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Okra mucilage act as a potential binder for the preparation of tablet formulation

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ABSTRACT

The present study was carried out with an aim of studying the ability of polysaccharide extracted from Abelmoschus esculentus (AE) to be used as a Binder in Drug delivery systems. Keeping in view the aim, the natural mucilaginous substances were collected from AE by Ethanol precipitation method and were undergone identification tests, quantitative determination of pectin by Carbazole tests and identification tests were carried out by FT-IR. After extraction of the mucilage these were used as a binder in various concentrations in the preparation of paracetamol tablet.

Keywords: Okra mucilage, Binder, Carbazole test, Paracetamol

INTRODUCTION

The okra plant, *Abelmoschus esculentus* (AE) Moench, a native plant from Africa, is now grown in many other areas such as Thailand, the Middle East and the southern states of the USA. The okra pod is often used as a vegetable. Its water extracts contain thick slimy polysaccharides and are used to thicken soups and stews [1, 2]. It is a high value functional fruit ingredient available in markets in the form of white to light brown powders and is used as gelling agents in several marketed products in jam, gellies etc [3]. This study was done with an aim to prepare PCM tablet by wet granulation method and direct compression by using okra mucilage as binding agent. The powdered mucilaginous substances were isolated from AE by Ethanol precipitation method [4] and identification tests of pectin in the natural mucilaginous extracts were done [5]. The identification tests shows the presence of pectin in the natural mucilaginous substances isolated from AE and the quantitative determination of pectin in the mucilaginous substances of AE was done by Carbazole test [6]. Thus the physical mixtures of model drug (Paracetamol) in solid form along with a series of natural polysaccharide isolated from AE was studied by Fourier Transform infrared spectroscopy (FT-IR).

MATERIALS AND METHODS

Fresh Okra fruit was collected from the local market of Godhra, Paracetamol was obtaining as a gift sample from Orley laboratories pvt.ltd. Ahmadabad, Crosspovidone from Chemdyes Corporation. Magnesium stearate from Signet chemicals, MCC 101 and Talc from S.D Fine chem., Ethanol from Triveni Chemicals.

Methods of extraction and isolation of mucilage from Okra fruit
Extraction of the mucilage
Aqueous Extraction
The natural mucilage substances was extracted using water as the Extracting medium

a. Preparation of the sample
The raw materials AE fruits are weighed (1 kg). It was cleanly wash with running tap water over a period of 1Hr. After washing these were thoroughly dried under sun light for 15 to 20 days. The dried materials were weight again (217 gm). The upper and lower ends of the fruit were cut and the seeds were removed completely, then the dry fruit was cut into small parts.

b. Heating of the sample
Mucilage was isolated in the following steps-
The heating mantle was set at 60-70 ^{0}C and preheated for 10 minutes. One beaker (1L) was taken and filled with chopped pieces of the dry fruits. Deionised water was added to it in the ratio 1:4 (217 gm okra + 1.5 kg water). The beaker was then placed on the heating mantle. The above set up was kept for about 7-8 hours for complete recovery of mucilage. The preparation was stirred regularly with glass rod. Temperature was checked at 15 minutes interval to keep it maintained at 60-70 ^{0}C. After about 8 hours the slurries was strained through a Buchner funnel (260ml). The filtrate was kept in room temperature in a beaker for overnight for sedimentation. The decanted filtrate was taken out and the supernatant was poured into a clean and dry beaker of 100 ml size.

c. Concentration of the Extract
The supernatant obtained from the above decantation process is concentrated by evaporating the solution in heating mantle at 50- 60 ^{0}C. The volume of the samples were reduced to 1/5 th of its original volume.

d. Precipitation of the Sample
The concentrated samples were washed with three volumes of Ethanol. The precipitate was collected and rewashed three times with three volumes of Ethanol and the precipitate was collected.

e. Drying of the precipitate
The precipitate was dried at first in sunlight over a period of 2Hr. then pass the dried substance through sieve no. 18. Place these sample in a Hot air oven for 1 hours and maintaining the temperature about 50 to 60 ^{0}C. And maintain the final LOD of the sample not greater than 3. On drying, the sample becomes hard and brownish in colour. It was powdered and the powdered samples were passed through sieve nos. 72.

