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Binding Properties of the Gum from Unripe Plantain Peels in Paracetamol Tablets

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ABSTRACT

Gum from the peels of unripe plantain, *Musa acuminata* was extracted, after crushing, with distilled water and bleached with sodium hypochlorite solution. Five different granule batches of paracetamol were prepared with different concentrations of the powdered gum at concentrations of 2, 4, 6, 8, and 10 % respectively, as mucilage. The disintegrant and lubricant were maize starch and magnesium stearate at 5 and 1 % total tablet weights, respectively. The wet granulation method was used with the incorporation of the disintegrant intragranularly. Similar granulations were made with a commercial binder - sodium carboxymethylcellulose (SCMC) for comparison. The flow properties of the granules were evaluated and the granules were compressed into tablets. The physicochemical properties of the tablets were evaluated. The plantain gum was fairly white. The granules produced with plantain gum showed similar flow properties with those produced with SCMC. The tablets formulated with plantain gum were more friable that the tablets formulated with SCMC, though, the values became close with increase in adhesive concentration. The tablets formulated with plantain peel gum disintegrated and released the drug faster than those formulated with SCMC. For example, the $T_{30\%}$ in 0.1 N HCl was 3 mins for granulations with 6% plantain gum, and 10mins for those formulated with 6% of SCMC. The results show that the gum from fresh peels of *Musa acuminata* could be a good alternative binder to the commercially sourced SCMC in pharmaceutical formulations.

Keywords: *Musa acuminata*, binder, sodium carboxymethylcellulose, paracetamol, tablets.

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INTRODUCTION

Binders (or adhesives) are used in the formulation of solid oral dosage forms to hold the active pharmaceutical ingredient and inactive ingredients together thus ensuring the formation of tablets and granules with the required mechanical strength[1]. These could be natural substances e.g starches, gums, polymers, or semi-synthetic and synthetic substances. Natural gums are biocompatible, cheap, and easily available. They are preferred to their semi synthetic and synthetic counterparts because of their lack of toxicity, low cost, availability, soothing action and non irritant nature[2]. The synthetic polymers have certain disadvantages such as high cost, toxicity, environmental pollution during synthesis, non-renewable sources, side effects, and poor patient compliance[2].

Several gums have been investigated as possible binders for pharmaceutical tablets. They include *Moringa oleifera* gum[3], *Mangifera indica* gum[4], *Okra* gum[5,6], *Guar* gum[7], *Albizia* gum[8], *Psyllium* seed gum,[9] *Occimum gratissimum*[10], khaya gum[11] to mention a few. All of these gums showed promising results for possible use when compared with the commercially available binders. However, a major limitation of gums from plants is that many of those plants are also food. Thus, there is competition between food and pharmaceutical use.

Plantain is a plant which is widely used as a nutritive agent as well as possessing excellent medicinal properties like wound healing effect due to the presence of allantoin. The peels are frequently discarded as waste. Conversion of this waste to a pharmaceutical excipient could reduce importation and create job as well as wealth.

MATERIALS AND METHODS

Reagents

Paracetamol powder, starch, sodium carboxymethyl cellulose (SCMC), magnesium stearate, sodium metabisulphate, sodium hypochlorite, were procured from their manufacturer (BDH, Poole England).

Equipment

Manesty F-3 Single Punch tableting machine (Manesty, England), manual grinding machine, spatula, electronic weighing balance (Ohaus, USA), mortar and pestle, sieve (1.0 mm), tablet hardness tester (Coslab, India), oven (Genlab, England), tablet disintegration test apparatus (VEEGO,India), friability test apparatus (Campbell electronics, India).

METHODS

Collection of plant material

Fresh ripened peels of Musa acuminata were bought from Nkwor Agu market, Nigeria and identified by a taxonomist, Mr A.O. Ozioko of the Bioresources Development Conservative Programme centre in Nsukka, Enugu state.

