

Full Length Research Paper

Preliminary investigations of the binding ability of lima bean (*Phaseolus lunatus*) starch in paracetamol tablets

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The binding properties of starch obtained from Lima bean (*Phaseolus lunatus*) were evaluated. The starch from the seeds was extracted and the binding ability of its mucilage compared with that of maize starch mucilage in paracetamol based tablets at concentrations of 0, 2.5, 5, 7.5 and 10% w/v. The following properties of the starch powders were evaluated; organoleptic properties, microscopy and reaction with iodine solution while for the paracetamol granules prepared with their mucilages; particle size analysis, moisture content, flow rate, and angle of repose. The starches and granules were also evaluated for bulk and tapped density, Hausner's ratio and Carr's compressibility index. Paracetamol tablets formulated using the starch mucilages were evaluated for uniformity of weight, dimensions, hardness, friability, disintegration time and dissolution rate. The paracetamol granules and tablets formulated with 0 to 10% w/v *P. lunatus* starch mucilage were comparable in granule flow properties, tablet weight variation and hardness, friability, disintegration times and dissolution rate with the granules and tablets prepared with maize starch B.P mucilage. The study revealed that the mucilage of *P. lunatus* starch when used as binder produced tablets of acceptable pharmaceutical quality.

Key words: Paracetamol tablets, wet granulation, *Phaseolus lunatus* starch, mucilage binder.

INTRODUCTION

Cohesiveness and structural strength are necessary qualities of powder particles meant for tablet production. A tablet must remain whole after compression, during handling, transportation, packaging and use. A good binding agent helps in achieving these objectives. The wet granulation method of tablet production uses a solution of binding agent to form a damp mass with a dry powder mix, which is then triturated, sieved and dried to obtain granules. The quantity and type of binding agent used determine the physicochemical characteristics of

tablets. It has been confirmed that increasing the binder concentration invariably causes a corresponding increase in the hardness and disintegration times of tablets (Odeku, 2005).

Starch mucilages are examples of some of the commonly used binders because of their abundant supply, low cost, biodegradability and ease of chemical modification. Starches are used extensively in pharmaceutical industries as disintegrants, binders and lubricants in tablet formulation. Examples of the commonly used

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starches include rice, potato, maize, corn, wheat, and tapioca starch. Maize starch is the most common of the starches used, however some authors have studied the use of starches from other sources (Iwuagwu and Onyekweli, 2002; Adane et al., 2006; Ibezim et al., 2008).

The production of starches (35 to 60%) from legumes or beans is a viable alternative to maize because legume starches contain a relatively high proportion of amylose and a higher resistance to swelling and rupture when compared to cereal starches and legume protein (15 to 40%) can be of economic value simultaneously (Singh and Nath, 2009). Lima bean (*Phaseolus lunatus*) is of Andean and Mesoamerican origin. It is grown locally in Nigeria for its economic and nutritional value. The bean seed contains 22% starch, with 34.5% amylose content. In water, it exhibits high single stage swelling with moderate solubility and its granules are highly resistant to acidic hydrolysis (Hoover et al., 1991).

This study was designed to evaluate the binding properties of Lima bean starch mucilage in comparison to maize starch mucilage in paracetamol tablets.

MATERIALS AND METHODS

P. lunatus starch was extracted from the seeds in our laboratory. Paracetamol (Nomagbon Pharmaceuticals Ltd, Benin City, Nigeria), maize starch (Roquette Freres, France), lactose (May and Baker, Nigeria), talc (BDH. Laboratories, UK) and magnesium stearate (Hopkin and Williams, UK) were all utilized as obtained.

Collection of *Phaseolus lunatus*

P. lunatus was purchased from a market in Nsukka and taken to Department of Pharmacognosy, Faculty of Pharmacy, University of Benin, Nigeria for authentication and certification at the herbarium.

Extraction of *Phaseolus lunatus* starch

About 1 kg of *P. lunatus* seeds was soaked for 24 h in water. The seeds were washed to remove the seed coat. The washed seeds were grounded into a paste using an electric grinder (Moulinex, France). The paste was mixed with sufficient water and then strained through a muslin cloth. The suspension obtained was washed several times with sufficient water, allowed to settle and the supernatant fluid decanted until a clear supernatant was obtained. The starch sediment was sun-dried, milled to fine powder and further dried in an oven at 60°C for 12 h.

