granules sufficient to produce a hundred (100) tablets were prepared per batch by triturating the required amount of paracetamol and microcrystalline cellulose powders with sufficient quantities of the binder mucilage before the required amounts of the disintegrant powder and lactose as a bulking/filling agent were added and properly triturated. The wet mass-produced was then forced through a 2.0 mm sieve and the wet granules dried in a hot air oven set at 60 °C for 30 min (Gallenkamp, UK). Granules produced were then rescreened with a 710 µm diameter sieve before drying again for 30 min. Calculated quantities of glidant (talc) and lubricant (magnesium stearate) were mixed and added to the produced granules before analysis.

Granule analysis

The formulated batches of paracetamol granules were subjected to the following granule flow properties analyses:

Bulk and tapped densities

About 30 g of granules was transferred into a 100 mL measure and the occupied volume was noted. The ratio of the weight of granule to the volume occupied was calculated as the bulk density. The 100 mL measure with the granules was tapped continuously on a padded wooden surface until a constant volume was obtained. The ratio of the granule's weight to the new volume was calculated as the tapped density of the granules.¹³

Hausner's ratio and Carr's compressibility index

The calculated ratio from the division of the tapped density by the bulk density of the granules was recorded as Hausner's ratios of the granules while Carr's index was calculated as the ratio of the difference between the tapped and bulked densities to the tapped density and the ratio expressed as a percentage.¹³

Flow rate and angle of repose

About 50 g of the granules were transferred gently into a closed funnel clamped about 5.0 cm above a horizontal flat surface. The funnel opening was opened with the granules falling under gravity onto the flat surface timed. Flow rate was computed from the division of the granule's weight by the time taken to empty the funnel. The height of the heap of granules and the radius of the base of the heap made from the free fall of the granules were recorded and used in calculating the angle of repose using Equation 1.¹³

$$\text{Angle of repose} = \tan^{-1} \frac{\text{height of heap (cm)}}{\text{radius of heap base (cm)}} \dots (1)$$

Drug-excipient interaction studies

The compatibility of paracetamol with the starch excipient was determined employing differential scanning calorimetry (DSC) and Fourier transform infra-red (FTIR) spectroscopy analysis of pure paracetamol powder and the granules formulated.

Differential scanning calorimetry

DSC was carried out using the Netzsch DSC 204F1 Phoenix apparatus (Netzsch-Geratebau GmbH, Selb, Germany). About 10 mg of the granule sample was transferred to an aluminium pan and hermetically sealed. The pan seal was broken by piercing and then placed in the sample holder of the calorimeter. Calibration of the calorimeter with indium was carried out with nitrogen as the purge gas. Heating the sample under nitrogen at the rate of 10°C per min was carried out from 30 to 350°C and at a flow rate of 70 mL/min.

Fourier transform infra-red spectroscopy

The FTIR analysis of the granule sample was carried out using a Fourier transform infrared spectrophotometer (Spectrum BX, Perkin Elmer, Beaconsfield Bucks, England). The potassium bromide tablet method

was used. About 5.0 mg of the granule sample was mixed with potassium bromide into a powder mix of about 200 mg. The powder mixture was compressed into a tablet with a sigma pneumatic press and placed in the sample holder. Scanning of the tablet sample at a range of 4000 - 500 cm⁻¹ was carried out.

Compression of granules to tablet

The formulated granules were compressed into tablets of uniform weights (600 mg) at 25 arbitrary unit load pressure in a single punch tableting machine (Manesty Machines, UK) using the 10 mm punch and die set. An elastic recovery period of 24 h was allowed for the tablets before evaluation.

Evaluation of tablets

The paracetamol tablets formulated were assessed based on the following tablet parameters; weight uniformity, hardness, friability as well as dissolution profiles.

