

# Isolation and characterization of jackfruit mucilage and its comparative evaluation as a mucoadhesive and controlled release component in buccal tablets

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## Abstract

**Background:** The purpose of the present research work was to extract jackfruit mucilage, use it as a mucoadhesive agent, and to develop extended release buccoadhesive tablets with an intention to avoid hepatic first-pass metabolism, by enhancing residence time in the buccal cavity. **Materials and Methods:** The mucilage was isolated from the jackfruit pulp by the aqueous extraction method and characterized for various physicochemical parameters as well as for its adhesive properties. Three batches of tablets were prepared (wet granulation method) and evaluated containing three mucoadhesive components: Methocel K4M, Carbopol 974P, and isolated jackfruit mucilage using chlorpheniramine maleate (CPM) as a model drug and changing the proportion of the mucoadhesive component (1:2:3), resulting in nine different formulations. **Results:** The results of the study indicate that the isolated mucilage had good physicochemical and morphological characteristics, granules and tablets conformed to the Pharmacopoeial specifications, and *in vitro* release studies showed the sustained action of drug with increasing concentration of the isolated natural mucoadhesive agent in the formulations. Permeability studies indicated that changing the mucoadhesive component, permeability behavior was not statistically different ( $P > 0.05$ ). FTIR and UV spectroscopy studies between mucilage and CPM suggested the absence of a chemical interaction between CPM and jackfruit mucilage. **Conclusion:** The developed mucoadhesive tablets for buccal administration containing natural mucilage (MF3) have a potential for the sustained action of drug release. Thus, mucoadhesive tablets for controlled release were successfully developed using natural jackfruit mucilage.

**Key words:** *Artocarpus heterophyllus*, chlorpheniramine maleate, mucoadhesive, natural polymers, release rate, wet granulation

## INTRODUCTION

Mucoadhesive drug delivery systems were developed to sustain drug delivery via various mucus membranes for either local or systemic delivery of poorly absorbed drugs such as peptides and proteins<sup>[1-3]</sup> as well as drugs that are subject to high first-pass metabolism.<sup>[4-6]</sup> Target sites include various mucus membranes such as the gastrointestinal tract,<sup>[7,8]</sup> eye,<sup>[9]</sup> cervix,<sup>[10]</sup> vagina,<sup>[11]</sup>

nasal cavities,<sup>[12]</sup> and oral cavities.<sup>[2,3,13,14]</sup> Mucoadhesive agents also increase residence time of the delivery system and provide intimate contact between the dosage form and the mucus membrane of interest, leading to increased drug transport. Such a method of drug delivery is less invasive than, and serves as an alternate to, the parenteral administration.

Most of the mucoadhesive materials are either synthetic or natural hydrophilic or water-insoluble polymers and are capable of forming numerous hydrogen bonds because of the presence of carboxyl, sulfate, hydroxyl, and amino functional groups. Formation of hydrogen bonds among the functional groups of the polymers and mucosal layer plays an important role. In general, stronger the hydrogen bonding stronger is the adhesion. Various polymers which have the ability to form strong hydrogen bonds include poly (vinyl alcohol), acrylic derivatives, celluloses, and starch.<sup>[15]</sup> Apart from the hydrogen bond formation, the presence of functional groups within the polymer structure may render the polymer chains as polyelectrolytes. The presence of charged functional groups in the polymer chain has a marked effect on the strength of the bioadhesion and can be demonstrated by the cell-culture-fluorescent probe technique.<sup>[16,17]</sup> Anionic

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	DOI: 10.4103/2230-973X.100039

polyelectrolytes have been found to form stronger adhesion when compared with neutral polymers.<sup>[7,13]</sup> Various synthetic materials tested for mucoadhesion include Carbopol 934P, Carbopol 974P, sodium carboxymethylcellulose (Sodium CMC), hydroxypropyl methylcellulose (HPMC), hydroxypropyl cellulose (HPC), polymethyl methacrylates (PMMA), and polycarbophil, whereas natural materials tested for mucoadhesive properties include carageenan, xanthan gum, sodium alginate, gelatin, acacia, and tragacanth.<sup>[18]</sup> All mucoadhesive materials interact with oligosaccharide molecules in the mucus layer that covers the mucosal epithelial surface.

For buccal administration, the conventional formulations like lozenges, troches, gels, oral rinses, or mouthwashes would be the simplest dosage forms for delivery of drugs through the mucosa of the oral cavity.<sup>[19,20]</sup> However, these conventional dosage forms have two major disadvantages which consist on an initial burst of activity followed by a rapid decrease in concentration<sup>[21,22]</sup> and in a limited stability *in situ* related to the constant flow of saliva and the mobility of the involved tissues. Buccal mucoadhesive formulations which control the drug release are expected to overcome these problems.

