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Research Article

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Preliminary study of *Annona reticulata* starch as binder in formulation of paracetamol tablets

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ABSTRACT

Binder properties of mucilage of starch extracted from Annona reticulata fruits were investigated in paracetamol tablet formulations prepared via wet granulation method. The starch paste in four concentrations (2.5%, 5%, 7.5% and 10%w/w) was evaluated for optimized binder concentration. Preformulation study of the drug with starch were analysed using Fourier transform infrared spectroscopy (FTIR) Preformulation study of the drug and starch showed no interaction in FTIR. The tablets were evaluated for physical properties, disintegration time and in vitro dissolution profiles, and all the parameters were found within the official specifications. The effect of binder on tablet properties was related to their viscosity and surface tension. Tablets at 7.5% w/w binder concentration showed more optimum results. Results suggest the suitability of Annona reticulata fruit mucilage as a binder to paracetamol tablets.

Key words: *Annona reticulata*, starch, binder, paracetamol, tablets.

INTRODUCTION

More than ever before, formulation development scientists have a need for high quality binders for oral dosage forms. As the structure and targeting of new drugs becomes more complex, additional demands are placed on the formulation chemist to develop formulations to deliver the drugs with optimum therapeutic efficacy. Furthermore, the globalization of the pharmaceutical industry has intensified the need to develop uniform testing procedures and global specifications for all excipients primarily used to develop pharmaceutical dosage forms including binders. This is being pursued by the International Pharmaceutical Excipients Council (IPEC) **[1].**

So the binder is a crucial ingredient in formulation of tablets and granules. The most commonly available plant ingredients with a range of applications are starches.

Annona reticulata is a small, deciduous or semi deciduous tree, upto 10 cm in height, native to tropical America. Dark rough, chocolate brown with longitudinal fissures, 1.4-4.0 mm thick, becoming double quilled when dry, leaves oblong lanceolate 10-20 cm × 2.5-7.4 cm with unpleasant odour. Berries in heart shaped syncarpium, yellowish, or brownish red when ripe. Acids black reddish, smaller, round, pulp dull white, less sweet than the other, rather insipid, and moderately adherent to seed. Reticulata upto 3m in height, compact, dome shaped, leaves lanceolate, wrinkled and folded syncarpium. Ethanolic extract of the fruit contains carbohydrates **[2].** Unripe fruits were used as an astringent, anthelmintic and antidyscenteric. Also possess insecticidal property. The objective of the present work was to isolate starch from the fruits of *Annona reticulata* and evaluate their tabletting properties as binder.

EXPERIMENTAL SECTION

2.1. Material collection

Paracetamol purchased from Paxmy specialty chemicals, Chennai was used as model drug in the study. Maize starch BP, magnesium stearate and gelatin were purchased from SD Fine chemicals, Mumbai. Aerosil was purchased from Degussa, Mumbai. All other solvents and chemicals were of pharmaceutical grade. *Annona reticulata* fruits were purchased from the local sellers of Ootacamund, India.

2.2. Isolation of Starch **[3].**

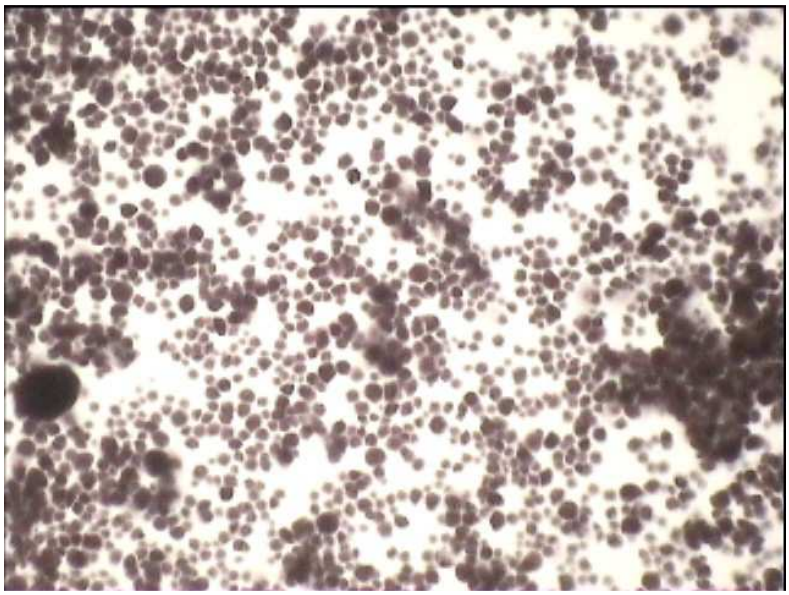
Fruits of *Annona reticulata* was peeled off and cut into small pieces. The fruits were then blended with 1% Nacl to free starch from the cells and the milky liquid is filtered through fine muslin. It was added with 2 litres of water and kept for 12 hrs for effective settling. On standing, starch granules settle at the bottom and the supernatant was then decanted. Finally settled starch sediment is washed with water and dried at 30-40 °C for half an hour in a tray drier. The dried product was stored in desiccator for further studies.