Preparation of the Plantain Gum Mucilage

The peels were washed with purified water. Bleached by soaking in a 0.02 % sodium hypochlorite solution for 36 hours, after which the bleaching solution was discarded. A 0.1% Sodium Meta bisulphate solution was added as an anti oxidant to prevent blackening of the peel upon exposure to atmospheric oxygen[13]. It was then dried and milled with grinding machine. The powder was sieved with sieve number 0.12 mm. The following quantities of powder 2, 4, 6, 8, and 10 % respectively, were used to prepare mucilage.

Preparation of Paracetamol Granules

A 50g quantity of paracetamol powder and a calculated quantity of starch based on the batch formula were weighed into a mortar and triturated slightly. Mucilage of powdered plantain gum of to give the required concentrations in the tablet formulation concentrations (2, 4, 6, 8, and 10 %) was added in bits while the powders in the mortar were mixed with a pestle.

The damp mass was screened through a sieve 1.0 mm. The formed granules were dried in an oven at 60 ^{0}C for 90 minutes. The dried granules were sieved through the sieve 1.0 mm. The procedure was repeated for 4, 6, 8, and 10 % concentration of the powdered plantain gum. The procedure above was repeated using SCMC as a binder.

Granule Flow Evaluation and Compression

The flow properties and the angle of repose of the granules were measured by transferring the granules to the funnel suspended at the height of 15 cm with a retort stand and the granules were allowed to drain onto a white paper to form a heap. The granules were weighed and sieved to separate out the fine particles which was also weighed and recorded. Triplicate determinations were carried out. Magnesium stearate was then mixed with granules. The mix was then compressed with a single punch tableting machine.

Evaluation of tablet properties

Weight uniformity test

Ten (10) tablets were randomly selected from each of the batches and weighed individually using an Electronic weighing balance (Ohaus, USA). The average tablet weight and standard deviation for each batch was determined.

Hardness or crushing strength determination

Six (6) tablets were randomly selected from each batch and crushed individually using the

Monsanto Hardness Tester. The pressure taken to crush the tablet was recorded in kgF. The mean and standard deviation of the tablet hardness were determined.

Friability testing

Ten (10) tablets were randomly selected from each batch and dedusted. The total weight of the ten tablets was determined using an electronic balance. The tablets were introduced into an Erweka Friabilator and rotated at 25rpm for four (4) minutes. The tablets were removed, de-dusted and reweighed. The loss in weight (friability) was expressed as a percentage thus:

$$\% \text{ friability} = \left(\frac{initial\ \ weig\,ht - final\ \ weig\,ht}{initial\ \ weig\,ht}\right) \text{X } 100$$

Disintegration Test

The Erweka disintegration unit with 0.1N HCl as the disintegration medium maintained at 37± 1^0C was used. Six (6) tablets selected at random were placed each in a tube of the disintegration unit. With the upward and downward movement of the medium, the time taken for each tablet to completely break down to particles and pass through the wire mesh was recorded. The mean of the determinations was calculated as described in the British Pharmacopoeia[12].

Table 1: Composition of the Paracetamol Tablets (500 mg)

Batch code	Paracetamol (mg)	Starch (mg)	Scmc (mg)	Plantain Peel (mg)	Mag. Stearate (mg)
A1	500.00	27.2	-	10.87	5.4
A2	500.00	27.8	-	22.2	5.6
A3	500.00	28.4	-	34.1	5.7
A4	500.00	29.1	-	46.5	5.8
A5	500.00	29.7	-	59.5	5.9
B1	500.00	27.2	10.87	-	5.4
B2	500.00	27.8	22.2	-	5.6
B3	500.00	28.4	34.1	-	5.7
B4	500.00	29.1	46.5	-	5.8
B5	500.00	29.7	59.5	-	5.9

A1 – 2 % plantain gum, A2 - 4% Plantain gum, A3 – 6 % Plantain gum, A4 – 8 % plantain gum, A5 – 10 % plantain gum, B1 – 2 % SCMC, B2 - 4 % SCMC, B3 – 6 % SCMC, B4 – 8 % SCMC, B5 – 10 % SCMC.

Dissolution Test

The dissolution rate of each of the batch was determined on the dissolution unit (Erweka Dissolution Apparatus). The volume of dissolution medium was 900 ml (GIF, SIF or distilled water). This was placed in the vessel immersed in the constant temperature bath and equilibrated at a temperature of 37± 0.5 ^{o}C. A tablet was placed in each of the six baskets. The paddles were adjusted to give a distance of 23-27 mm between the paddle and the inside bottom of the vessel.