Weight uniformity

Twenty paracetamol tablets from each batch were randomly selected and weighed with an electronic balance (Scout-Pro, China). Subsequently, the respective mean and standard deviation values were calculated.¹⁴

Tablet hardness

The tablet hardness was determined using a motorized digital hardness tester (Campbell Electronic Hardness Tester. Model HT 3050, India). This assessment was performed by determining the load required to cause diametric fracture on ten tablets randomly selected from the individual batches, and the mean values computed.¹⁵

Tablet friability

The friability test was performed by weighing ten randomly selected dedusted tablets. These were placed in the drum of an Erweka Friabilator (Erweka, Germany) and treated to free fall and cascading stress for 4 min, at the rate of 25 rpm. Subsequently, the tablets were removed, dusted again and weighed to ascertain the percentage weight loss.¹⁵

Disintegration time

Six (6) tablets from each batch were placed in each of the six (6) compartments of the disintegration tester containing 600 mL of distilled water and maintained at 37 ± 0.5 °C (MK IV, Manesty machines, UK). The disintegration tester was operated and the time taken for all the fragments of the disintegrated tablets to pass through the compartment's mesh was noted and the average was computed as the disintegration time.¹⁴

Dissolution profiles

Preparation of standard calibration curve for paracetamol

Exactly 100 mg of pure paracetamol powder was dissolved in 75 mL of 0.1 N HCl solution and made up to 100 mL in a volumetric flask with more HCl solution. The wavelength of maximum absorption of the stock solution was obtained using a UV/Visible spectrophotometer (T70 PG instrument Ltd, UK). Serial dilutions of the stock solution ranging from 10 - 100 µg/mL were made. The absorbances of the serially diluted samples were recorded at 245 nm and plotted against the corresponding concentrations to produce a straight-line graph. The equation of the line, R² value and intercept were generated for further evaluation.¹⁶

In vitro dissolution

Dissolution was performed *in vitro* using a US Pharmacopoeia dissolution Type II apparatus with 900 mL dissolution medium at 37 ± 0.5°C, which was set at a paddle rotation speed of 50 rpm/min (ST7, G.B. Caleva Ltd, England). Two (2) tablets were randomly selected from the formulated batches of tablets and used for the test. Dissolution testing was carried out in 0.1 N HCl for 1.0 h. Aliquot samples were withdrawn from the dissolution fluid at stipulated time intervals and replaced with an equivalent volume of fluid maintained at the same

temperature. Samples taken were analyzed for paracetamol using a UV spectrophotometer set at an absorbance of 245 nm (T70 PG Instrument Ltd, UK). The concentration of drug present in each sample was evaluated from the line of regression equation generated from the calibration curve of pure paracetamol.

Statistical analysis

Statistical analysis of data was carried out with GraphPad Instat (v. 3.06). Experiments were carried out in triplicates and results were reported as mean and standard deviations. Differences between means were determined using One-way Analysis of Variance (ANOVA), where $p < 0.05$ was considered significant.

Table 1a: Formula used in the preparation of paracetamol granules and tablets using avocado starch powder (ASP) as disintegrant

Ingredients	Batches							
	A	B	C	D	E	F	G	H
Paracetamol (mg)	500	500	500	500	500	500	500	500
Avocado starch powder (ASP) (mg) (%w/w)	15 (2.5%)	30 (5%)	45 (7.5%)	60 (10%)	75 (12.5%)	90 (15%)	-	-
Maize starch BP powder (MSP) (mg) (%w/w)	-	-	-	-	-	-	30 (5%)	45 (10%)
Microcrystalline cellulose (mg)	5	5	5	5	5	5	5	5
Maize starch BP mucilage (15%w/v)	qs	qs	qs	qs	qs	qs	qs	qs
Lactose (mg)	72	62	47	32	17	2	62	47
Talc (mg)	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium stearate (mg)	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
	600	600	600	600	600	600	600	600

Key: A: (2.5% ASP), B: (5.0% ASP), C: (7.5% ASP), D: (10.0% ASP), E: (12.5% ASP), F: (15.0% ASP), G: (5.0% MSP), H: (10% MSP)

Table 1b: Formula used in the preparation of paracetamol granules and tablets using avocado starch mucilage (ASM) as binder