2.3. Characterization of starch

The starch was characterized for surface character, gelatinization and gelling concentration, pH, viscosity and surface tension **[4].**

The surface character of *Annona reticulata* starch (Figure. 1) was analysed by Digital Microscope attached to the computer system (Motis instruments, Bangalore). Samples (1g each) previously moistened with water were loaded into a capillary tube by means of intrusion. The temperature of gelatinization (°C) and time from swelling to full gelatinization were measured with a melting point apparatus. Different concentarion of dry powders were mixed with distilled water using laboratory stirrer and the gel forming concentration of starch (%) was found out. Each starch (1g) was made into mucilage with distilled water (100 ml) and pH was determined using digital pH meter (Merck, Mumbai). Brookfield Viscometer (Engineering labs, INC, Middlebord, USA) was used to determine viscosity (cp) of starch mucilage (5% w/v) at 28 °C. The surface tension of starch solution (0.1% w/v) solution was determined by dropweight method using stalagmometer. Infrared (IR) spectra were matched for detection of any possible chemical interaction between drug and starch on an Perkin Elmer FTIR series (model 1615) Spectrophotometer in the range of 450 to 4000 cm^{-1}using potassium bromide discs. The IR spectrum of physical mixture was compared with those of pure drug and starch and matching was done to detect any appearance or disappearance of peaks.

Fig 1. *Annona reticulata* starch



2.4. Preparation and evaluation of granules

The starch paste in four concentrations (2.5-10.0 % w/w) of paracetamol granules were prepared using mucilage and maize starch by wet granulation method **[5].** Here maize starch was used as standard binder for comparison. All the ingredients were mixed thoroughly except aerosil and magnesium stearate using the formula as shown in Table 1.The starch paste in four concentrations (2.5-10.0 % w/w) was used as binder. The coherent mass obtained was then passed through 16/20 mesh and then dried at 60^0Cfor 1 hour and used for tablet preparation. Aerosil and

magnesium stearate were finally added to the formulation. The granules were evaluated for micromeritic properties like bulk density, tapped density, percentage of fines, angle of repose, compressibility carr's index, hausner's ratio and loss on drying which were measured by the method described in our earlier studies **[5].**

Table 1. Formulation compositions of paracetamol tablets

Ingredients	Mg/tab
Paracetemol	250
Annona/maize starch in water *(2.5 to 10 % w/w)	Variable (9.37 to 37.5)
Corn starch (10 %w/w)	37.5
Microcrystalline cellulose	Variable (44.25 to 72.5)
Magnesium stearate 1 % w/w	3.75
Aerosil 0.5 % w/w	1.805

2.5. Evaluation of binding efficacy of mucilage

Tablets (375mg) of 10 mm diameter were prepared from the prepared granules using Rotary tablet compression machine (10 stations, Rimek,Karnavati Eng. Ltd., Ahmedabad, India) The prepared tablets were evaluated for weight variation, thickness, hardness, friability and content uniformity according to the method described in our earlier studies **[6].** Disintegration time was determined in Disintegration apparatus (Veego Equipments, Mumbai, India) using distilled water at 37.0±0.5 °C. The rate of dissolution was studied in a rotary paddle USP (XXIII)apparatus II,(Electro lab, Mumbai, India) operated at 50 rpm. The dissolution medium was phosphate buffer at pH 5.8 at 37±0.5 C. The amount of paracetamol in each sample was analysed spectrophotometrically with UV-160A recording spectrophotometer (Shimadzu India, Chennai, India **[7].**