Natural polymers are easily available and have some advantages when employed in controlled release drug delivery systems such as bioacceptability, biocompatibility, biodegradability, and nontoxicity. Mucilages are most commonly used adjuvant in pharmaceutical preparations. They consist of sugar and uronic acid units. They swell in water and form a gel.<sup>[23]</sup> Mucilages are most commonly used adjuvant in pharmaceutical preparations as binding, disintegrating, suspending, emulsifying, and sustaining agents because of their low cost, ready availability, non-toxicity, and non-irritancy.<sup>[24,25]</sup>

The buccal cavity has a very limited surface area of around 50 cm<sup>2</sup> but the easy access to the site makes it a preferred location for delivering active agents. The site provides an opportunity to deliver pharmacologically active agents systemically by avoiding hepatic first-pass metabolism in addition to the local treatment of the oral lesions. The sublingual mucosa is relatively more permeable than the buccal mucosa (due to the presence of large number of smooth muscle and immobile mucosa), hence formulations for sublingual delivery are designed to release the active agent quickly while mucoadhesive formulation is of importance for the delivery of active agents to the buccal mucosa where the active agent has to be released in a controlled manner. This makes the buccal cavity more suitable for mucoadhesive drug delivery.<sup>[26]</sup>

In the light of this information and to overcome the drawbacks of conventional oral drug delivery system, the present study was designed to evaluate the mucilage from jackfruit for its extended release and mucoadhesive properties. Chlorpheniramine maleate (CPM) was used as a model drug to evaluate the sustained-release potential of the mucilage. CPM has been used extensively as an antihistamine for symptomatic relief of the common cold and allergy.<sup>[27]</sup>

The scientific name of the jackfruit tree is *Artocarpus heterophyllus* Lam. (Moraceae). It is popular fruit crop that is originated in India at the foot of the Western Ghats, and is now very popular throughout South East Asia. Elsewhere in humid tropical areas it is a common garden tree. Jackfruit is the largest tree-borne fruit in the world, reaching up to 50 kg in weight and 60–90 cm in length. The ripe fruit contains well-flavored yellow sweet bulbs and seeds (embedded in the bulb). Fruits are oblong-cylindrical in shape, typically 30–40 cm (12–16 in) in length but sometimes up to 90 cm (35 in). They usually weigh 4.5–30 kg (10–66 lb) although a weight of 50 kg (110 lb) has been reported.<sup>[28]</sup> The pulp constitutes 25–40% of the fruit's weight. It is a nutritious fruit, rich in vitamins A, B and C, potassium, calcium, iron, proteins, and carbohydrates. Due to the high levels of carbohydrates, jackfruit supplements other staple foods in times of scarcity in some regions. It is also a relatively cheap fruit in some countries such as Bangladesh, where it has been declared the “national fruit” because of its socioeconomic importance.<sup>[29]</sup> Potassium rich in jackfruit may help to regulate blood pressure. Jackfruit contains lignans, isoflavones, saponins, that are called phytonutrients and their health benefits are wide ranging from anti-cancer to antihypertensive, anti-aging, antioxidant, and anti-ulcer.<sup>[30]</sup> The study is carried out varying the ratio of the jackfruit mucilage as well as the existing standard polymers in order to investigate the influence of various parameters on the technological and biopharmaceutical behavior of the tablet. The compatibility between the drug and the different excipients and the technological characteristics of the granulate<sup>[31]</sup> and of the tablets were determined. Moreover, studies for the evaluation of the bioadhesive force,<sup>[32,33]</sup> the release of the drug from the dosage form, and the diffusion of the drug through a goat buccal mucosa were carried out.

## MATERIALS AND METHODS

### Materials

CPM was received as gift sample from Alembic Ltd. Vadodara, Gujarat, Jackfruit was procured from local market. Ethyl alcohol, Methocel K4M, Carbopol 974P were procured from Loba Chem (Mumbai, India) and used as received. All other reagents used were of analytical grade.

### Methods

#### *Isolation of mucilage from jackfruit*

The fresh fruits were obtained from local market of Vadodara town in the month of June. The fruits were thoroughly washed with water to remove dirt and debris. Incisions were made on them, left over night and then cut it into pieces. The seeds which were present inside the fruit were removed. The pulps of the fruits were crushed and soaked in water for 5–6 h, boiled for 30 min, and left to stand for 1 h to allow complete release of the mucilage into the water. The mucilage was extracted using a multi layer muslin cloth bag to remove the marc from the solution. Ethanol (three times the volume of filtrate) was added to precipitate the mucilage. The mucilage was separated, dried in an oven at 35°C,

collected, grounded, passed through a #80 sieve, and stored in desiccator till use.<sup>[34]</sup>

### Characterization of isolated mucilage from jackfruit

The isolated dried mucilage was studied for percentage yield and characterized for various physiochemical parameters such as solubility, weight loss on drying,<sup>[35]</sup> thin layer chromatography,<sup>[36,37]</sup> viscosity, pH, swelling index, total carbohydrate content, and test for chloride, sulfate, and tannins.<sup>[38,39]</sup>

### Compatibility study

Mixtures consisting of different ratios of CPM/mucilage, and either CPM or mucilage alone were scanned in the wavelength range 190–300 nm. The peak at 262 nm was monitored for any wavelength shift on a model Shimadzu UV-1800 spectrophotometer.

Spectra were obtained for physical mixtures of CPM/ mucilage, and either CPM or mucilage alone using a model Bruker Alpha T FT-IR spectrophotometer.