Ingredients	Batches						
	I	J	K	L	M	N	O
Paracetamol (mg)	500	500	500	500	500	500	500
Avocado starch mucilage (ASM) (%w/v)	qs (5%)	qs (7.5%)	qs (10%)	qs (12.5%)	qs (15%)	-	-
Maize starch BP mucilage (MSM) (%w/v)	-	-	-	-	-	qs (5%)	qs (10%)
Maize starch BP powder (5%w/w) (mg)	30	30	30	30	30	30	30
Microcrystalline cellulose (mg)	5	5	5	5	5	5	5
Lactose (mg)	62	62	62	62	62	62	62
Talc (mg)	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium stearate (mg)	1.5	1.5	1.5	1.5	1.5	1.5	1.5
	600	600	600	600	600	600	600

Key: I: (5.0% ASM), J: (7.5% ASM), K: (10.0% ASM), L: (12.5% ASM), M: (15.0% ASM), N: (5.0% MSM), O: (10.0% MSM)

Results and Discussion

Flow and bulk properties of the paracetamol granules

Evaluation results of the prepared paracetamol granules are presented in Table 2. Generally, the granule batches prepared with avocado starch as binder (I, J, K, L and M) showed better flow properties than those batches prepared with the starch as disintegrants (A, B, C, D, E and F) while their maize starch controls in both cases (G, H and N, O) exhibited excellent flow characteristics.

Lower Carr's indices ($\leq 31.80\%$), Hausner's ratios (≤ 1.47) and angles of repose ($\leq 30.26^\circ$) were observed in the granule batches prepared with avocado starch as binder when compared with granule batches prepared with the starch as disintegrants. Similarly, the flow rate values of the granule batches prepared with avocado starch as binder were comparatively higher than its counterpart granule batches prepared with the starch as disintegrants.

These better flow properties exhibited by the granule batches prepared with the starch as binder could be attributed to less powder particle densification occasioned by voids created in the bulk granules as a result of uneven sizes of the granule particles.^{17,18} The extent of mucilage coating of powder particles has been shown to determine granule sizes and this in turn affects some of the granule bulk properties and

consequently, some physicochemical properties of tablets produced with the granules.^{19,20}

Drug-excipient interaction studies

The DSC thermograms and FTIR spectra obtained from the compatibility studies are shown in Figures 1 and 2, respectively. The thermogram and spectrum for pure paracetamol powder and the granule mixture of the pure drug with the starch and other excipients were similar in pattern.

The DSC thermogram of pure paracetamol powder (Figure 1) showed two endothermic transitions, a sharp one at 169 °C, corresponding to its melting point and a semi-broad one at 310 °C. The sharp trough appeared as a spike which is an indication of its crystallinity and purity. The thermograms of the granules containing paracetamol and all the other granule ingredients including the avocado starch showed the characteristic trough of pure paracetamol. This observation suggests no interaction between the drug and the test starch.

The FTIR spectrum of pure paracetamol (Figure 2) showed characteristic absorption bands at 1080 - 1195 (C-O-C and C-O stretch), 1690 (O-H bend), 2947 (-CH₂ stretch) and 3010 cm⁻¹ (O-H stretch). These bands observed for acetylsalicylic acid remained unchanged when compared with the spectral data of the granules containing the combination of paracetamol and all the other granule ingredients

including the avocado test starch. This observation ruled out the possibility of chemical interaction and complex formation between paracetamol and other ingredients in the granule formulation during the mixing process.