RESULTS AND DISCUSSION

The pH of *Annona reticulata* starch mucilage was 5.86 while that of maize starch was 6.21. Both the starches had low viscosity values (2.162 cp for *Annona reticulata* starch and 2.186 cp for maize starch) The gelatinization temperature was found to be between 70-80 °C and the gelling concentration was in the range of 2-4% for both the starches respectively. The starch mucilage of *Annona reticulata* exhibited surface tension value of 62.6 dynes/cm whereas it was 66.8 dynes/cm for maize starch. The lower viscosity and surface tension of starch mucilage probably enabled better penetration and spreading over paracetamol powder during wet massing thereby producing more porous granules. Surface tension and viscosity of mucilage binders are important determinants of other physical phenomena of granulation such as adhesion, cohesion, wetting and spreading. The binder solubility and the properties of the binder solution, its surface tension and viscosity affect granulation and tabletting processes in addition to the binder-excipient and binder–drug interactions. In the preformulation study, the compatibility between the drug and starch was evaluated using FTIR peak matching method. The IR spectra of drug, starch and physical mixture are shown in figures 2 to 4 respectively. There was no appearance or disappearance of peaks in the starch-drug mixture, which confirmed the absence of any chemical interaction between the drug and the selected starch indicating that the drug and starch are compatible. Physical properties of the granules such as bulk density, tapped density, percentage of fines, angle of repose, carrs index, hausner ratio and loss on drying were evaluated. The results are given in tables 2-3. It was observed that as the concentration of starch was increased the percentage of fines were decreased and the flow properties increased as evident by decrease in the angle of repose values. However, 0.5 %w/w Aerosil was included as the glidant to avoid any flow problems during large scale manufacturing.

Table 2. Percentage of fines of formulations with different binder concentration

S.No	Binder	Concentration of Binder (%)	Retained on sieve 44 (g)	Passed through sieve 44 (g)	% of fines
1	*Annona reticulata starch*	2.5	24.1	5.9	24.48
		5.0	24.5	5.5	22.40
		7.5	25.3	4.7	18.57
		10	25.8	4.2	16.27
2	Maize starch	2.5	23.1	6.7	28.20
		5.0	23.4	6.4	27.92
		7.5	23.8	6.3	26.96
		10	24.5	5.4	27.98