Characterization of starch powders

Organoleptic properties

The taste, odour and colour of the starches were recorded.

Solubility

100 mg of starch was placed in 2 ml of cold water in a test-tube and

shaken. The state of solubility was recorded.

Chemical test

A 5 ml of the starch suspension was prepared and a few drops of 0.01 M iodine solution were added. The resulting colour change was recorded.

Microscopy

The starch sample was thinly spread over a glass slide and viewed under a light microscope (Labo Microsystems GmbH, Germany) via a calibrated eyepiece and the sizes and shape of the particles was recorded.

Bulk density

A 30 g quantity of the starch powder was poured gently into a 100 ml graduated measure. The volume of the powder was read and the bulk density calculated.

Tapped density

The measure containing the 30 g of starch powder was tapped 100 times on a wooden platform. The volume was noted and used in calculating the tapped density.

Carr's index

The difference between the tapped and bulk density of the starch powder divided by the tapped density was calculated and the ratio expressed as percentage.

Hausner's ratio

The ratio of the tapped density to the bulk density of the starch powder was calculated as the Hausner's quotient.

True density

A 25 ml specific gravity bottle (glass pycnometer) was filled with liquid paraffin, cleaned of any residual liquid paraffin and weighed (a). The bottle was emptied, rinsed with acetone and dried. About 1 g (b) of the starch powder was poured into the bottle and then filled with liquid paraffin. It was weighed (c) after cleaning off the residual paraffin on the bottle. The various weights recorded were used to calculate the true density of the starch using equation 1. All the tests were carried out for both starches in triplicates.

$$\rho = b/[(a+b)-c]S \quad (1)$$

Where ρ is the particle density of the starch and S is the specific gravity of liquid paraffin

Preparation of granules

The wet granulation method of massing and screening was used in preparing all the batches of paracetamol granules using the

Table 1. Formula of prepared paracetamol tablets.

Item	Ingredients	Quantity/tablet	Quantity/batch
Drug	Paracetamol	500 mg	100 g
Filler	Lactose	50 mg	10 g
Intragranular disintegrant	Maize starch	25 mg	5 g
Binder solution	Maize starch or <i>P. lunatus</i> starch	0, 2.5, 5, 7.5, 10 % w/v	-
Extragranular disintegrant	Dried maize starch	25 mg	5 g
Glidant	Magnesium stearate	1% w/w	1% w/w
Lubricant	Talc	1% w/w	1% w/w

calculations shown in Table 1. Calculation was made for 100 tablets per batch. A batch was prepared for each of the binder concentrations tested with *P. lunatus* starch and maize starch. The paracetamol powder, lactose and *P. lunatus* starch or maize starch were carefully weighed into a mixer and dry mixed for five minutes. The intragranular disintegrant was gradually added to the powder mix in geometric proportions during the mixing. Various concentrations of the starch mucilages (*P. lunatus* starch and maize starch) were prepared. This was carried out by dispersing the appropriate weights of the starch in about 10 ml of water in a beaker and then making up to the 100 ml mark with hot boiling water to form a thick mucilage (binder). Sufficient quantities of the binder solution required to form a wet mass was gradually added to the dry powder mix. The wet mass was passed through a 710 μm sieve mesh screen and the resulting granules dried at 60°C for 30 min in a hot air oven (Gallenkamp, UK). The granules were rescreened through the same sieve and further dried for another 30 min. The dry granules were subjected to various analyses after which the extragranular disintegrant, glidant and lubricant previously weighed and mixed in a mortar were added in geometric proportion and intimately mixed in readiness for compression.

Analysis of granules

Particle size analysis

Five Endecotts sieves were stacked in a test sieve shaker in decreasing order of aperture sizes (500, 250, 150, 125 and 90 μm , in that order). A 30 g quantity of the granules was placed on the sieve at the top and shaken for 10 min. The weight of granules retained on each sieve was recorded (Musa et al., 2010).