### Comparative mucoadhesive characterization of natural mucilage with Methocel K4M, Carbopol 974P as standard polymers; shear stress measurement

Different concentrations of the mucoadhesive agent solution, a such as, 1%, 2%, and 3% w/v, using Methocel K4M, Carbopol 974P, and a natural isolated mucilage from jackfruit were prepared. Shear stress was calculated by self-fabricated apparatus made of wooden board with scale and two glass slides having two pans on the both sides mounted on a pulley. An excess of prepared solution was placed between two glass slides and 1000 g weight was placed on glass slide for 5 min to compress the sample to uniform thickness. Weight (250 g) was added to the pan. The weight required to separate two slides was taken as a measure of shear stress.<sup>[40]</sup>

### Preparation and evaluation of granules for buccal tablets using isolated natural mucilage

The wet granulation method was used for the preparation of granules. The obtained granules were evaluated for flow property, apparent density, tapped density, compressibility index, and Hauser's ratio.<sup>[41,42]</sup>

### Formulation and evaluation of buccal tablets containing natural mucilage, Methocel K4 M and Carbopol 974 P

Three batches of tablets each containing 4 mg of CPM as model drug were prepared changing the proportion of the mucoadhesive component (1:2:3) by the conventional wet granulation method using flat face 6 mm punch (Rimek Mini Press-I machine), resulting in nine different formulations (CF1, CF2, CF3 for Carbopol 974P; MF1, MF2, MF3 for Natural mucilage; HF1, HF2, HF3 for Methocel K4M). The tablet weight was adjusted to 150 mg [Table 1]. The prepared tablets were evaluated for average thickness, hardness,

**Table 1: Composition of tablets**

Ingredients	Quantity/Tab (mg)		
	F1	F2	F3
Drug (CPM)	4	4	4
Dicalcium phosphate	119	94	69
Mucoadhesive component <sup>a</sup> (Ratio-1:2:3)	25	50	75
Magnesium stearate	1	1	1
Talc	1	1	1

<sup>a</sup>Carboxyvinyl polymer (Carbopol 974P) or Natural Jackfruit Mucilage or Hydroxypropylmethyl cellulose (Methocel K4M) resulting in g formulations as CF1, CF2, CF3 for Carbopol 974P; MF1, MF2, MF3 for Natural mucilage; HF1, HF2, HF3 for Methocel K4M.

friability test, weight variation test, and mucoadhesive strength measurement.<sup>[43,44]</sup>

### Dissolution testing

Dissolution studies were performed using a USP dissolution apparatus 2 (paddle method) at 50 rpm. The dissolution medium consisted of 900 ml phosphate buffer (pH 6.8) at 37°C. Samples were analyzed for CPM by UV spectrophotometry at 262 nm. Tablets were tested and the experiments were performed in triplicate. For each formulation, the time to reach 90% of CPM release (t<sub>90%</sub>) was calculated from the mean dissolution data by reading from the respective dissolution curve.

The tablet was designed to absorb water and swell, changing into a gelling mass that would release a high percentage of the drug before disintegration occurred. Therefore, the drug release from a tablet can be considered as release from a swelling matrix rather than a release from a disintegrating matrix. The release kinetics of each tablet can be assessed by inserting the experimental data in the semi-empirical equation  $M_t/M_\infty = Kt^n$  where  $M_t/M_\infty$  is the fractional amount of the drug at the time  $t$ ,  $K$  is a kinetic constant of the system which indicates rate of the release and the  $n$  is the release exponent, indicative of the mechanism of release. Values for  $n$  and  $K$  for each system were obtained from the logarithmic plot of the fractional release against the time, considering data between the first withdrawal at 30 min and the one corresponding to the release of the 60% of the dose.<sup>[45]</sup> The slope of the line is  $n$  while  $\log K$  is the intercept. The values of  $n$  and  $K$  were calculated by regression analysis and the statistical parameter  $R^2$  was established to evaluate the fitting of the semi-empirical equation to the release kinetics.

### Mucoadhesion studies

The aim of this study was to quantitate the force of detachment (mucoadhesive strength) of CPM buccal tablets applied to freshly excised goat buccal mucosa as a model membrane. The force of detachment was measured in grams by using self-fabricated apparatus (modified physical balance) as per the reference given in the literature with little modifications.<sup>[46]</sup>

### In vitro drug permeation

The *in vitro* buccal drug permeation studies of CPM through the goat buccal mucosa were done by using modified Franz diffusion cell at 37°C ± 0.5°C (diameter of 1.5 cm with a

diffusional area of 1.76 cm<sup>2</sup>). Fresh goat buccal mucosa was mounted between the donor and receptor compartments. The buccal tablet was placed in donor compartment with the core facing the mucosa and the compartments clamped together. The receptor compartment (15 ml capacity) was filled with phosphate buffer of pH 6.8. The temperature of media was maintained at 37 ± 0.5°C with the help of temperature-controlled water jacket and the hydrodynamics in the receptor compartment was maintained by stirring with a magnetic bead at 100 rpm. A 2 ml sample was withdrawn at predetermined time intervals and analyzed for drug content at 262 nm using a UV spectrophotometer. The volume of release media was maintained by adding equal volume of the fresh media after every sampling.