Identification Test of Pectin [7]
a. Stiff gel Test
200 mg of powered was heated with 10ml of water on a water bath till a solution was formed, on cooling stiff gel was formed.

b. Test with 95% Ethanol
On adding an equal volume of Ethanol (95%) to 1% w/v solution of pectin sample, a translucent, gelatinous precipitate was produced. (Distinction from most gums).

c. Test with Potassium Hydroxide (KOH)
To 5ml of a 1% w/v solution of pectin sample, 1ml of a 2% w/v solution of KOH was added and set aside for 15 minutes. A transparent semi gel was produced When the above gel was acidified with dilute HCl and shaken well, a voluminous, colourless gelatinous ppt. was formed .This upon boiling became white and flocculent.

d. Carbazole test [8]
Preparation of Reagents
0.150 g of reagent grade Carbazole was dissolved in 100 ml of ethyl alcohol. The dissolution of Carbazole was slow and required stirring.

Method
2ml of sample was chilled in 10ml distilled water. 12 ml of conc. H_2SO_4 was added slowly and carefully through the side of the test tube. The above preparation was heated for 20 minutes on a water bath and cooled. 1 ml 0.1% Carbazole in absolute alcohol was added to it and kept for 2 hours. The solution was scanned in the range of 400 to 800 nm to fix the maximum wave length and UV spectrum can be obtained.

Drug – Excipient Compatibility Study [9]
The FT-IR spectra of pure pectin, Paracetamol and both the powdered mucilaginous substances were obtained individually and compared. Physical mixture of drug with powdered mucilaginous substances taking one of them with drug was prepared and FT-IR spectra were obtained. Another FT-IR spectrum was also obtained for the physical mixture of drug with both the mucilaginous substances.

Table 1: Compression of PCM Tablet Containing Okra Mucilage

Ingredients	Qty (mg/Tab)							
	PC1	PC2	PC3	PC4	PC5	PC6	PC7	PC8
	Wet granulation				Direct Compression			
Paracetamol	500	500	500	500	500	500	500	500
MCC101	44	35	29	20	44	29	20	17
SSG	24	24	24	24	24	24	24	24
Okra Mucilage	12	21	30	39	12	30	39	42
Water	qs	qs	qs	qs	---	---	---	---
Lubrication								
Talc	10	10	10	10	10	10	10	10
Mag. striate	10	10	10	10	10	10	10	10
Total	600	600	600	600	600	600	600	600

Procedure for Preparation of Paracetamol Tablet

Weighing and Shifting

All the ingredients were weighed accurately, according to their respective weight. Paracetamol and remaining excipient passed through sieve no # 40. Okra mucilage was passing through sieve no # 30.

Preparation of Granules and Dry Blend

In the above formulation PCM tablet were prepared by wet granulation and direct compression method. The main aim is to check the binding capacity of okra in wet granulation method and direct compression method.

A. In the formulation from batch (PC1-PC4) PCM and MCC101 are mix properly in the PLM. Okra Mucilage was dissolved in required amount of boiled water under constant stirring till it form a jel mass. Granulation was carried out in PLM by adding above binding solution of okra adopting the following parameter.

i) Shifting PCM and MCC101 was loaded in PLM and dry mixing for 15 minute.

ii) Binding solution was added for 10 minute at slow speed of PLM.

iii) Kneading continue for 20 minute at 200 rpm.

Wet shifting was carried out through sieve no #10. Granules were dried by using rapid dryer for 90 minute at 40 ^{0}C. Dry shifting was done through sieve no #20. Then add the SSG in the require amount and mix it for 10 minute.

B. In the batch from (PC5-PC8) PCM, MCC101 and Okra are mix properly in the PLM for 20 minute and finally add SSG and mix it over for 10 minute.