Moisture content

A 1 g quantity of the granules was dried in a hot air oven for 4 h at 105°C. The initial weight of the granules and the weight after drying were recorded and used to calculate the moisture content of the granules (Musa et al., 2010).

Flow rate of granules

An Erweka flow tester was used. The time taken for 50 g of the paracetamol granules to pass through its orifice was recorded. This was carried out in triplicates and the mean values recorded (Musa et al., 2010).

Angle of repose

The hollow tube method was used. A short hollow tube of 3 cm in internal diameter sitting on a circular horizontal surface of same diameter was filled with granules. The tube was withdrawn vertically and excess granules allowed to fall off the edge of the circular horizontal surface. The height of the heap was measured. The angle of repose, θ , was calculated using equation 2.

$$\theta = \tan^{-1} (h/r) \quad (2)$$

Where h is the height of the heap of granules and r is the radius of the circular base.

Bulk density, tapped density, Carr's index and Hausner's ratio

The methods of obtaining these parameters for the starches were the same used for the paracetamol granules.

Compression of Granules

Batches of the granules were compressed into tablets using a single punch tableting machine (F-3 Manesty Machines, UK) at compression pressure of 30 arbitrary units. The die volume was adjusted to compress tablets of uniform weight by using granules weighing 675 mg. The tablets made were then kept in air tight containers and stored in a desiccator until evaluation.

Evaluation of tablets

The following tests were carried out on the compressed tablets using standard procedures: tablet weight uniformity, hardness, friability, disintegration time and dissolution rate (BP, 2003).

Tablet weight uniformity

The weight of each of 20 tablets was determined from each batch using an electronic balance (College B154, Mettler Toledo, Switzerland) and the mean weight and standard error were computed.

Tablets' hardness

The hardness of each of ten tablets per batch was determined (Campbell Electronics, Model HT-30/50, India). The mean hardness

Table 2. Some physical properties of the starches studied.

Properties		Maize starch	<i>Phaseolus lunatus</i> starch
Organoleptic	Appearance	White	White
	Taste	Tasteless	Tasteless
	Odour	Odourless	Odourless
	Texture	Smooth	Rough
	Solubility (cold water)	Insoluble	Insoluble
Microscopy	Size Range	10-20 μm	10-50 μm
	Form	Polyhedral or subspherical	Oval to elliptical
	Hilum	Hilum is central and triangular	Hilum is an elongated cleft
	Striations	No striations	Eccentric and faint striation
Powder parameters	Bulk density (g/ml)	0.49	0.57
	Tapped density (g/ml)	0.62	0.78
	True density (g/ml)	1.20	1.56
	Carr's index (%)	21.73	26.05
	Hausner's ratio	1.28	1.35

was calculated.

Friability test

The weight of ten tablets was determined on the electronic balance. The tablets were then placed in the drum of a friabilator (Erweka GmbH, Germany) revolving at 25 rpm which exposed the tablets to rolling and repeated shock resulting from free fall within the apparatus. After four minutes, the tablets were brought out, dedusted and reweighed. The weight was then recorded and friability calculated as percentage loss in weight.

Disintegration time

The disintegration times of six tablets per batch of the tablets were determined in distilled water at $37 \pm 0.5^\circ\text{C}$ using the B.P. disintegration tester (MK IV, Manesty Machines, UK).

Dissolution studies

The dissolution profiles of the paracetamol tablets were determined using the BP basket method for the various batches of the tablets (Caleva ST7, UK). A dissolution medium of 900 ml of 0.1M HCl solution maintained at $37 \pm 0.5^\circ\text{C}$ with a basket revolution of 50 rpm was used. A 5 ml volume of leaching fluid was withdrawn at various intervals and replaced with an equivalent volume maintained at same temperature ($37 \pm 0.5^\circ\text{C}$) of the dissolution medium. The samples were filtered and diluted with an equal volume of 0.1 M HCl. This was continued for 60 min. The absorbances of the resulting solutions were measured at λ_{max} of 245 nm (T70, PG Instruments Ltd). The concentration and the percentage of drug released at each time interval was determined using the equation from the standard calibration plot obtained from the pure drug. A minimum of triplicate determinations were carried out for all experiments and the results were reported as mean \pm SD.

