Research Article

Effect of Mucilage of *Abelmoschus esculentus* as Tablet Binder in Diclofenac Sodium Matrix Tablets

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ABSTRACT

The present investigation is an effort to study the suitability of mucilage obtained from *Abelmoschus esculentus* as tablet binder. Diclofenac sodium matrix tablets by using this natural polymer and evaluating its release property and to produce sustained effect of Diclofenac sodium. Matrix tablets were formulated employing mucilage in different concentrations by wet granulation method. The granules prepared have flowability decreased with increase of mucilage concentration and are with good compressibility. Tablets were subjected to thickness, weight variation, drug content, hardness, friability, swelling index and in-vitro release studies. Results were found that hardness 4.4- 5.2 kg/cm^2 and friability test was found to be less than 0.1% in all the cases. The release mechanisms and the release rate kinetics of the tablets were examined using in vitro dissolution testing model. The release was found to follow the zero order kinetics. It reveals that increase in the mucilage concentration decrease the release of Diclofenac from matrix tablet and its shows that mucilage component exhibited excellent retarding effect on drug release from the matrix tablets even at very low concentrations.

Keywords: Diclofenac Sodium, *Abelmoschus esculentus'* mucilage, Matrix Tablet, Sustain release.

INTRODUCTION

Excipients of natural origin have attracted the attention of formulators due to lack of toxicity and ease of availability. Many studies have proved mucilages as good pharmaceutical excipient. Mucilages are plant hydrocolloids and metabolic products formed within the cell (intracellular formation). These are polymers of a monosaccharide or mixed monosaccharides combined with uronic acids. Mucilage form slimy masses when added to water. They are found in different plant parts like epidermal cells of leaves (senna), in seed coats (linseed, psyllium), roots (marshmallow), barks (slippery elm) and middle lamella (aloe). *Abelmoschus esculentus* is a flowering plant belonging to family Malvaceae1. Its mucilage is an amorphous polysaccharide was found to be composed of D-galactose, L-rhamnose and L-galactouronic acid, Glucose2. Studies shows that it can be used as tablet binder and to achieve sustain release. Natural mucilage polymers are prone to microbial contamination, moisture instability and batch to batch variation.

Diclofenac sodium is a non-steroidal anti-inflammatory drug, widely used to control pain and inflammation of rheumatic and non-rheumatic origin. Due to the rapid systemic clearance repeated daily dosing of 3 to 4 times a day is required to maintain therapeutic plasma drug concentration which effects patient compliance. To increase patient compliance Diclofenac sodium is formulated as sustain release dosage form. The purpose of this study was to isolate mucilage from *Abelmoschus esculentus* and to compare its efficiency as an effective tablet binder

MATERIALS AND METHODS

Materials

Abelmoschus esculentus pods were purchased from local market, Guntur. Diclofenac sodium was obtained as gift sample from Apo thec, Bangolre. Lactose, magnesium stearate and Starch are obtained from Qualigens fine chemicals, Mumbai. Ethanol was purchased from National scientific laboratories, Guntur.

Isolation and extraction of mucilage

Okra pods are cut into small pieces and are soaked in about sufficient amount of water & left overnight for release of mucilage into water with occasional shaking. After 24 hours the solution is passed through muslin cloth & marc is pressed, solution is slightly warmed for 5min to 75^o C to inactivate enzymes. Then mucilage solution is poured into 6 times volume of alcohol & precipitate formed is collected & dried in hot air oven at temperature less than 30^0 C for less time & stored in dessicator until further use.

Identification tests of okra mucilage[1]

Molisch's test

To dried mucilage powder Molisch's reagent was added and conc. H_2SO_4 was added from the side of a test tube.

Iodine test

To 10ml distilled water dried mucilage powder was added to make solution and to it 1 ml 0.2 N iodine solution was added.

Ruthenium red test

Take a small quantity of mucilage powder, mount it on a slide with ruthenium red solution, and observe it under microscope. If mucilage is present particles appear in pink colour.