Tablet properties

Physicochemical properties of the paracetamol tablets

Table 3 shows the physicochemical properties of paracetamol tablets formulated using the avocado test starch at different disintegrant and binder concentrations. The weight uniformity test highlighted no significant difference between all the batches of tablets produced, which was consistent with the BP specifications, which recommends that not more than two tablets deviate from the average tablet weight with $\pm 5.0\%$ and that no tablet should deviate with $\pm 10.0\%$.²¹ Based on the hardness test results, all tablets formulated using the test avocado starch as binder showed higher values than those prepared with the test starch as disintegrant, although the values were within the pharmacopoeial specification of 5 to 8 kp.¹⁴

These satisfactory hardness values of the tablets may be due to the effective inter-particulate bond formation of the binders used in the formulations; which were maize starch mucilage in the batches of tablets where the test avocado starch was used as disintegrant and the test avocado starch mucilage, where the test starch was used as binder. Also, the acceptable hardness values may be the result of some contribution by the MCC attributable to its inherent binding ability to promote increased bond formation between the granules as a result of the formation of plastic deformation during compaction.^{22,23}

The friability of the formulated paracetamol tablets ranged from 0.14 - 1.56% with the batches of tablets formulated with the avocado starch as binder having higher values. The friability values seemed to decrease in these batches of tablets with increase in the concentrations of the starch as binder but no pattern was discernible in those batches of tablets where the starch was used as a disintegrant. Nevertheless, all the tablet batches did not meet the official BP recommendation of a maximum tablet weight loss of 0.8 - 1.0%.¹⁹

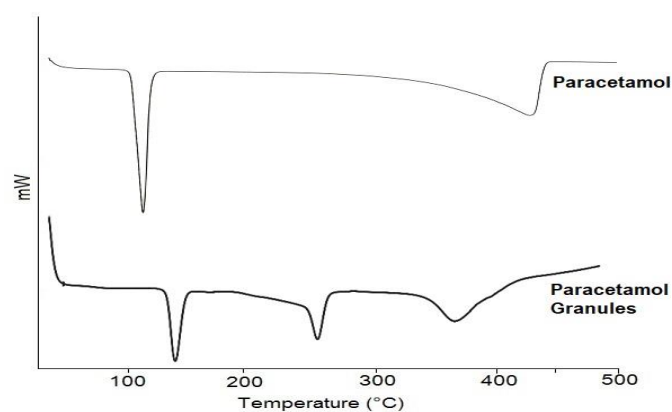


Figure 1: DSC thermograms of paracetamol powder and paracetamol granules formulated with avocado starch

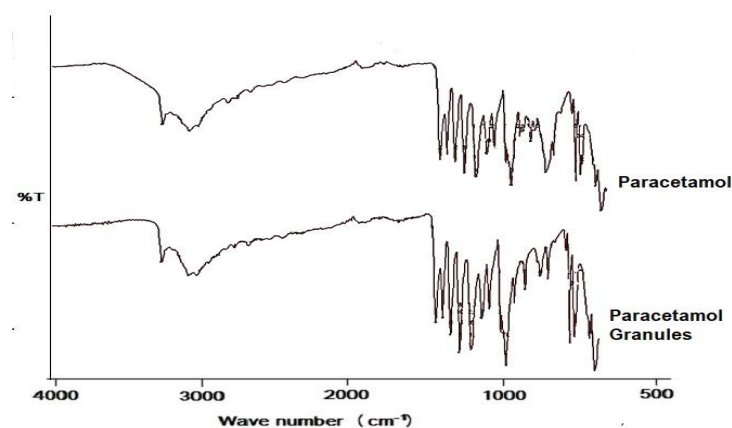


Figure 2: FTIR spectra of paracetamol powder and paracetamol granules formulated with avocado starch