A test on the reference suspension was carried out by placing 2 ml of the suspension in the donor compartment. The suspension was obtained adding an excess of drug in purified water at room temperature. The system was heated up to 50 ± C in order to dissolve the drug and then equilibrated at 37°C ± 0.5°C for 24 h.<sup>[47,48]</sup>

Permeation through the membrane can be considered as a passive diffusion process and can be described by Fick's law equation:

$$J_s = dQ_r / A dt$$

where  $J_s$  is the steady-state buccal mucosa flux in mcg/cm<sup>2</sup> per h,  $dQ_r$  is the change in quantity of material passing through the membrane into the receptor compartment expressed in mcg,  $A$  is the active diffusion area in cm<sup>2</sup>, and  $dt$  is the change in time in hours. The steady state flux of CPM through the goat buccal mucosa was calculated from the slope of the linear portion of the cumulative amount permeated through the membrane per unit area versus time plot. For the CPM suspension, the permeability coefficient was calculated using the equation:

$$K_p = J_s / C_d$$

Where  $K_p$  is the permeability coefficient,  $J_s$  is the flux calculated at the steady time, and  $C_d$  is the donor concentration.<sup>[49]</sup>

## RESULTS AND DISCUSSION

### Characterization of isolated mucilage from jackfruit

The main aim of this work was to isolate and evaluate mucilage from jackfruit for its extended release and mucoadhesive properties in buccal tablets. Carbopol 974P, Methocel K4M, and Natural Jackfruit Mucilage were selected as buccoadhesive polymers. Jackfruit yielded 12–15% w/w mucilage using alcohol as mucilage precipitating solvent. The isolated mucilage was characterized for various physicochemical properties and specifications were set as per the Pharmacopoeial guidelines. The mucilage was tested for the presence of carbohydrates and a positive result was obtained. Total carbohydrates content was found to be 80.05%. The pH was found to be 6.4, indicating that the natural mucilage might not irritate the epithelium and mucus membrane of oral cavity. All other physicochemical parameters conferred to the pharmacopoeial guidelines. The results are shown in Table 2.

### Compatibility study

Results of FTIR and UV spectroscopy studies suggested the absence of a chemical interaction between CPM and jackfruit mucilage. The FTIR spectra of jackfruit mucilage showed characteristic peak C = O of amide at (1631 cm<sup>-1</sup>). The spectrum also showed usual bands for hydroxyl (915–955 cm<sup>-1</sup>) and ester carbonyl (1730 cm<sup>-1</sup>) groups and protein (carbonyl stretch 1660–1680 cm<sup>-1</sup>).

### Shear stress measurement

While demonstrating shear stress measurement, jackfruit mucilage was found to possess comparable and remarkable adhesiveness to that of Carbopol 974P and more adhesiveness than Methocel K4M within 60 min as shown in Table 3.

### Evaluation of granules

The results for evaluation of granules for buccal tablets using isolated natural mucilage are shown in Table 4. The flowability of the granulates was quite good according to the Carr's Index and Hausner ratio. Moreover, results showed that the granulate behavior is affected by both the type and the ratio of the mucoadhesive component. The increase in the mucoadhesive

**Table 2: Physicochemical parameters of jackfruit mucilage**

Parameter	Observation
Solubility with water	Colloidal solution formed in cold water
pH (1% w/v)	6.4
Loss on drying	2.73%
Swelling index*	21.4
Test for carbohydrates (Molish test )	Positive
Test for Tannins (Ferric chloride test)	Negative
Test for chloride (Silver nitrate test )	Positive
Test for sulfate (Barium chloride test)	Negative
Viscosity (3.0% solution in water)	1324 cp
Total carbohydrates content (Phenol Sulfuric Acid Method)	80.05%
Thin layer chromatography (Acetonitrile : Ethyl acetate : Propanol : Water; 85 : 20 : 20 : 15)	Spot corresponding to glucose and mannose
Yield	120–150 g/kg

\*Values are the mean of three readings

percentage causes an increase in granulometry followed by a reduction in the granulate flowability and in the apparent density. The granules containing Methocel K4M showed remarkable differences when compared to the granulates containing Carbopol 974P and Natural mucilage (which are very similar). It confirms the fact that the polymers are member of two different classes: cellulose derivatives and polyacrylic acid derivatives, respectively.

### Evaluation of buccal tablets

Three batches of tablets each containing 4 mg of CPM as model drug were prepared changing the proportion of the mucoadhesive component (1:2:3) by the conventional wet granulation method, resulting in nine different formulations [Table 1]. The results of evaluation of tablets are shown in Table 5. The thickness of all formulations F1 to F3 was in the range of  $2.10 \pm 0.3$  to  $2.40 \pm 0.05$  mm. The hardness of all formulations F1 to F3 was in the range of 4 to 6 kg/cm<sup>2</sup>. The percentage friability in

all formulations F1 to F3 was found to be less than 0.1%. The average weight for all formulations F1 to F3 was in the range of  $148 \pm 0.81$  to  $152 \pm 0.81$ . The percentage of drug content for all formulations F1 to F3 was in the range of  $97.2 \pm 0.5$  to  $99.8 \pm 0.4\%$ . All the formulations passes test for weight variation, hardness, content uniformity and show acceptable results with respect to drug content ( $99.8 \pm 0.4$ ) and % friability.