Statistical analysis

Descriptive statistics was done for all data using Microsoft Excel (2007). Mean and standard deviations of triplicate determinations was computed and reported. Differences between mean was determined using analysis of variance (ANOVA) while $p < 0.05$ was considered significant.

RESULTS AND DISCUSSION

The starch powder of *P. lunatus* was white, odourless and tasteless with a rough texture. Microscopic examination of the starch particles showed a larger particle size range as against the medium size range of maize starch which was oval to elliptical in shape (Table 2). The starch of *P. lunatus* is likely to absorb more moisture than maize starch because of its large grain size which will lead to large pore sizes which may trap water and result in high moisture content (Olayemi et al., 2008). Moisture contents as high as 3 to 4% w/w is generally argued as appropriate to produce maximum disintegration and dissolution of tablets.

P. lunatus starch exhibited higher density than maize starch which could be as a result of wide size range of its particles with the smaller particles filling the void spaces created by larger ones. This is in line with Newman (1967) who showed that low densities result when void spaces created by powder particles are not filled by smaller particles, leading to consolidation of the powder particle and this is a feature of maize starch. Results from the particle size analysis of the paracetamol granules from both the maize and *P. lunatus* starches showed no significant difference in the particle size distribution at the

Table 3. Some physicochemical properties of the paracetamol granules.

Starch	Starch concentration (% w/v)	Bulk density (g/L)	Tapped density (g/L)	Carr's Index (%)	Hausner's ratio	Angle of repose (°)	Flow rate (g/s)	Moisture content (%)
Maize	10	0.46	0.49	6.12	1.07	34	4.52	3
	7.5	0.39	0.42	7.14	1.08	41	4.33	3
	5	0.45	0.51	11.76	1.13	43	4.15	4
	2.5	0.40	0.46	13.00	1.15	45	3.68	3
	0	0.39	0.61	36.06	1.56	48	-	3
<i>P. lunatus</i>	2.5	0.45	0.56	19.64	1.24	48	3.65	2
	5	0.45	0.55	18.00	1.22	47	3.88	3
	7.5	0.43	0.49	12.24	1.14	45	4.18	3
	10	0.41	0.45	8.09	1.09	43	4.37	2

various binder concentrations tested. Also, the moisture loss of all the granules was between 2 to 4%, which met the BP (1980) specification that not more than 15% of the granule weight should be lost on drying.

As shown in Table 3, the bulk and tapped densities of both the maize and *P. lunatus* starch paracetamol granules decreased with increase in binder concentration. This is consistent with the formation of larger granules as the concentration of binder increased leading to larger voids in between the larger granules. As the concentration of the binder increased, the percentage of large granules also increased while the percentage of smaller granules and fine particles decreased. This was due to increase in the formation of bonds between the paracetamol particles and other excipients. The effect of bond formation on the density of granules may be the reason behind the fact that the paracetamol granules produced with maize starch mucilage had lower density values compared to those of the *P. lunatus* starch mucilage that produced granules of a slightly higher density.

The flow properties were found to increase with increase in binder concentration (Table 3). This may be due to the decrease in density with increase in binder concentration and also due to the resultant increase in particle size, leading to decrease in surface free energy of the granule particles and decrease in frictional forces between the granules leading to faster flow. The flow rate of granules which is a measure of flowability is necessary for successful tableting. A good flowability could be attributed to the increase in particle size of the paracetamol particles through the wet granulation technique. The particle size of a drug can be affected by the processing technique such as granule growth during wet granulation and the characteristics of the resulting granulate (Badawy et al., 2000). In comparison, the paracetamol granules prepared with maize starch

mucilage flowed better than that prepared using *P. lunatus* starch mucilage. This could be explained by the effect of the density of the respective starches.