Fig 2. FTIR spectrum of paracetamol

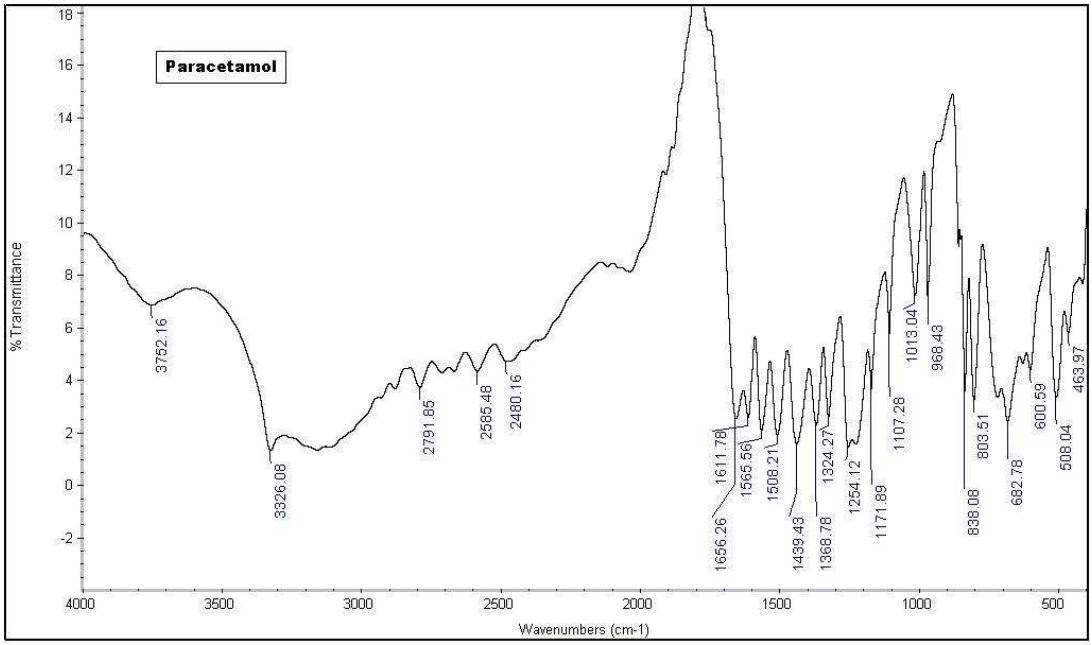


Figure 3. FTIR spectrum of *Annona reticulata* starch

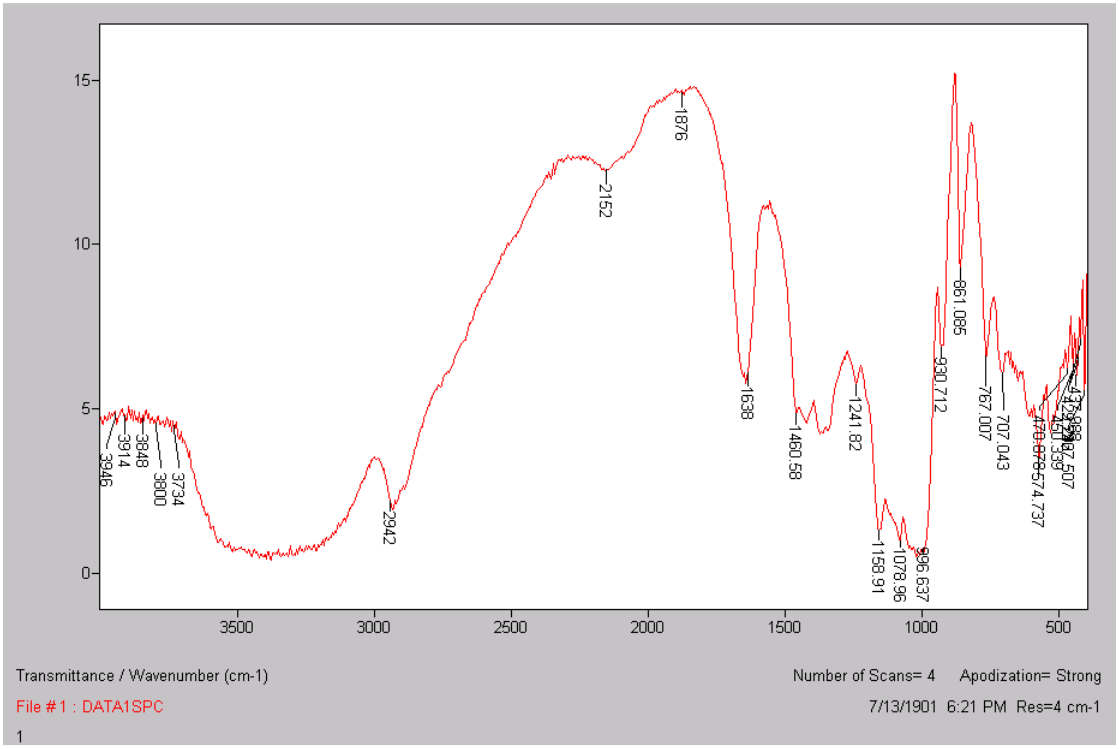
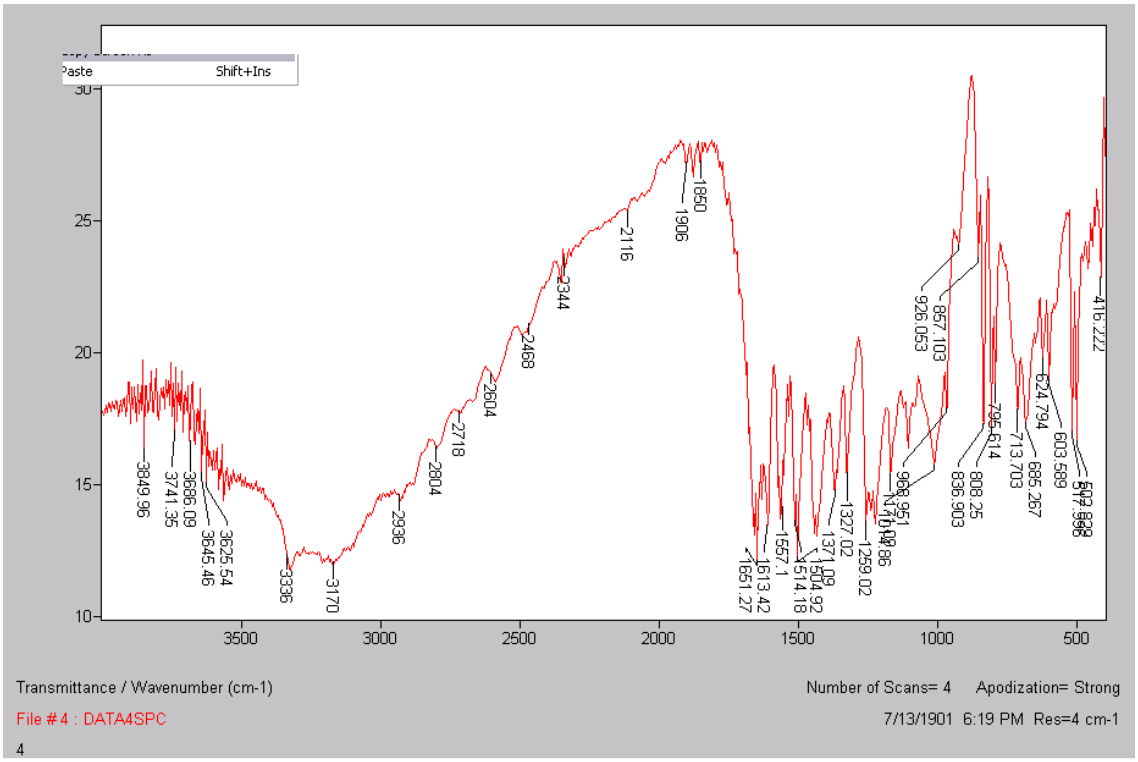