### Mucoadhesion studies

The results for mucoadhesion studies are shown in Table 6. The mucoadhesive strength of natural mucilage was observed more as compared to Methocel K4M and comparable to that of Carbopol 974P. The mucoadhesive characteristics were affected by ratio of mucoadhesive agents. Due to a higher concentration of the isolated natural mucilage in formulation F3, it showed more mucoadhesive strength than F1 and F2. The highest mucoadhesive strength may be due to possibility of proper hydration and erosion of natural polymer adhered to mucosal surface with strong bond which have been supported by maximum mucoadhesive force.

### Dissolution testing

The percentage of drug released from tablets containing the different mucoadhesive agents at the different concentrations is represented in Figures 1–3. The values of n, K, and R<sup>2</sup> for these release rates are represented in Table 7. From the R<sup>2</sup> values it is observed that the semi-empirical equation described by Ritger and Peppas is able to fit the release from tablets containing Carbopol 974 P and Natural Mucilage ( $0.9853 < R^2 < 0.9301$ ) but not the release from tablets containing Methocel K4M ( $0.9573 < R^2 < 0.9657$ ). In this case, n and K values did not show significance. The plots revealed that tablets containing Methocel K4M have an initial burst with a release, on average, of 50% in

**Table 3: Shear stress measurement**

Name of the polymer	Contact time (minutes)	Weight required <sup>a</sup> (grams)
Carbopol 974P	5	23.5 ± 1.20
	10	58.0 ± 1.30
	15	80 ± 1.40
	30	94.5 ± 1.20
Natural mucilage	5	24.5 ± 1.70
	10	60 ± 1.50
	15	82 ± 1.30
	30	96.5 ± 1.10
Methocel K4M	5	11.0 ± 1.20
	10	18.0 ± 1.21
	15	24.5 ± 2.0
	30	28.5 ± 1.50

<sup>a</sup>Each value represents the mean ± S.D. n = 3

**Table 4: Evaluation of granules**

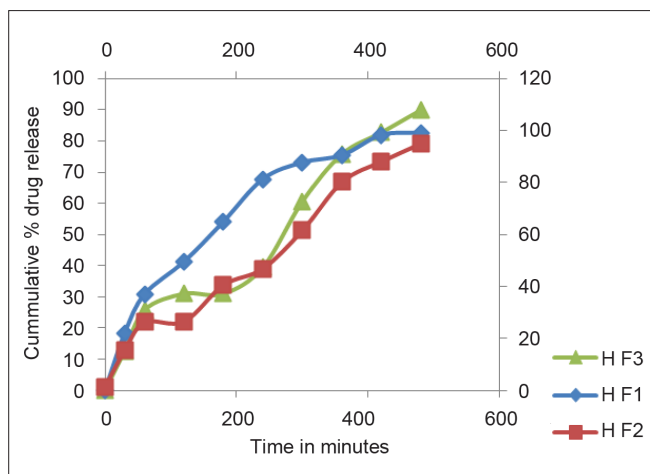
Parameters	Carbopol 974P			Natural mucilage			Methocel K4M		
	F1	F2	F3	F1	F2	F3	F1	F2	F3
Apparent density (g/ml) <sup>a</sup>	0.4233 ± 0.0012	0.3973 ± 0.0020	0.357 ± 0.0024	0.487 ± 0.0024	0.47 ± 0.0016	0.4523 ± 0.0020	0.4456 ± 0.0026	0.431 ± 0.0008	0.4113 ± 0.0020
Hausner's ratio <sup>a</sup>	1.2224 ± 0.0084	1.2489 ± 0.0145	1.2765 ± 0.0065	1.2394 ± 0.0028	1.2492 ± 0.0039	1.2705 ± 0.0037	1.2889 ± 0.0070	1.3136 ± 0.0038	1.3244 ± 0.0138
Carr's index (%) <sup>a</sup>	18.19 ± 0.5639	19.92 ± 0.9345	21.66 ± 0.4017	19.31 ± 0.1882	19.94 ± 0.2566	21.29 ± 0.2324	22.41 ± 0.4212	23.87 ± 0.2238	24.48 ± 0.7868