Hausner's ratio and Carr's index are indirect methods of assessing the flow properties of granules. For Hausner's ratio, values greater than 1.6 are indicative of poor flowability while values greater than or equal to 1.25 show good flowability. Carr's index values less than or equal to 16% indicates good flowability while values greater than 23% demonstrate poor flowability (Stanifort, 2002). The result shown in Table 3 indicate that all the batches of granules prepared with both starch mucilages have good flow properties which is necessary for successful tableting except that of 0% binder concentration, that exhibited poor flowability. Comparing both starches, maize starch paracetamol granules exhibited better flow properties than *P. lunatus* starch paracetamol granules.

The angle of repose is also another indirect method of accessing the flow properties of granules. As a general guide, powders with angle of repose greater than 50° have unsatisfactory flow properties, whereas minimum angles close to 25° correspond to very good flow properties (Stanifort, 2002). The results obtained for all the batches where above 25° but below 50°. Therefore, all the batches of granules can be said to have fair flow properties, with that of maize starch flowing better than that of *P. lunatus* starch granules. Hence the need to add a glidant to further enhance flow.

Table 4 shows some physicochemical parameters of the paracetamol tablets formulated from both starch mucilages. The weight uniformity test on the tablets indicated no significant differences ($p > 0.5$) in the weights of tablets from the various batches (Table 4) and hence conformed to the British Pharmacopoeia (2003) specification, that is, that not more than two of the individual weights should deviate from the average weight by

Table 4. Some physicochemical characteristics of the paracetamol tablet.

Starch	Starch Concentration (% w/v)	Batch	Tablet Weight* (g)	Tablet dimensions (mm)		Tablet Hardness* (KgF)	Friability (%)	Disintegration Time* (s)
				Diameter*	Thickness*			
Maize	10	A	0.59(0.002)	12.22(0.002)	4.33(0.004)	14.96(0.042)	0.33	84(0.010)
	7.5	B	0.59(0.002)	12.24(0.004)	4.33(0.004)	14.68(0.073)	0.67	30(0.019)
	5	C	0.58(0.004)	12.22(0.009)	4.35(0.035)	14.52(0.049)	0.70	24(0.009)
	2.5	D	0.59(0.002)	12.24(0.007)	4.32(0.007)	10.40(0.050)	1.02	21(0.009)
	0	E	0.58(0.003)	12.24(0.003)	4.26(0.003)	5.60(0.058)	1.39	15(0.008)
<i>P. lunatus</i>	2.5	F	0.58(0.003)	12.23(0.002)	4.34(0.004)	6.04(0.050)	1.04	15(0.010)
	5	G	0.59(0.002)	12.23(0.004)	4.04(0.005)	8.38(0.050)	0.99	15(0.009)
	7.5	H	0.58(0.002)	12.23(0.003)	4.37(0.003)	8.94(0.040)	0.71	18(0.010)
	10	I	0.59(0.003)	12.22(0.004)	4.22(0.042)	8.92(0.049)	0.67	21(0.008)