The motor knob was set so that the basket rotates at 100 rpm. A 5 ml sample was withdrawn each time at 1, 3, 6, 10, 20, and 30 minutes interval with 5 ml pipette. A 5-ml volume of fresh dissolution medium at the same temperature was used to replace the withdrawn sample. The absorbance of the sample was read using the spectrophotometer at 257 nm. The concentrations were then calculated using the constant K gotten from Beer's calibration:

$$A=KC.$$

Where, A= Absorbance, C= Concentration, K= constant

RESULTS AND DISCUSSION

Yield of the Gum and Appearance

The yield of the gum was 97% (w/w and this shows that it could be processed in bulk for commercial purposes. The colour was pale white. Thus, it was expected not to add extra colour to the formulation.

Granule and Tablet Properties

Table 2: Granule Properties

Batch codes	Flow rate (mm/sec)	Angle of repose (degree)	Percentage fine (%)
A1	7.7	30.5	26.0
A2	8.1	27.3	25.4
A3	15.3	28.2	21.8
A4	14.0	30.5	23.2
A5	13.0	27.8	25.4
B1	12.5	28.7	32.8
B2	11.1	30.4	34.5
B3	8.5	30.0	19.9
B4	13.0	24.1	27.8
B5	14.0	30.9	23.9

Diameter of orifice: 1cm (10 mm); height of flow: 15 cm (150 mm)

With the plantain peel gum, fine particle composition decreased with increase in gum concentration up to 6 % (Table 2). The percentage of fine particles was more with the plantain peel gum than with SCMC. However, both batches exhibited a high percentage of fine particles, possibly due to method of processing.

The flow rates of the granules formulated with the plantain gum increased with increase in concentration till 6 %, after which the flow rates decreased with further increase in adhesive concentration (Table 2). Thus it appears the best concentration for optimum flow is 6%. The flow rates of the granules prepared with the plantain gum were slightly less than those obtained with granules formulated with SCMC. These results corresponded with the angle of repose

results. The variations could be attributed to the shape of the powder, size and size distribution of the granules[14].

Table 3: Tablet Physico-technical Properties

	Hardness (kg/cm)	**Weight variability (mg)**	**Friability (%)**	**Disintegration time (min)**
Limit →	At least 5 kg/cm	Mean ± 5% S.D	Not more than 1%	Within 15 minutes
Batch Number ↓				
A1	2.5 ± 0.18	540 ± 16.66	48.03	0.16
A2	3.2 ± 0.11	550 ± 12.51	30.60	0.30
A3	3.5 ± 0.09	560 ± 13.49	20.47	1.20
A4	4.0 ± 0.06	580 ± 15.49	16.57	2.45
A5	4.6 ± 0.14	520 ± 20.02	7.38	4.00
B1	3.2 ± 0.11	540 ± 13.16	46.58	4.00
B2	4.1 ± 0.14	520 ± 16.6	26.00	33.2
B3	4.6 ± 0.14	550 ± 13.49	29.70	14.0
B4	5.2 ± 0.19	560 ± 13.64	8.93	21.0
B5	5.7 ± 0.14	520 ± 14.29	7.82	30.0

The temperature of the disintegration medium (purified water) was maintained at 37 ± 2^0C.

The hardness values of the tablets prepared with SCMC were generally moderately higher than those of tablets prepared with the plantain gum (Table 3). Hardness values increased with increase in adhesive concentration in either case. Thus, the plantain peel showed moderately lesser adhesive ability than SCMC.

The tablets prepared with the plantain gum were generally more friable than tablets prepared with SCMC (Table 3). However, as adhesive concentration increased, tablet friability remarkably decreased and the values with the two excipients (batch 5) approximated each other. Thus, at higher concentrations, plantain peel gum could replace SCMC as binder in paracetamol tablet formulations.