<sup>a</sup>Each value represents the mean ± S.D. n = 3

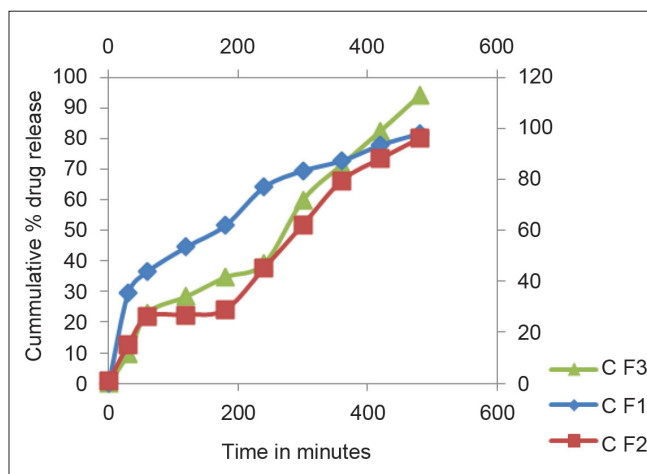
**Table 5: Evaluation of tablets**

Parameters	Carbopol 974P			Natural mucilage			HPMC (Methocel K4M)		
	F1	F2	F3	F1	F2	F3	F1	F2	F3
Avg weight (mg) <sup>a</sup>	149 ± 0.8164	148.66 ± 0.9428	148 ± 0.8164	150.66 ± 0.4714	152 ± 0.8164	149.66 ± 0.4714	148 ± 0.8164	150 ± 0.8164	151 ± 0.8164
Hardness (kg/cm <sup>2</sup> ) <sup>a</sup>	5 ± 0.81	5.1 ± 0.62	6 ± 0.81	4 ± 0.81	5.3 ± 0.47	6.1 ± 0.62	5.2 ± 0.52	5.1 ± 0.32	5.1 ± 0.23
Drug content (%) <sup>a</sup>	99.8 ± 0.4	97.2 ± 0.5	98.4 ± 0.5	99.8 ± 0.4	98 ± 1.1	98.6 ± 0.3	99 ± 0.4	98.1 ± 0.2	99 ± 0.3
Thickness (mm) <sup>a</sup>	2.11 ± 0.02	2.10 ± 0.03	2.40 ± 0.01	2.30 ± 0.04	2.40 ± 0.05	2.15 ± 0.02	2.28 ± 0.05	2.36 ± 0.01	2.33 ± 0.03
Friability (%)	Less than 0.1% in all formulations								

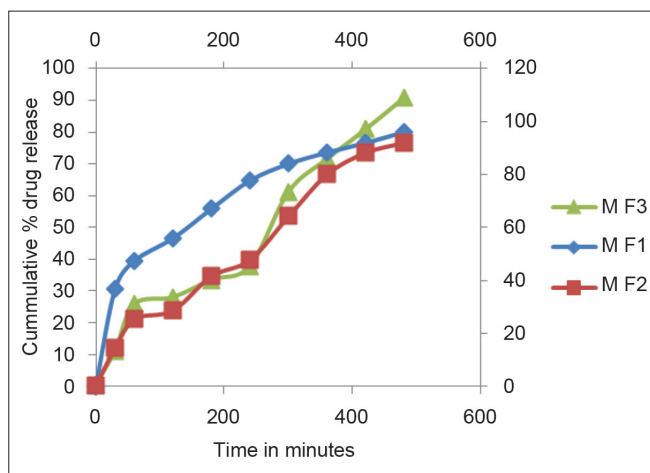
<sup>a</sup>Each value represents the mean ± S.D. n = 3



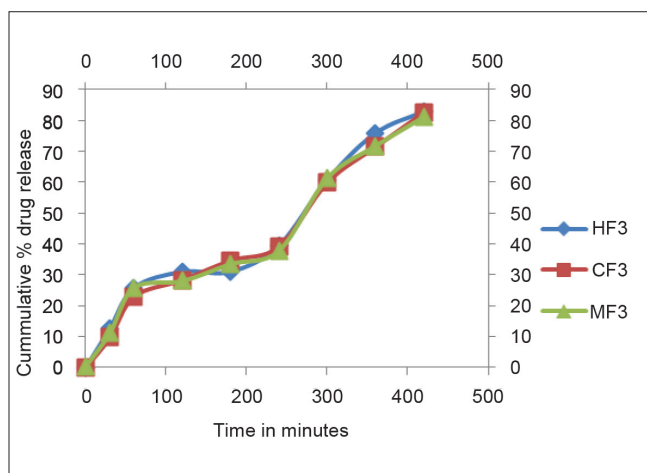
**Figure 1:** Percentage release of tablets containing Methocel K4M at 1:2:3 ratio



**Figure 2:** Percentage release of tablets containing Carbopol 974P at 1:2:3 ratio



**Figure 3:** Percentage release of tablets containing Natural Mucilage at 1:2:3 ratio



**Figure 4:** Comparison between the percentage release of tablets containing Methocel K4M, Carbopol 974P, and Natural Mucilage at higher ratio

Table 6: Mucoadhesive strength determination	
Formulation	Mucoadhesive strength* (grams)
HF1	10.30 ± 1.10
HF2	11.41 ± 1.82
HF3	20.50 ± 1.03
CF1	26.31 ± 1.17
CF2	37.80 ± 2.0
CF3	41.40 ± 1.83
MF1	29.60 ± 1.74
MF2	40.39 ± 1.81
MF3	45.72 ± 1.79