*Standard error in parenthesis

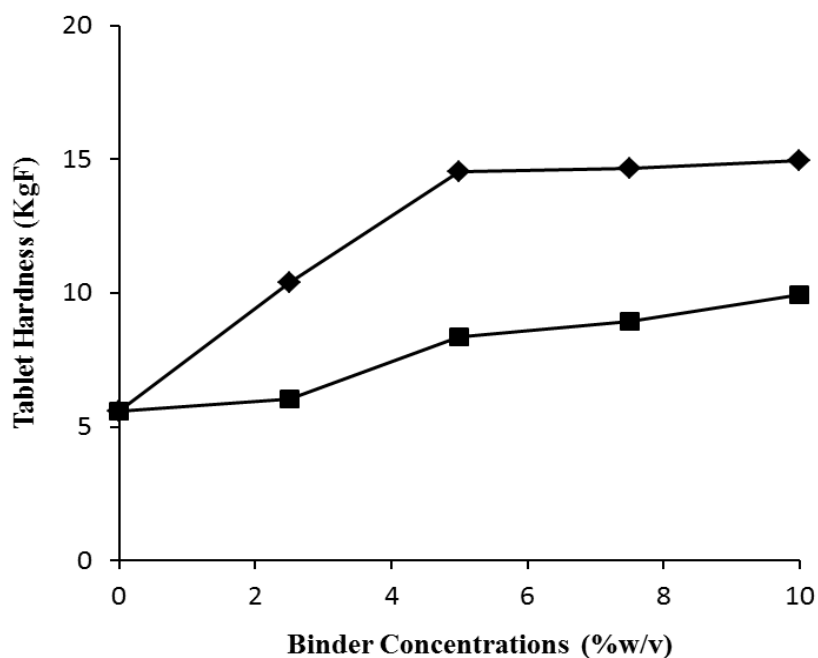


Figure 1. Plots of hardness against binder concentration in paracetamol tablets produced using *P. lunatus* (■) and maize (◆) starch mucilages as binders.

more than $\pm 5\%$ and none should deviate by more than $\pm 10\%$. Also, although there were no significant differences amongst the tablet dimensions, the slight variation in tablet thickness among the batches of tablet made with *P. lunatus* starch could be as a result of the density of granulation (Oyi et al., 2009).

A good tablet is expected to possess sufficient mechanical strength to withstand fracture and erosion during handling, while maintaining good disintegration and dissolution properties. The mechanical strength (hardness and friability) of a tablet is primarily due to

inter-particulate bonding which could be Van Der Waal's forces, mechanical interlocking or the formation of solid bridges via the binder. Uncoated tablets with hardness greater than or equal to 5 KgF are considered optimal and acceptable (Ofoefule et al., 1998). Table 4 shows that all the tablets from all the batches of granules have hardness values above 5 KgF. Increase in starch mucilage concentrations caused a corresponding increase in the paracetamol tablets hardness with the hardness values of tablets from maize starch significantly higher than that of *P. lunatus* starch (Figure 1). This increase in

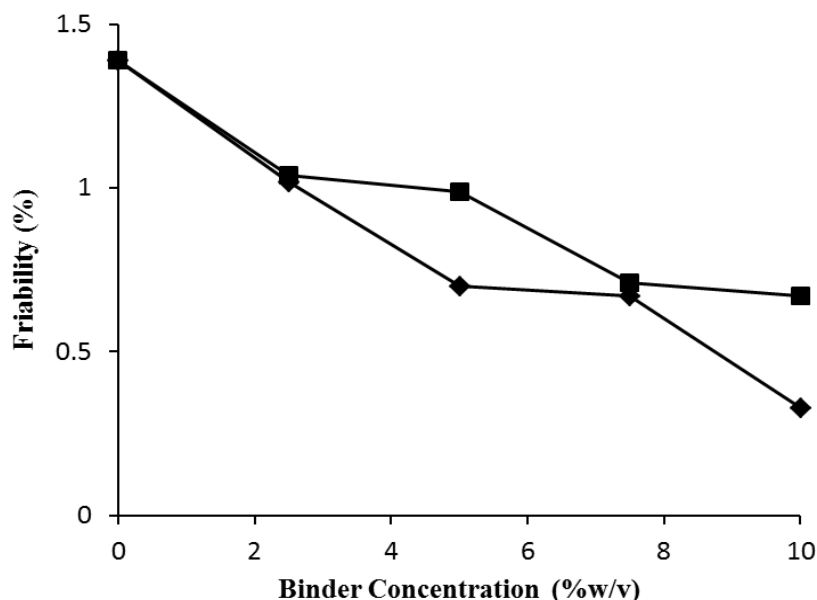


Figure 2. Plots of friability against binder concentration in paracetamol tablets produced using *P. lunatus* (■) and maize (◆) starch mucilages as binders.

increase in hardness might be due to the adhesive nature of the binder, leading to increased bond formation between the granules as a result of formation of plastic and elastic deformation and asperity melting of the particles during compaction (Musa et al., 2008). Binders also promote plastic deformation of particles, thereby increasing the area of contact for interparticulate bonding (Uhumwangho et al., 2006) and subsequently leading to the formation of more solid bonds in the tablet.