Table 2: Micromeritic properties of the formulated paracetamol granules

Batch	Bulk density (g/mL)	Tapped density (g/mL)	Hausner's ratio	Carr's index (%)	Flow rate g/sec	Angle of repose (°)
A	0.457 ± 0.005	0.679 ± 0.005	1.49 ± 0.20	32.90 ± 0.10	0.568 ± 0.12	30.49 ± 0.42
B	0.470 ± 0.004	0.701 ± 0.010	1.49 ± 0.60	33.45 ± 0.02	0.587 ± 0.22	30.26 ± 0.14
C	0.466 ± 0.002	0.717 ± 0.015	1.54 ± 0.42	34.02 ± 0.30	0.542 ± 0.20	30.10 ± 0.16
D	0.474 ± 0.001	0.697 ± 0.002	1.47 ± 0.44	32.01 ± 0.42	0.527 ± 0.14	30.06 ± 0.20
E	0.470 ± 0.003	0.701 ± 0.012	1.49 ± 0.22	33.00 ± 0.23	0.461 ± 0.40	30.86 ± 0.14
F	0.474 ± 0.004	0.667 ± 0.050	1.41 ± 1.00	28.40 ± 0.12	2.631 ± 0.20	20.46 ± 0.16
G	0.517 ± 0.002	0.739 ± 0.025	1.43 ± 0.80	29.27 ± 0.22	2.872 ± 0.20	20.26 ± 0.13
H	0.521 ± 0.002	0.745 ± 0.020	1.43 ± 0.12	29.20 ± 0.40	5.212 ± 0.12	15.26 ± 0.22
I	0.475 ± 0.006	0.699 ± 0.004	1.47 ± 0.30	31.80 ± 0.04	0.475 ± 0.22	30.26 ± 0.14
J	0.476 ± 0.004	0.733 ± 0.013	1.44 ± 0.20	31.02 ± 0.42	0.433 ± 0.30	30.26 ± 0.18
K	0.480 ± 0.003	0.686 ± 0.010	1.43 ± 0.42	29.10 ± 0.22	2.400 ± 0.20	23.26 ± 0.14
L	0.465 ± 0.002	0.665 ± 0.020	1.43 ± 0.12	30.00 ± 0.12	0.567 ± 0.20	30.26 ± 0.14
M	0.483 ± 0.001	0.690 ± 0.015	1.43 ± 0.14	30.00 ± 0.22	1.610 ± 0.12	30.26 ± 0.21
N	0.531 ± 0.004	0.737 ± 0.012	1.39 ± 0.42	27.00 ± 0.20	4.423 ± 0.20	18.26 ± 0.14
O	0.531 ± 0.004	0.738 ± 0.030	1.39 ± 0.40	27.01 ± 0.14	2.213 ± 0.22	22.26 ± 0.24

Table 3: Some physicochemical properties of the formulated paracetamol tablets

Batch	Weight (g)	Hardness (kp)	Friability (%)	Disintegration time (min)
A	0.604 ± 0.005	6.70 ± 0.05	0.70 ± 0.10	1.15 ± 1.20
B	0.610 ± 0.004	8.70 ± 0.10	0.48 ± 0.02	1.66 ± 0.60
C	0.626 ± 0.002	8.25 ± 0.15	0.14 ± 0.30	0.91 ± 0.42
D	0.599 ± 0.002	7.30 ± 0.02	0.70 ± 0.42	0.63 ± 0.44
E	0.608 ± 0.005	7.25 ± 0.12	0.71 ± 0.23	0.51 ± 0.22
F	0.599 ± 0.001	6.05 ± 0.50	1.47 ± 0.12	0.51 ± 0.10
G	0.606 ± 0.003	7.40 ± 0.25	0.76 ± 0.22	> 15.00
H	0.606 ± 0.001	6.50 ± 0.20	1.04 ± 0.40	4.67 ± 0.12
I	0.609 ± 0.002	8.00 ± 0.04	1.50 ± 0.04	0.25 ± 0.30
J	0.609 ± 0.004	8.00 ± 0.13	1.56 ± 0.02	0.50 ± 0.20
K	0.608 ± 0.005	8.35 ± 0.25	1.12 ± 0.10	0.51 ± 0.40
L	0.609 ± 0.002	8.55 ± 0.11	1.10 ± 0.11	0.58 ± 0.10
M	0.610 ± 0.002	8.70 ± 0.50	0.92 ± 0.05	0.78 ± 0.30
N	0.606 ± 0.002	7.30 ± 0.12	0.96 ± 0.04	> 15.00
O	0.608 ± 0.001	8.10 ± 0.20	0.76 ± 0.10	11.12 ± 0.30