Lubrication

A. The granules from Batch PC1-PC4 were blended with Mg. Stearate and talc for 5 minute in a double cone blender.

B. The powder mixture from Batch PC5-PC8 was blended with Mg. Stearate and talc for 5 minute in a double cone blender.

Compression

All the above granules/blend of every batch was compressed by 12 mm circular standard concave punch having a break line in one side.

Evaluation of Granules/Blends [10]

Prepared granules were evaluated for pre compression parameters like bulk density, Tapped density, Compressibility index, Hauser ratio and Angle of repose.

Friability of granules [11]

Friability was measured using Electrolab Friability testing apparatus (Electrolab Ltd, Mumbai, India). Took a # 40 mesh and place the granule over the mesh and shake for 15 mins. Took 10 gm of granules which retain over the sieve and place in friabilator by tumbling 10 g of the granules for 4 min at 25 rpm. The tested granules were gently tapped on ASTM # 40mesh to remove the fines generated and the weight loss was measured.

Friability (%) = $[(I_{wt} - F_{wt})/ I_{wt} \times 100]$

Evaluation of Tablets [12]
Prepared tablet was evaluated for post compression parameters like hardness, friability, weight variation, thickness, disintegration time (USP).

Uniformity of Content
Weigh and powered twenty tablets. Weigh accurately a quantity of the powered containing about 0.5gm PCM. Add 50ml of 0.1M NaOH, dilute with 100ml of water, shake for 15min and add sufficient water to produce 200ml mix filter and dilute 10ml of filtrate to 100ml with water. To 10ml of resulting solution add 10ml of 0.1 M NaOH, dilute to 100ml with water and mix. Measure the absorbance of the resulting solution at 248nm.

Dissolution Studies [13]
The release rate of PCM tablets will determine using USP Dissolution Testing Apparatus II (Paddle type). The dissolution test was performed using 900 ml of water, at 37 ± 0.5 °C and 100 rpm. Aliquot volume was withdrawn from the dissolution apparatus at specified interval, and the samples were replaced with fresh dissolution medium. After filtration and suitable dilution the amount of drug release was determined from the calibration curve.

Comparison of dissolution profiles by statistical analysis with marketed product
Dissimilarity factor (f_1) [14]
It was calculated in the comparison with reference or with the innovator product to know the dissimilarity. The dissimilarity factor (f_1) should be always less than 15 (f_1<15).

$$f_1 = \frac{\sum R_t - T_t}{\sum R_t} \times 100$$

Similarity factor (f_2)
The similarity factor (f_2) was defined as the logarithmic reciprocal square root transformation of one plus the mean squared difference in percent dissolved between the test and the reference products. This was calculated to compare the test with reference release profiles.

$$f_2 = 50 \times \log 10 \times \frac{1}{\sqrt{1 + 1/n \times \sum (R_t - T_t)^2}} \times 100$$

Where, n= numbers of sampling points, the similarity factor (f_2) should be always greater than 50 (f_2>50)

Stability Studies of the Standardized Formulations [15]
The stability studies were carried out on the most satisfactory formulations as per ICH guidelines. The most satisfactory formulation sealed in aluminum packaging and kept in humidity chamber maintained at 35 ± 2 °C / 60 ± 5 %RH and 40 ± 2 °C / 75 ± 5 %RH for 2 months. At the end of studies, samples were analyzed for the drug content, in vitro dissolution and other physicochemical parameters

RESULTS AND DISCUSSION

Identification Test
After the extraction process, tests were done to ascertain the presence of pectin in the sample. The results of the various identification tests performed are show in Fig. 1 and 3. All the performed tests showed positive results towards the presence of Pectin in the Sample. Further confirmation was done by acidifying the Semi-gel formed in the Test No. 3**.** With dilute HCl and shaken well voluminous, colourless gelatinous ppt. was formed. This upon boiling becomes white and flocculent. This confirmed the presence of Pectin. The observation of identification of pectin was similar for both the powdered mucilaginous substances.