Table 3. Granular properties of formulations using *Annona reticulata*/maize starch

Parameters	Binder concentration (%) *Annona reticulata* starch				Binder concentration (%) Maize starch			
	2.5	**5.0**	**7.5**	**10.0**	**2.5**	**5.0**	**7.5**	**10.0**
Angle of repose (°C)	$28^0$10'	$28^0$20'	$28^0$45'	$28^0$16'	$28^0$19'	$28^0$45'	$28^0$86'	$28^0$58'
LBD(g/cm3)	0.444	0.418	0.426	0.429	0.456	0.434	0.419	0.424
TBD(g/cm3)	0.542	0.551	0.526	0.534	0.521	0.536	0.529	0.536
Loss on drying (%)	5.12	5.34	5.16	5.01	6.12	6.45	5.26	5.48
Carr s index (%)	18.60	18.74	18.19	18.45	18.21	18.52	18.21	18.47
Hausner s ratio	1.221	1.222	1.216	1.219	1.218	1.220	1.217	1.220

Figure 4. FTIR spectrum of *Annona reticulata* starch with Paracetamol



The formulated granules were compressed into tablets on a 10 station rotary tablet machine. The prepared tablets were evaluated for weight variation, thickness, hardness, friability, content uniformity and disintegration time. The results are given in table 4. All the formulation showed uniform thickness. The average percentage deviation of 20 tablets of each formula was less than ± 5 % and hence the formulations passed the test for uniformity of weight. Good uniformity in drug content was found among the different batches.

The effect of binder concentration on the tablet hardness indicated that increase in the concentration of the binder resulted in increase in the hardness which may be due to stronger cohesive bond formation between the granules. All the formulated batches have acceptable hardness which can withstand the abrasion during the transit.