All values were expressed as mean ± standard deviation

The disintegration times of the batches of paracetamol tablets prepared with the test avocado starch ranged from 0.25 - 1.66 min as against the control tablets formulated with maize starch which ranged from 4.67 - > 15.00 min. Therefore, all the tablets formulated with the test starch met the 15 min official disintegration time requirement stipulated in the British Pharmacopoeia for uncoated tablets.²¹ The tablets exhibited a decrease in disintegration times with increase of the test starch as disintegrant and an increase in disintegration times with increased test starch as binder. Despite the increase in disintegration times of the tablets prepared with the test starch as binder, their disintegration time values were still lower than those batches of tablets prepared with the avocado starch as disintegrants.

These low disintegration times of the tablets may be attributed to swelling and hydration properties of the avocado test starch both in its powder and mucilage (gel) form.¹³ Swelling is an important parameter that reveals the ability of starch granules to absorb water and it has been shown that gelatinization increases the swelling factor and water absorption index of starch.²⁴ The swelling and hydration properties of the avocado starch may have enhanced tablet breakup on contact with fluid leading to fast disintegration.^{11,25,26} Furthermore, it can be inferred from the less than 3 min disintegration times of the tablets that the test avocado starch may be a potential super-disintegrant with possible application in the formulation of fast disintegration tablets.^{27,28}

In vitro dissolution

Figures 3a and 3b show the release profile of the different batches of the formulated paracetamol tablets. Generally, all batches of tablets exhibited increased drug release with increase in the avocado starch either as disintegrant or binder with those batches of tablets with the test starch as disintegrant having a higher overall drug release.

However, not all the batches of the tablets formulated passed the British Pharmacopoeia requirement for dissolution for tablets, which stipulates a minimum drug release of 70% after 45 min.¹⁹ The difference in drug release from these tablet formulations was observed to be significant at $p < 0.05$ when comparison is made between those batches with the starch as disintegrant or binder and the control batches with maize starch as disintegrant or binder. Again, it can be seen that even though tablets containing the test starch as binder disintegrated faster, the disintegration-dissolution theory was not followed here, as the fast disintegration of the tablets did not equate to a prompt release of the drug. Though the tablets were quick to break up into their primary particles, drug dissolution from the particles was slower. This may be

due to the poor solubility of paracetamol in the dissolution fluid and the possible formation of a mucilaginous layer around the paracetamol powder particles by the binder used, thereby contributing to its slow release.^{16,29,30}

Conclusion

Tablets formulated with avocado (*Persea americana*) seeds starch as disintegrant and as binder met pharmacopoeial specifications in their tablet properties and these properties were comparable to maize starch BP. The fast disintegration times exhibited by the tablets make the starch a potential super-disintegrant in the formulation of fast disintegrating tablets.

Conflict of Interest

The authors declare no conflict of interest.

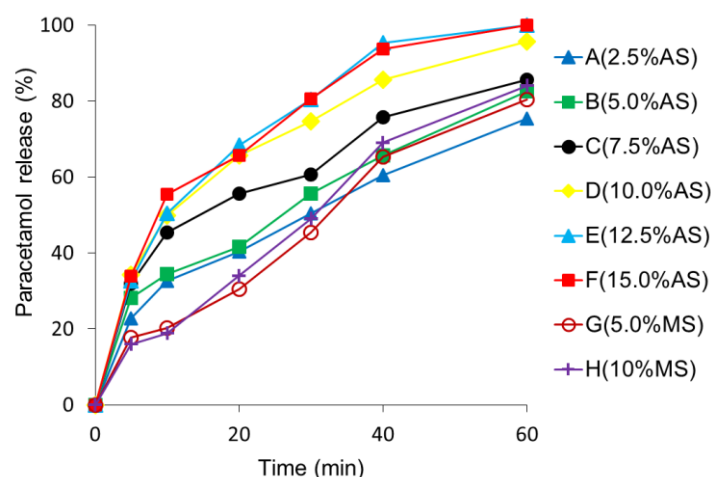


Figure 3a: Dissolution profiles of batches of paracetamol tablets formulated with avocado starch (AS) and maize starch (MS) powders as disintegrants.