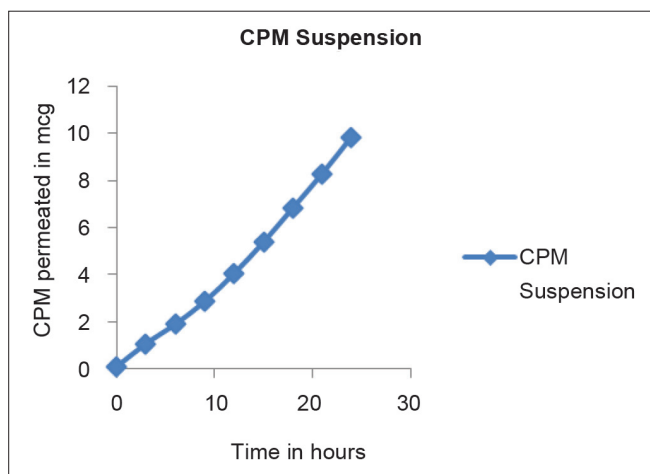
\*Each value represents the mean ± S.D. n = 3

the 2 h. The polymers, Carbopol 947P, and Natural Mucilage showed a better modulation capacity, with a release on average, of 25% and 26% respectively at the 2 h. This aspect is shown by the comparison between tablets containing the three mucoadhesive polymers, at highest concentration (Formulation F3), in Figure 4. Methocel K4M did not allow a significantly controlled release. Tablets containing Carbopol 974 P and Natural Mucilage showed a controlled release, characterized by an exponent *n* that

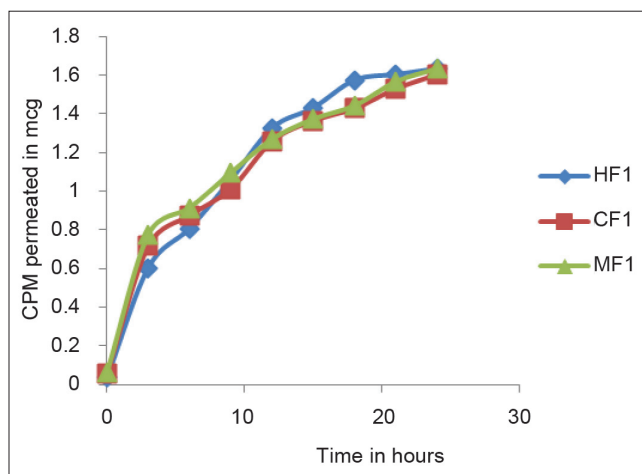
changed according to the type of mucoadhesive polymer. For tablets containing Carbopol 974 P, *n* was between  $0.3461 \pm 0.01$  and  $0.6504 \pm 0.07$  and for Natural Mucilage between  $0.3296 \pm 0.01$  and  $0.5041 \pm 0.03$ . A *n* value of 0.5 indicates a Fickian process that describes release of a drug from a matrix governed by diffusion.

**In vitro drug permeation**

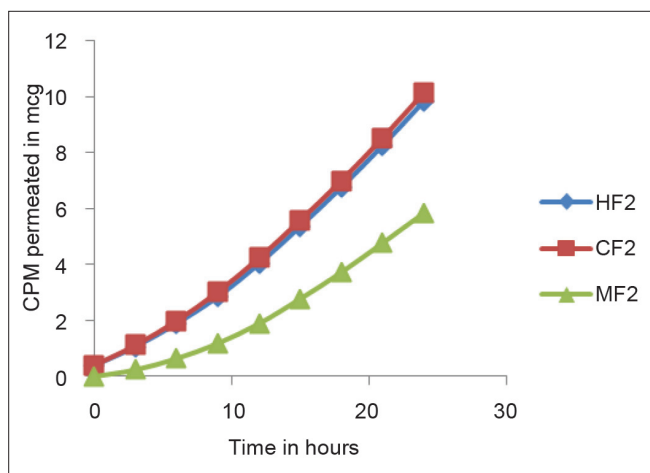
The permeation profile of the CPM suspension in water is shown in Figure 5, while Figures 6-8 show permeation profiles of tablets. The fluxes and *Kp* values in these profiles are reported in Table 8 that also shows the values for the CPM suspension in water. Permeation tests from the CPM suspension showed a *Kp* value of  $8.99 \times 10^{-2}$  corresponding to a flux of  $0.1799 \text{ mcg}^* \text{ cm}^{-2} \text{ h}^{-1}$ . Tablet permeation profiles are lower than those obtained from the suspension (tablet fluxes as a whole fell under  $0.0575 \pm 0.002$  and  $0.1789 \pm 0.033 \text{ mcg}^* \text{ cm}^{-2} \text{ h}^{-1}$ ) which can be explained when considering that CPM present in tablets must be dissolved and released before permeation occurs. From the comparison



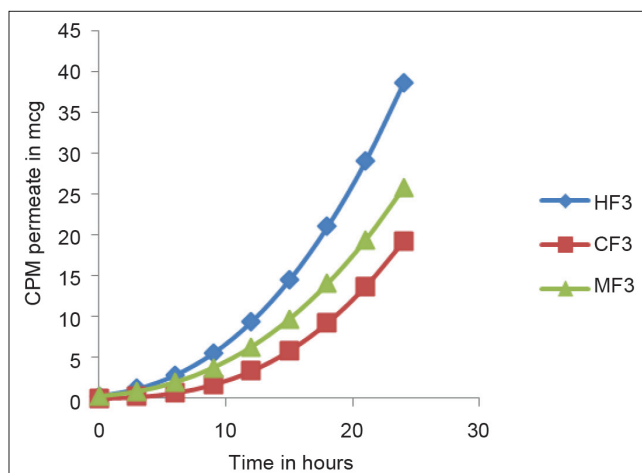
**Figure 5:** Cumulative amount of permeated CPM from a saturated solution in purified water