Another measure of tablet's strength is friability. In the present study, the percentage friability for all the formulations was below 1 % w/w, indicating that the friability for all the formulations was below 1 % w/w indicating that the friability is within the prescribed limits.

Table 4.Tablet properties of formulations using *Annona reticulata*/maize starch

Parameters	Binder concentration (%) *Annona reticulata* starch				Binder concentration (%) Maize starch			
	2.5	**5.0**	**7.5**	**10.0**	**2.5**	**5.0**	**7.5**	**10.0**
Wt variation (mg)	380.25 (1.26)	383.26 (1.78)	382.56 (1.58)	382.06 (1.23)	375.15 (1.06)	373.12 (0.68)	382.25 (1.28)	372.68 (0.93)
Thickness(mm)	3.98	3.97	4.1	4.3	3.92	3.96	3.98	4.01
Hardness (kg/cm^2)	4.0	4.3	4.4	5.6	4.3	4.4	4.6	4.6
Friablilty (%)	0.321	0.326	0.481	0.521	0.624	0.527	0.624	0.629
Content uniformity (%)	97.27	99.56	97.32	95.71	98.35	97.17	98.12	96.14
Disintegration time (min)	190	202	220	229	150	162	181	145
% release after 60 minutes	32.92	60.21	72.86	72.92	37.27	71.21	72.86	72.97

The effect of binder concentration on the disintegration of the formulated paracetemol tablets was investigated. It was observed that, there was increase in the disintegration time with the increase in the binder concentration. There was only marginal increase in disintegration time in batches formulated with starch above 7.5 % w/w concentration. This can be related to the increased swelling and capillary effect at high concentration. However, the disintegration time of all the batches was well within the acceptable limits. Drug release from the tablets containing 7.5 to 10% was more than 70% in 60 minutes. Tablets at 7.5% w/w concentration show more optimum results as tablet binder while at higher concentration *Annona reticulata* starch formed a viscous mass that makes barrier in movement of

dissolution medium into the pores of dosage form. The drug release from tablets showed slight decrease with increase in binder concentration. In case of maize starch as binder, the optimized concentration could be 5% w/w to formulate paracetamol tablet.

CONCLUSION

An immediate release tablets were formulated using natural starch by wet granulation technique. Preformulation studies indicate the compatibility of starch with paracetemol. The physicochemical parameter observed support the ideal flow nature of the formulated granules and the applicability of the selected starch as binder. A credible association exists between binder physical properties such as surface tension and viscosity and the physicochemical and *invitro* dissolution rate of the resulting tablets. The effect of binder concentration on the flow properties, *in vitro* disintegration time behavior was significant. In general an increase in the binder concentration improves the flow and increases the disintegration time.

Based on these observations, it was concluded that the formulated tablets showed acceptable pharmacotechnical properties and compiled with the specifications for weight variation, content uniformity, hardness, friability, *in vitro* disintegration and dissolution studies. It also can overcome the disadvantages associated with the synthetic polymers.

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REFERENCES

[1] Kistensen HG, In: Swarbrick J; Boylam JC, Encyclopaedia of Pharmaceutical Technology, Marcel Dekker, 2nd ed, New York, 451-465, **1988**.
[2] Anonymous In: The Wealth of India, Raw materials, I, CSIR, New Delhi, 284-289, **1998**.
[3] Saleemulla Khan, Ramu G, Krishna Mohan G, Jayaveera KN, Chetan Bhalgat. *Journal of Scientific and Industrial Research*. **2011**, 70: 149-155.
[4] Adebayo AS, Itiola OA. *Pharmaceutical Technology*. **2003**, 3: 78-90.
[5] Akhilesh V Singh, Anudwipa Singh, Lila K Nath, Nihar R Pani. *Asian Pacific Journal of Tropical Biomedicine*. **2011**, 1: 86-89.
[6] Ramu G, Krishna Mohan G, Jayaveera KN, Suresh N, Chandraprakash K, Ramesh B, et al. *Indian Journal of Natural Products and Resource*s. **2010**, 1(3): 342-34
[7] Gowthamarajan K, Kanaka Phani Kumar G, Narayan Babulal Gaikwad, Suresh B. *Carbohydrate Polymers*. **2011**, 33: 506-511.