Drug and Excipient Compatibility Study
From the F.T.IR study of okra it was found that O-H stretch at 3408.56 cm^{-1} Very board due to strong hydrogen binding, C-H stretching at 2925.07 cm^{-1} methyl C-H stretching associated with aromatic ring, O-H bending at 1611.72 cm^{-1} assigned to the O-H bending of water. From the F.T.I.R study of PCM it was found that the N-H amide stretch at 3326.35 cm^{-1} This band can be seen quite clearly although it is on top of the broad OH stretch, Phenolic OH Stretch at 3162.30 cm^{-1} Very board due to strong hydrogen binding, C-H stretching at 2880.63 cm^{-1} Not clear due to underlying OH absorption, C=O amide stretch at 1654.89 cm^{-1} Stretching in amides occurs at a low

wave number, Aromatic C=C Stretching at 1610.84 cm^{-1} This band is strong since the aromatic ring has polar substituent's which increase the dipole moment of the C=C bonds in the ring, Aromatic C=C Stretch at 1506.31 cm^{-1} Evidence of a doublet due to interaction with ring substituent's. From the FTIR study of okra PCM mixture it was found that N-H amide stretching at 3326.35 cm^{-1} This band can be seen quite clearly although it is on top of the broad OH stretch, Phenolic OH Stretch at 3162.30 cm^{-1} Very board due to strong hydrogen binding, C-H stretching at 2880.63 cm^{-1} Not clear due to underlying OH absorption, C=O amide stretch at 1654.89 cm^{-1} Stretching in amides occurs at a low wave number. Thus the FT-IR report shows the absence of any interaction of mucilaginous substances isolated from AE with pure Pectin and PCM are compatible.

Evaluation of powder blend

The evaluation of various powder blends was performed with regards to bulk density, Tapped density, Carrs Compressibility index, Hausners ratio and Angle of repose was performed for drug as well as for excipients and result were indicated in Table No.2. The results of all these tests were complied with specification in I.P Standards.

Evaluation of Tablets

The physical attributes of the tablet were found to be satisfactory. Typical tablet defects, such as capping, chipping, and picking, were not observed, the compression was done with 10 mm standard concave punches. Results for other physical evaluations were also found to be within an acceptable range. For instance, weight variation ranges for all formulation are from 598.2 to 601.7 Hardness of the tablet was found to be 3.2 to 6.81. Thickness was found to be fixed during the compression cycle; values were 3.40 to 3.48 respectively. The range of Friability of only PC3 and PC4 batches was calculated 0.86 and 0.58 which was well within the acceptable range of 1% and all other batch fails to pass the friability test.

In-Vitro Dissolution Studies

To achieve the good dissolution profile, the tablet should be formulated so that it releases the drug in a predetermined and reproducible manner. By considering the drug's biopharmaceutic and pharmacokinetic profile, one can determine the required release from the tablet 4 and Figure 7 shows the in vitro drug release profile of Paracetamol. It was found that PC3and PC4 19.4% and 23.4% of the drug was released during eith in 5mins, and 95.2 and 95.7% at the end of 30 mins. All the formulation are compare with the marketed product and among these formulation PC4 shows less Dissimilarity (*F*1) factor 3.05 and highest Similarity (*F*2) 82.66.