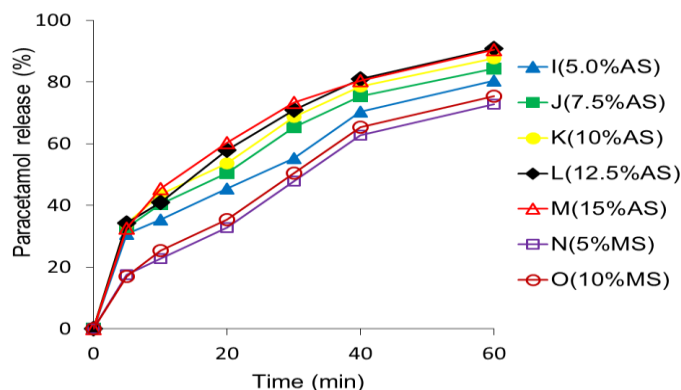


Figure 3b: Dissolution profiles of batches of paracetamol tablets formulated with avocado starch (AS) and maize starch (MS) mucilages as binders

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

References

- Popoola-Akinola OO, Raji TJ, Olawoye B. Lignocellulose, dietary fibre, inulin and their potential application in food. *Heliyon*. 2022; 8(8): e10459.
- Onyeaka H, Obileke K, Makaka G, Nwokolo N. Current research and applications of starch-based biodegradable films for food packaging. *Polymers*. 2022; 14(6): 1126.
- Abd El-Ghany NA, Elella MHA, Abdallah HM, Mostafa MS, Samy M. Recent advances in various starch formulation for wastewater purification via adsorption technique: a review. *J Polym Environ*. 2023; 31: 2792-2825.
- Tosif MM, Najda A, Bains A, Kaushik R, Dhull SB, Chawla P, *et al*. A comprehensive review on plant-derived mucilage: Characterization, functional properties, applications and its utilization for nanocarrier fabrication. *Polymers*. 2021; 13(7): 1066.
- Falcao LS, Coelho DB, Veggi PC, Campelo PH, Albuquerque PM, de Moraes MA. Starch as a matrix for incorporation and release of bioactive compounds: Fundamentals and applications. *Polymers (Basel)*. 2022; 14(12): 2361.
- Kumar Y, Shikha D, Guzmán-Ortiz FA, Sharanagat VS, Kumar K, Saxena DC. Starch: Current production and consumption trends. In: Sharanagat VS, Saxena DC, Kumar K, Kumar Y (Eds). *Starch: Advances in Modifications, Technologies and Applications*. Cham: Springer, 2023.
- Manchanda S, Chandra A, Bandopadhyay S, Tekade RK. Formulation additives used in pharmaceutical products: Emphasis on regulatory perspectives and GRAS. In: Tekade RK (Ed). *Dosage Form Design Considerations*. Vol. 1. Cambridge: Academic Press, 2018. 773-831 p.
- Le-Corre DB, Bras J, Dufresne A. Starch nanoparticles: A review. *Biomacromolecules*. 2010; 11(5): 1139-1153.
- Fatokun O. Fostering local production of essential medicines in Nigeria. *Bull World Health Organ*. 2020; 98(7): 507-508.
- Santos DM, Ascheri D, Bukzem AL, Morais C, Carvalho C, Ascheri J. Physicochemical properties of starch from avocado seed (*Persea Americana* Mill). *Bol Cent Pesqui Process Aliment*. 2016; 34(2): 1-12.
- Macena JFF, Souza JCA, Camilloto GP, Cruz RS. Physicochemical, morphological and technological properties of the avocado (*Persea americana* Mill. cv. Hass) seed starch. *Sci Agrotechnol*. 2020; 44: e001420.
- Martins SHF, Pontes KV, Fialho RL, Fakhouri FM. Extraction and characterization of the starch present in the avocado seed (*Persea americana* mill) for future applications. *J Agric Food Res*. 2022; 8: 100303.
- Enadeghe OD, Eraga SO, Obarisiagbon JA. Characterization of avocado (*Persea americana*) seed starch - Physicochemical and powder properties. *J Sci Pract Pharm*. 2022; 9: 447-458.
- British Pharmacopoeia. Volume III. British Pharmacopoeia Commission. London: The Stationery Office Limited, 2009. 6578-6585 p.