**Figure 6:** Cumulative amount of permeated CPM from the tablets (F1) containing Methocel K4M, Carbopol 974P, and Natural Mucilage



**Figure 7:** Cumulative amount of permeated CPM from the tablets (F2) containing Methocel K4M, Carbopol 974P, and Natural Mucilage



**Figure 8:** Cumulative amount of permeated CPM from the tablets (F3) containing Methocel K4M, Carbopol 974P, and Natural Mucilage

**Table 7: *n* and *k* values of the different tablets**

Parameters	Carbopol 974P			Natural mucilage			Methocel K4M		
	F1	F2	F3	F1	F2	F3	F1	F2	F3
$K(\text{cm} \cdot \text{h}^{-1})^a$	-0.9389 ± 0.03662	-1.604 ± 0.09682	-2.116 ± 0.1728	-0.8874 ± 0.02430	-1.650 ± 0.06771	-1.678 ± 0.1001	-1.940 ± 0.1121	-1.564 ± 0.07944	-1.694 ± 0.08376
$n^a$	0.3461 ± 0.01600	0.4767 ± 0.04594	0.6504 ± 0.07732	0.3296 ± 0.01061	0.5041 ± 0.03213	0.4581 ± 0.04748	0.7749 ± 0.05161	0.4720 ± 0.03770	0.4740 ± 0.03975
$R^2$	0.9853	0.9389	0.9218	0.9928	0.9724	0.9301	0.9657	0.9573	0.9531

<sup>a</sup>Each value represents the mean ± S.D. *n* = 3

of profiles of the different tablets, it is observed that changing the mucoadhesive component, permeability behavior was not statistically different ( $P > 0.05$ ). The higher fluxes shown by Methocel K4 M and Natural Mucilage can be explained by its rapid disaggregation. On the other hand, in all tablets, the cumulative amount of permeated CPM increased in respect to the concentration of the mucoadhesive polymer, probably because an increase in the mucoadhesive component allowed a closer contact between the tablet and the mucosa.

## CONCLUSION

All granulates and tablets satisfied the Pharmacopoeia specifications. FTIR and UV studies showed that there is no interaction between the CPM and the natural mucilage. The CPM release kinetics showed that tablets containing natural mucilage were the best formulations because they showed a prolonged drug release with linear kinetics, comparable to Carbopol 974 P. Tablets containing Methocel K4M did not show

**Table 8: Flux (Js) and Kp values of CPM from tablets and from the suspension in purified water**

Parameters	Carbopol 974 P			Natural mucilage			Methocel K4M			CPM suspension in purified water
	F1	F2	F3	F1	F2	F3	F1	F2	F3	
Js (mcg*cm <sup>-2</sup> * h <sup>-1</sup> ) <sup>a</sup>	0.0575 ± 0.002	0.1881 ± 0.021	0.1876 ± 0.029	0.0601 ± 0.031	0.0845 ± 0.012	0.3101 ± 0.034	0.5630 ± 0.041	0.4652 ± 0.049	0.1789 ± 0.033	0.179957 ± 0.027  0.089979 ± 0.031
Kp <sup>a</sup>	0.5436 ± 0.013	2.3099 ± 0.021	2.9776 ± 0.024	0.5598 ± 0.036	1.1709 ± 0.031	4.5163 ± 0.034	0.5580 ± 0.029	0.0006 ± 0.037	2.2213 ± 0.033	

<sup>a</sup>Each value represents the mean ± S.D. n = 3

a good release profile because they released significant portion of drug within the two hours, thus they did not allow a prolonged drug release. Permeability tests showed that all tablets showed a satisfactory drug permeability flux, compared with the flux from a saturated solution of drug in water. The permeability behavior was not statistically different ( $P > 0.05$ ) on changing the mucoadhesive component.

In conclusion, the developed mucoadhesive tablets for buccal administration containing natural mucilage (MF3) have a potential for the sustained action of drug release. Thus, mucoadhesive tablets for controlled release were successfully developed using natural jackfruit mucilage.

Our future studies will be directed at determining the bioavailability of CPM from the prototype jackfruit mucilage-based buccal tablets following application to the buccal mucosa of rabbits. These studies will also investigate histopathological studies whether any histological changes to the underlying tissue are observed following application and removal of the mucoadhesive buccal tablets.

## ACKNOWLEDGEMENTS

The authors wish to acknowledge the assistance of Dr. Pradip Wahile (The Alembic Ltd. Vadodara) for the kind supply of CPM as gift sample and Dr. Devanshu Patel (Managing Trustee, Parul Trust) for providing the facilities to carry out the research work.

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**How to cite this article:** Sabale V, Patel V, Paranjape A. Isolation and characterization of jackfruit mucilage and its comparative evaluation as a mucoadhesive and controlled release component in buccal tablets. *Int J Pharma Investig* 2012;2:61-9.  
**Source of Support:** Nil. **Conflict of Interest:** None declared.

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