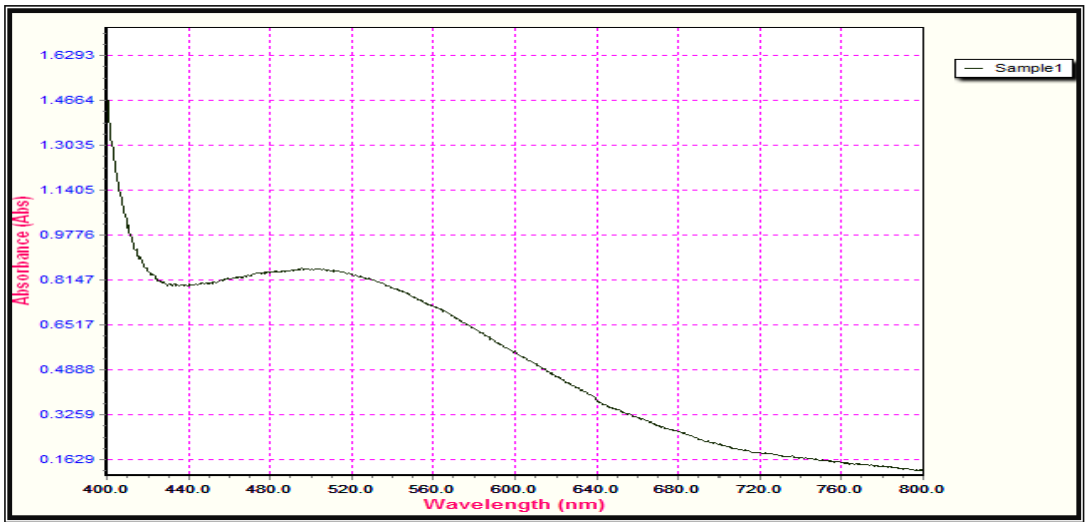

Fig 1: Carbazole test for identification of pectin

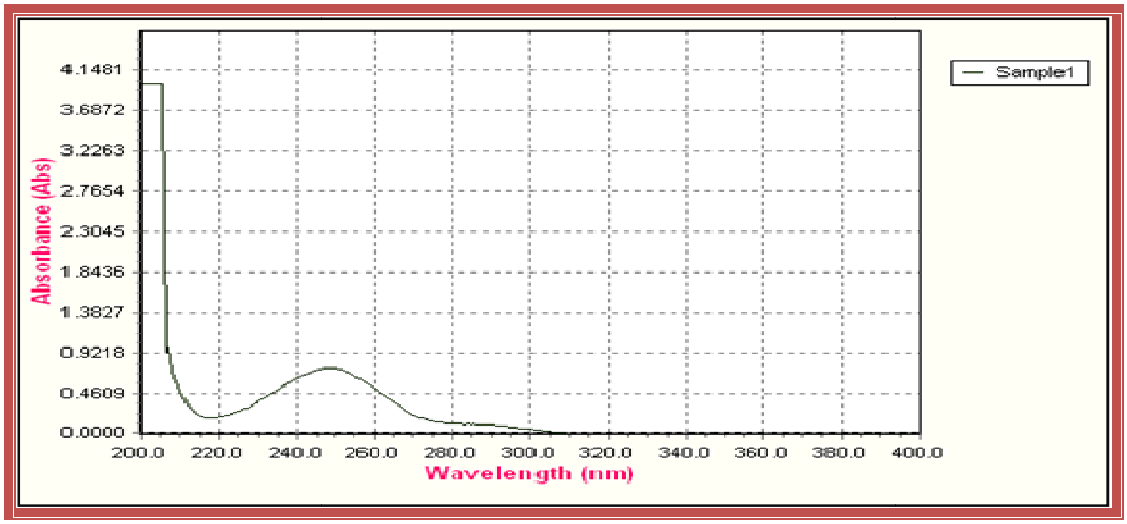

Fig 2: UV spectrum of pure PCM in Phosphate buffer pH 5.8

Fig 3: Photograph of dry okra mucilage and photograph of a Sticky golden brown gel was formed after cooling