The friability values of the tablets were a reverse to that of hardness (Figure 2); friability decreased with increasing concentrations of the binders (Table 4). There was an inverse correlation between the hardness of the tablet and its friability as the harder tablets gave lower friability values. This was expected since like hardness, friability is consequent upon interparticulate bonding and bridges in tablets. Increased binder concentration will lead to a reduction in the size of the capillary spaces between the particles (Oyi et al., 2009) by filling up of the interparticulate spaces, thereby increasing area of contact between the particles leading to the formation of additional solid bonds, and these confer resistance to tablet fracture and abrasion. However, all the tablets met the BP specification of a maximum loss of 1% of the mass of the tablets tested or a 0.8 to 1.0% loss in weight of the tested tablets with no capping, lamination or breaking up in the course of the test.

The reduction of capillary spaces between the particles, as a result of the increase in the concentration of binder, will lead to a reduction in the penetration of water into the tablet to break bonds. This will lead to longer disintegration

times (Oyi et al., 2009). All the formulated tablets disintegrated within 15 min (Figure 3 and Table 4) as specified by British Pharmacopoeia (1980) for uncoated tablets. The results of the disintegration time testing of all the tablets compliment the result of the hard-ness test of the tablets. This indicates that the increase in disintegration time is attributable to an increase in the bonding bridges formed during compaction of the tablet mass as series of linkages, bridges and bonds are formed in order to hold the tablet compacts (Bangudu, 1993).

In the dissolution studies, the dissolution pattern agreed with the disintegration-dissolution theory, which indicates that disintegration usually plays a vital role in the dissolution process since it determines to a large extent, the area of contact between the solid and liquid (Odeku and Itiola, 2003). However, all the batches of the tablets formulated passed the BP 2003 dissolution test for tablets which specifies that at least 70% of the drug should be in solution after 30 mins. From the results obtained, the dissolution rate increased with decrease in concentration of binder and hardness of the tablets (Figure 1), which is probably due to the fact that dissolution is a subject of disintegration. That is to say that tablets would disintegrate before the drug is released into solution. However, it is not always the case, as disintegration could be rapid, but the tablet may actually disintegrate into hard coarse particles from which dissolution may be slow (Musa et al., 2008). Some authors maintain that disintegration and dissolution times are correlated (Proudfoot, 1988) as particle size, and consequently the surface area into which a tablet disintegrates

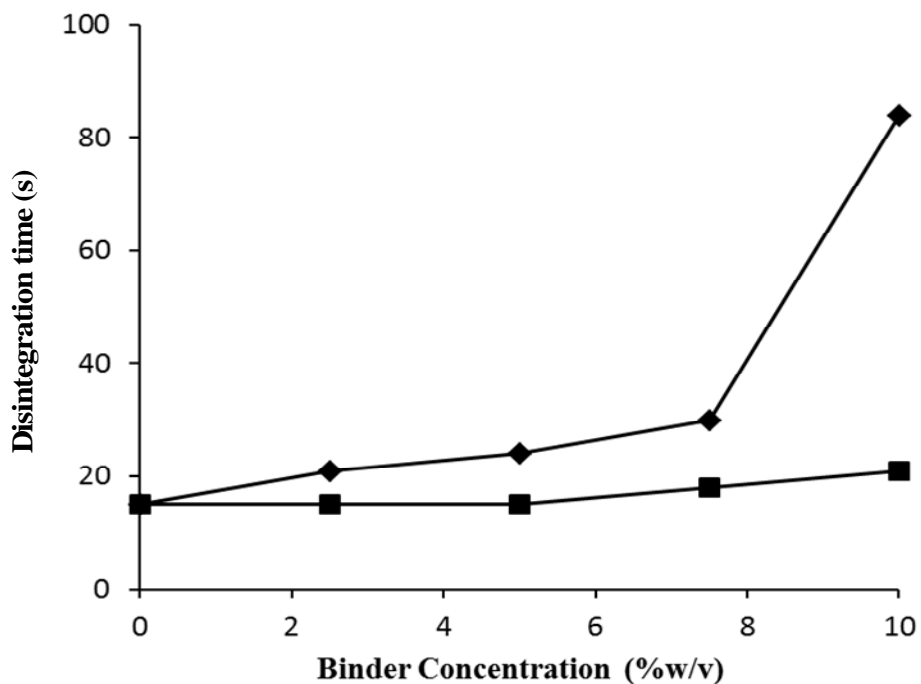


Figure 3. Plots of disintegration time against binder concentration in paracetamol tablets produced using *P. lunatus* (■) and maize (◆) starch mucilages as binders