The weight variation deduced from the standard deviation, is more in the tablets prepared with plantain gum than that of the SCMC (Table 3). This weight variation could be attributed to the presence of more fine granules which form powder compacts that retard flow of powders.

The tablets with plantain gum as binder disintegrated fast (in less than 5 minutes) (Table 3). These results conformed to the Pharmacopoeia limits of disintegration of immediate release tablets - within 15 minutes. Tablets formulated with SCMC had higher disintegration times than those of the plantain gum. The tablets formulated with plantain gum would thus be expected to have a faster onset of action.

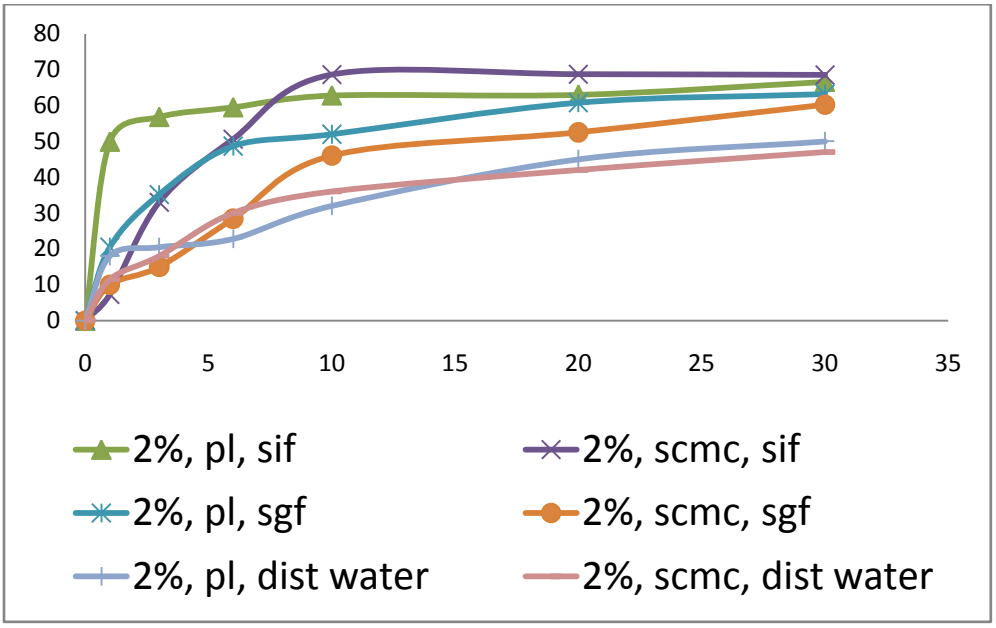

Figure 1: Release profile of paracetamol tablets formulated with 2 % binder