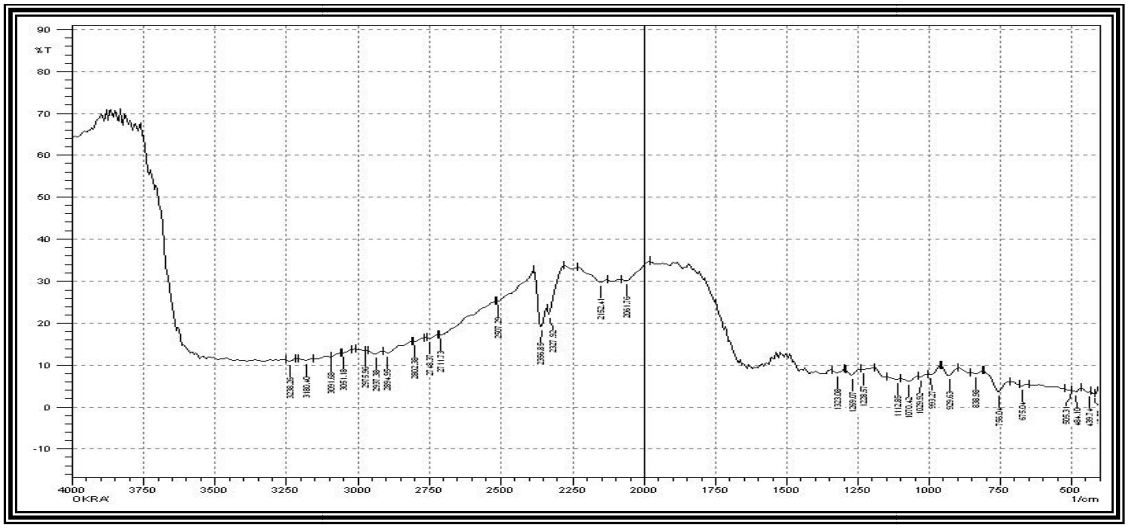

Fig 4: FTIR spectra of okra mucilage

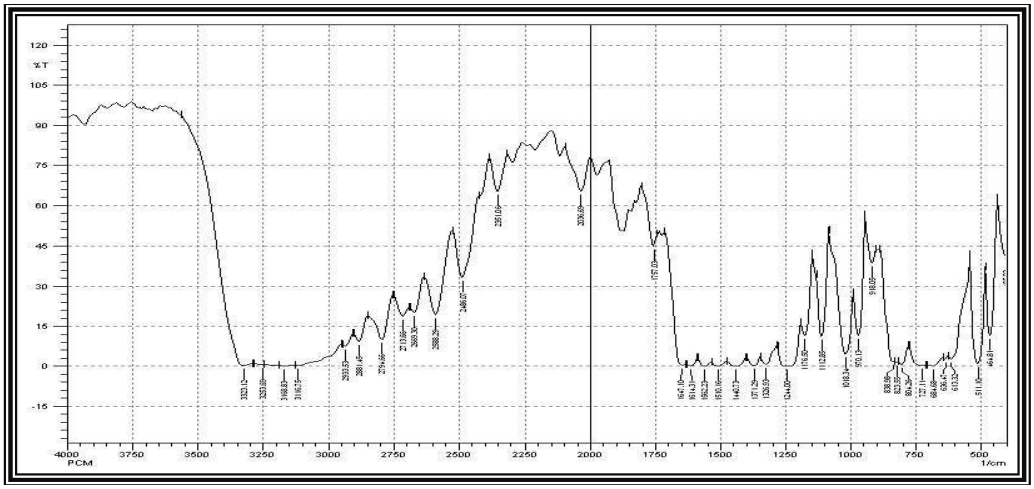

Fig 5: FTIR spectra of Pure Paracetamol

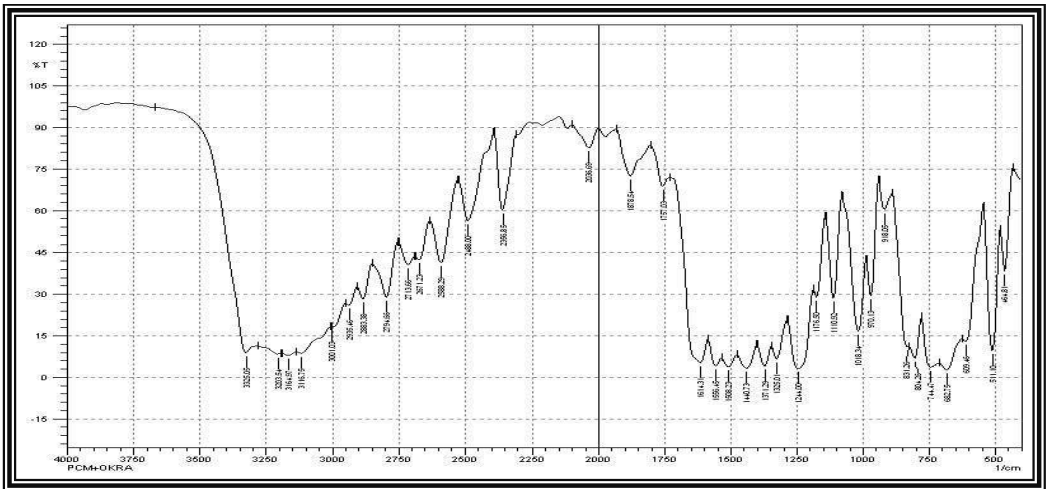

Fig 6: FTIR spectra of Pure Paracetamol and Okra mucilage

Table 2: Precompression Parameter of Paracetamol granules

Batch code	B.D (g/ml)	T.D (g/ml)	C.I (%)	Hausner's Ratio	Angle of Repose (θ)	Friability %w/w
PC1	0.464±0.2	0.541±0.01	14.2±0.02	1.16±0.08	29.9±0.03	1.72
PC2	0.450±0.3	0.515±0.04	11.62±0.05	1.14±0.04	24.12±0.05	1.21
PC3	0.456±0.1	0.521±0.01	12.30±0.06	1.14±0.09	20.12±0.03	0.86
PC4	0.441±0.5	0.598±0.04	11.44±0.01	1.12±0.01	18.86±0.02	0.42
PC5	0.430±0.2	0.480±0.03	10.41±0.08	1.11±0.11	34.86±0.01	---
PC6	0.43±0.2	0.50±0.1	13.3±0.2	1.27±0.06	32.9±0.21	---
PC7	0.47±0.1	0.55±0.1	14.1±0.4	1.17±0.11	31.5±0.36	---
PC8	0.49±0.4	0.57±0.2	11.7±0.5	1.16±0.03	31.2±0.12	---

Table 3: Post-compression evaluation of Paracetamol tablets