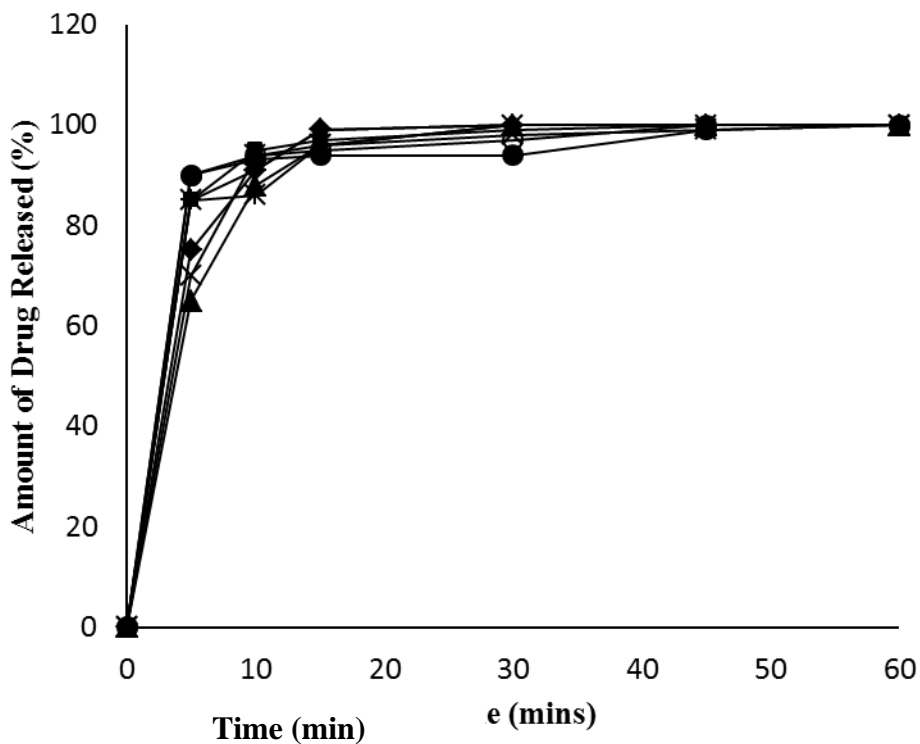


Figure 4. Dissolution profile of paracetamol tablets using varying amounts and types of binders Maize Starch Mucilage: 2.5%w/v (◆), 5%w/v (▲), 7.5%w/v (*), 10%w/v (+) *P. lunatus* Starch Mucilage: 2.5%w/v (■), 5%w/v (x), 7.5%w/v (○), 10%w/v (●).

correlate with dissolution time of the active drug (Rubeinstein and Wells, 1997; Iwuagwu et al., 2001) while some others continue to disagree (Wagner, 1971).

The dissolution rate for tablets produced using maize starch mucilage as binder had the least percentage of drug release at initial time of dissolution. This could be due to its high bond strength. At 30 min, the tablets released 100% of paracetamol. This was not the case with tablets produced using the *P. lunatus* starch mucilage as binder; a large percentage of the drug was released at the initial time of dissolution, and release was continuous for 60 min. This could be due to the fact that tablets containing starch with large particles have smaller starch-particle ratio (less starch separating individual drug particles), leading to faster release of the drug.

Conclusion

Maize starch mucilage formed harder paracetamol tablets than *P. lunatus* starch mucilage. This implies that the inter-granule bonds formed by maize starch were stronger than those of *P. lunatus* starch mucilage. *P. lunatus* starch mucilage gave tablets with shorter disintegration times and faster dissolution rate than the tablets formed with maize starch mucilage. *P. lunatus* starch can therefore be used as a suitable substitute for maize starch as a binder in the formulation of paracetamol tablets.

Conflict of Interest

The author(s) have not declared any conflict of interests.

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