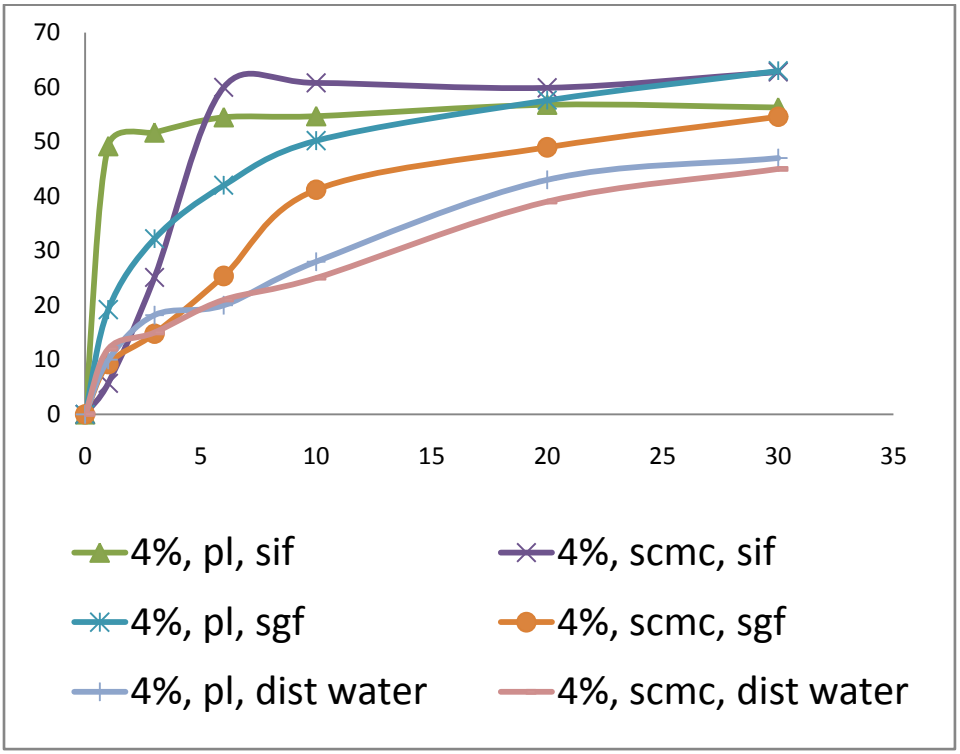

Figure 2: Release profile of paracetamol tablet formulated with 4% binder

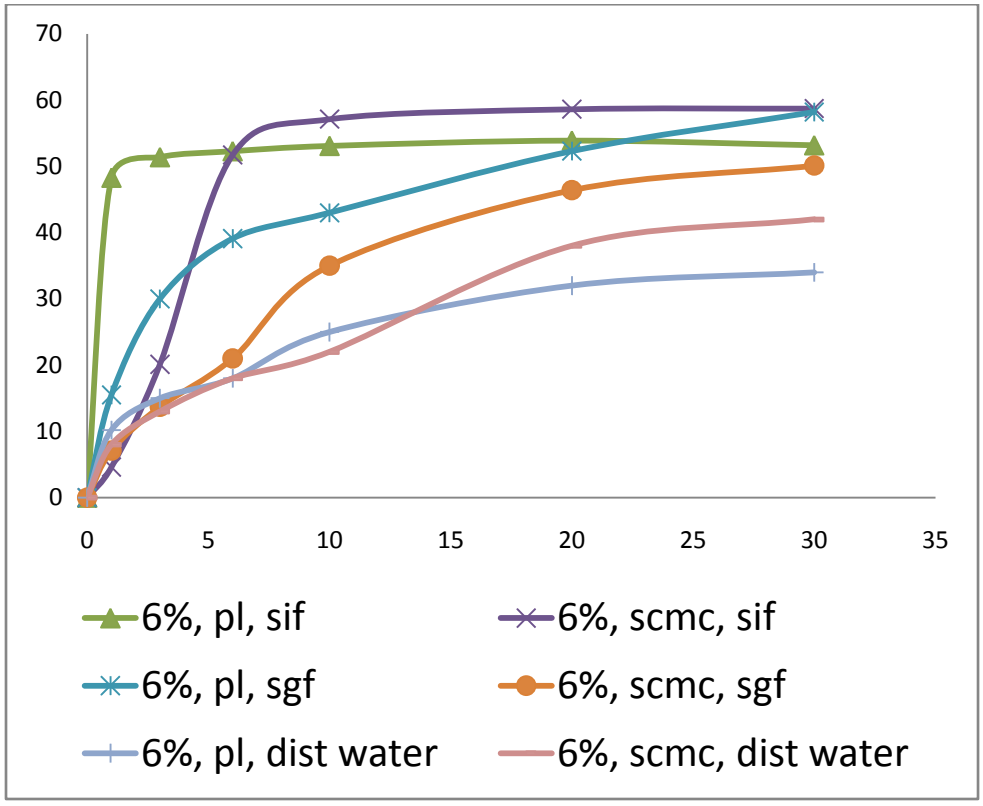

Figure 3: Release profile of Paracetamol tablets with 6% binder

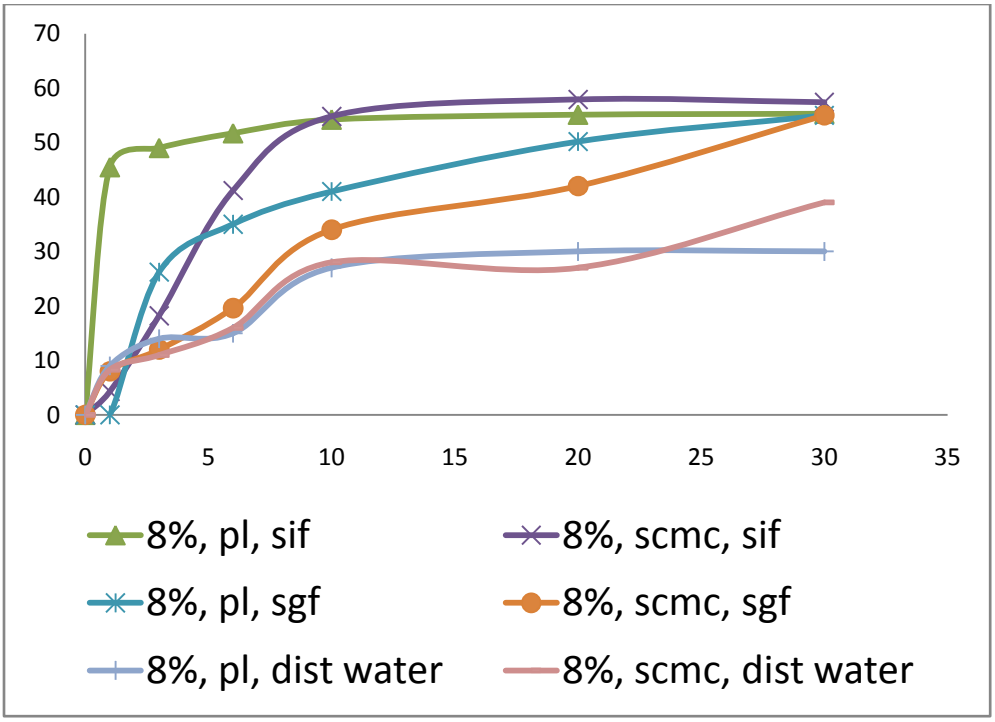

Figure 4: Release profile of Paracetamol tablets with 8% binder

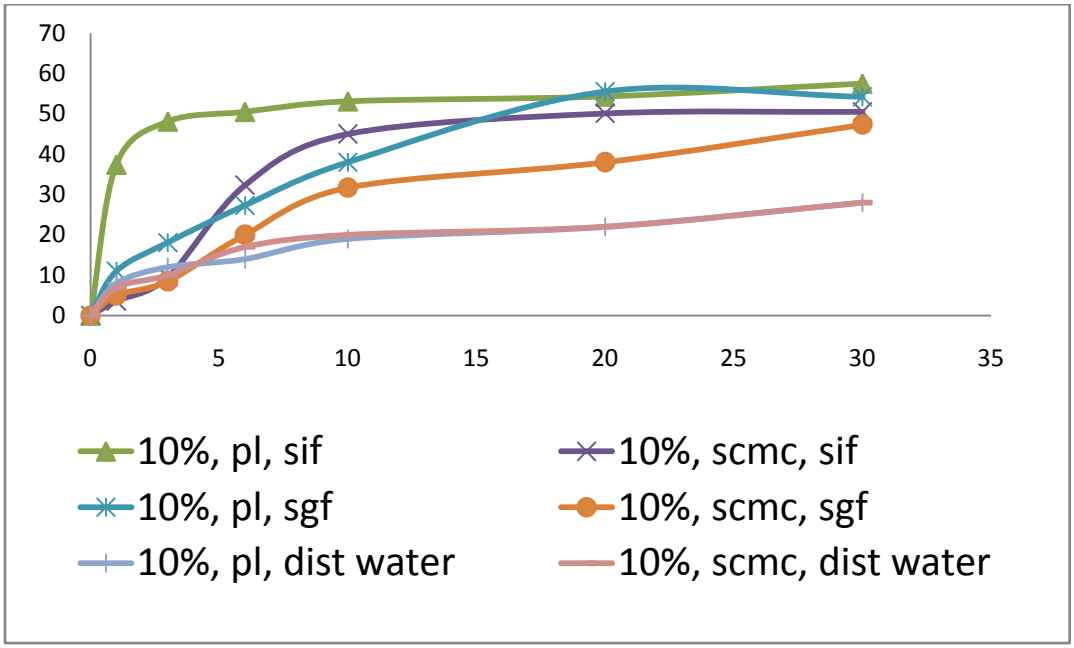

Figure 5: Release profile of paracetamol tablets formulated with 10 % binder

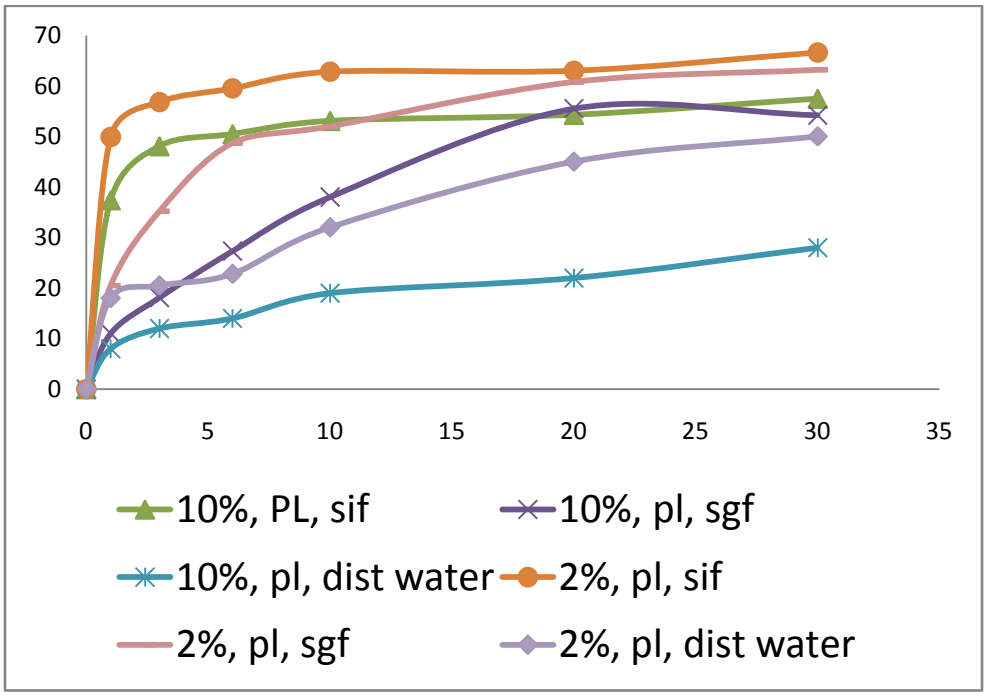

Figure 6: Release profile of paracetamol tablets formulated with 2% and 10 % plantain gum in different media

Tablet Dissolution

The drug absorption and physiological availability depend on having the drug substance dissolved in physiological fluid. Suitable dissolution characteristics are an important property of a satisfactory tablet. The dissolution test measures the amount of time required for a given percentage of the drug substance in a tablet to go into solution. Generally, the tablets formulated

with plantain gum dissolved faster than those with SCMC with almost the same total percentage release (figure 1-5). Tablets formulated with plantain gum had highest release in SIF and least in distilled water (Figure 1-6). This is likely due an ionic effect since acidic drugs tend to dissolve faster in alkaline environment. Also, there might be uncoiling of the polymeric structure of the gum in alkaline environment leading to more swelling and hence more drug release[15]. Increase in plantain gum concentration led to decrease in paracetamol release (Figure 6). The dissolution of the tablets formulated with plantain gum conformed to the British Pharmacopoeia (2009) standard.

CONCLUSION

Extraction of the gum from fresh plantain peels is a simple process and the yield is high. At higher binder concentrations the gum has similar binding properties as sodium carboxymethyl cellulose (SCMC). Tablets formulated with plantain gum disintegrate and release their contents much faster than those formulated with SCMC at all formulation concentrations. Thus, plantain gum could be a good replacement for SCMC in paracetamol tablet formulation and it is more economical, being processed from a "waste product". Also, the processing is simple and cheap. However, more studies need to be carried out on optimizing it for commercial use.

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