Batch code	Thickness (mm) N=10	Hardness kg/cm^2 N=10	Friability (%) N=3	Drug Content (%)	Weight variation N=20	DT (Min)
PC1	3.48±0.59	4.2±0.2	1.26±0.02	96.10±3.2	598.2±4.2	3
PC2	3.46±0.41	5.3±0.3	1.03±0.06	96.86±4.4	602.4±3.9	4
PC3	3.45±0.44	6.2±0.7	0.86±0.03	96.77±4.1	599.3±4.3	7
PC4	3.43±0.22	6.8±0.1	0.58±0.02	96.90±4.3	601.6±3.4	12
PC5	3.40±0.35	3.2±0.1	2.1 ±0.04	97.88±3.6	600.3±5.2	3
PC6	3.44±0.28	3.9±0.7	1.76±0.08	98.22±3.2	601.7±4.2	3
PC7	3.46±0.31	4.2±0.5	1.31±0.03	97.62±4.1	600.8±4.7	4
PC8	3.41±0.39	4.9±0.4	1.07±0.08	99.88±3.6	599.3±5.2	5

Table 4: *Invitro* drug release study

Time (min)	% Cumulative release								
	RT	PC1	PC2	PC3	PC4	PC5	PC6	PC7	PC8
0	0	0	0	0	0	0	0	0	0
5	24.7	39.2	30.2	19.4	23.3	49.9	40.2	32.8	25.2
10	37.9	60.3	42.1	28.6	38.2	66.3	61.5	50.8	39.1
15	56.9	75.4	59.2	47.2	54.1	81.2	76.7	61.4	54.2
20	71.7	84.2	74.3	64.1	68.4	96.3	84.3	75.6	70.3
25	84.5	93.1	89.5	81.5	84.1	99.2	92.7	88.5	86.4
30	99.1	99.2	98.6	92.5	95.7	99.0	99.6	99.2	98.5