- Eraga SO, Elue DN, Iwuagwu MA. Evaluation of the direct compression properties of microcrystalline cellulose obtained from cassava fermentation waste in paracetamol tablet formulations. *Nig J Pharm Res*. 2020; 16(1): 31-37.
- Alalor CA, Okafo SE, Avbunudiogba JA, Atimah CO. Solubility and dissolution optimization of paracetamol using in situ micronization by solvent change method. *Int J Biosci*. 2022; 21(3): 8-19.
- Guo Z, Chen X, Liu H, Guo Q, Guo X, Lu H. Theoretical and experimental investigation on angle of repose of biomass coal blends. *Fuel*. 2014; 116: 131-139.
- Al-Hashemi HMB, Al-Amoudi OSB. A review on the angle of repose of granular materials. *Powder Technol*. 2018; 330: 397-417.
- Eichie FE, Kudehinbu AO. Effect of particle size of granules on some mechanical properties of paracetamol tablets. *Afr J Biotechnol*. 2009; 8(21): 5913-5916.
- Gajjar P, Johnson CG, Carr J, Chrispeels K, Gray JMNT, Withers PJ. Size segregation of irregular granular materials captured by time-resolved 3D imaging. *Sci Rep*. 2021; 11: 8352.
- British Pharmacopoeia. Vol. I and IV: Her Majesty's Stationary Office, Cambridge: University Press, 2015.
- Zhang Y, Law Y, Chakrabarti S. Physical properties and compact analysis of commonly used direct compression binders. *AAPS PharmSciTech*. 2003; 4: 489-499.
- Verheyen P, Steffens KJ, Kleinebudde P. Use of crospovidone as pelletization aid as alternative to microcrystalline cellulose: Effects on pellet properties. *Drug Dev Ind Pharm*. 2009; 35(11): 1325-1332.
- Nakom KN, Tongdang T, Sirivongpaisal P. Crystallinity and rheological properties of pregelatinized rice starches differing in amylose content. *Starch/Starke*. 2009; 61(2): 101-108.
- Wang J, Li Y, Jin Z, Cheng Y. Physicochemical, morphological, and functional properties of starches isolated from avocado seeds, a potential source for resistant starch. *Biomolecules*. 2022; 12(8): 1121.
- De Dios-Avila N, Tirado-Gallegos JM, Rios-Velasco C, Luna-Esquivel G, Isirdia-Aquino N, Zamudio-Flores PB, *et al*. Physicochemical, structural, thermal and rheological properties of flour and starch isolated from avocado seeds of Landrace and Hass cultivars. *Molecules*. 2022; 27(3): 910.
- Gupta A, Hunt RL, Shah RB, Sayeed VA, Khan MA. Disintegration of highly soluble immediate release tablets: A surrogate for dissolution. *AAPS PharmSciTech*. 2009; 10(2): 495-499.
- Markl D, Zeitler JA. A review of disintegration mechanisms and measurement techniques. *Pharm Res*. 2017; 34(5): 890-917.
- Ogunjimi AT, Alebiowu G. Neem gum as a binder in a formulated paracetamol tablet with reference to acacia gum BP. *AAPS PharmSciTech*. 15, 2014; 500-510.
- Alwossabi AM, Elamin ES, Ahmed EMM, Abdelrahman M. Solubility enhancement of some poorly soluble drugs by solid dispersion using *Ziziphus spina-christi* gum polymer. *Saudi Pharm J*. 2022; 30(6): 711-725.