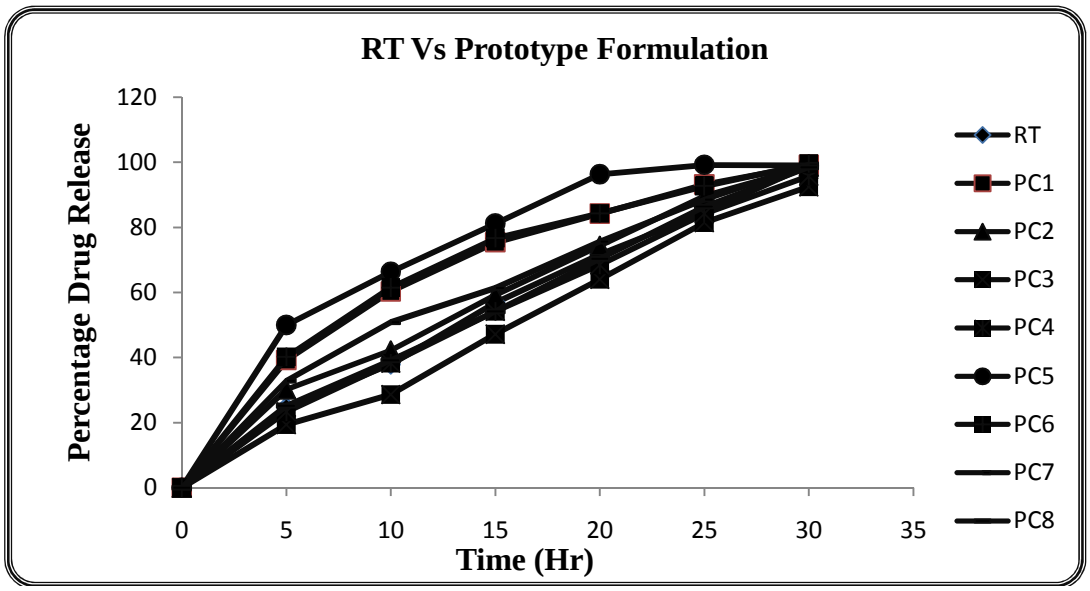

Fig. 7: *In-vitro* drug release of Prototype formulation Vs Marketed formulation

CONCLUSION

The mucilage of okra was successfully isolated and extracted from the dry okra fruit, the isolation procedure was done with the distilled water with a ratio 1: 4. Finally to obtain pure water soluble mucilage the supernent was washed with the help of ethanol. It was done because the water insoluble material were completely removed from the mucilage, and to obtained a pure water soluble precipitate. After drying the mucilage it was pass through sieve no 72 to obtain a fine particle size of the mucilage. The above okra mucilage was used in wet granulation and direct compression method in the different formulation of paracetamol. From the Okra gum used as a binding agent in some tablet formulations with good hardness, friability, and dissolution rate. However, this natural binder the dissolution rate of some slightly soluble drugs and may be consider as a good candidate for binding the formulations. From the study it is clear that the binding property of fruit polymer of *Abelmoschus esculentus* (okra) is much better. Natural gums are promising biodegradable polymeric materials. Many studies have been carried out in fields including food technology and pharmaceuticals using gums and mucilage. It is clear that gums and mucilage have many advantages over synthetic materials. Therefore, in the years to come, there will be continued interest in natural gums and their modifications aimed at the development of better materials for drug delivery systems. The results presented here shows that the mucilage obtained from *Abelmoschus esculentus* can be used as a binder in paracetamol tablets formulations with good physical properties. Tablets of long disintegration times were produced; hence it's potential in binding and prepares the granules for pharmaceutical formulations.

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