Preparation of matrix tablets

Different tablets formulations were prepared by wet granulation method. All the powders were passed through 60 mesh sieve. Required quantity of drug and other ingredients were mixed thoroughly. Then, the polymer is dissolved in water was added slowly with uniform mixing to get a wet mass. The wet mass was passed through sieve no. 10 to obtain wet granules. The granules were dried at 50 º C for 5 to 6 hrs in tray dryer. The dried granules were passed through sieve.no.22, after blending with Magnesium sterate were compresses into tablet compression using tablet compression machine. Each tablet contained 100mg of Diclofenac sodium and other pharmaceutical ingredients as listed in Table 1.

EVALUATION OF MATRIX TABLETS OF DICLOFENAC SODIUM

Weight variation test[3]

The weight variation test was performed as per procedure of IP. Randomly twenty tablets were selected after compression, weighed individually and average weight was determined. The individual weight was compared with average weight for determination of percent deviation.

Drug content[4]

Five tablets were weighed individually and powdered. The powder equivalent to average weight of tablets was weighed and drug was extracted in Phosphate buffer pH 6.8, the drug content was determined measuring the absorbance at 276 nm after suitable dilution using a UV- Vis double beam spectrophotometer.

Hardness[5]

The hardness of the tablets was determined using Montanso hardness tester. It is expressed in kg/cm^2. Three tablets were randomly picked and hardness of the tablets was determined.

Thickness

The thickness of the tablets was determined by using Vernier calipers. Five tablets were used, and average values were calculated.

Friability test[4]

The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed and transferred into friabilator. The friabilator was operated at 25rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again. The % friability was then calculated by,

%F = 100 (1-W0/W)

% Friability of tablets less than 1% is considered acceptable.

In Vitro dissolution studies[5]

The in vitro release of Diclofenac sodium from the formulated tablets was carried out in tablet dissolution USP type I apparatus using 900 ml of dissolution medium maintained at 37.0±0.5°C and a stirring rate of 100 rpm. Tablets from each formulation were tested individually in 0.1N HCl for the first 2 hours and in phosphate buffer (pH 6.8) for the following hours. Samples of 5 ml were withdrawn from the dissolution medium and replaced with fresh medium to maintain the volume constant & time intervals are noted. After filtration and appropriate dilution, the amount of drug present in each sample was determined spectrophotometrically at 278 nm (for medium 0.1N HCl) and at 276nm (for phosphate buffer pH 6.8).

Kinetics of drug release

Drug release kinetics and mechanism was examined by fitting the cumulative release data to models representing zero order (Q v/s t), first order [log(Q_0-Q) v/s t], Higuchi's square root of time (Q v/s $t^{1/2}$) and Peppas double log plot (log Q v/s log t) respectively, where Q is the cumulative percentage of drug released at time t and (Q_0-Q) is the cumulative percentage of drug remaining after time t. The results obtained from in vitro release studies were plotted in four kinetics models of data treatment as follows:

- Cumulative percentage drug release Vs. Time (zero order rate kinetics)
- Log cumulative percentage drug retained Vs. Time (first order rate kinetics)

- Cumulative percentage drug release Vs. √T (Higuchi's classical diffusion equation)
- Log of cumulative percentage drug release Vs. log Time (Peppas exponential equation)

RESULT AND DISCUSSION

9.35 g of mucilage/kg was isolated from the pods of *Abelmoschus esculentus*. On treatment with ruthenium red, mucilage particles showed red color thereby confirming it as polysaccharide. A violet ring was formed at the junction of two liquids on reaction with Molisch's reagent confirming the presence of carbohydrates; mucilage does not show blue color when treated with 0.2 N iodine solution confirming the absence of starch. Three batches of matrix tablets were prepared. The results of pre-compression and post-compression analysis were given in Table 2 and 3 respectively. The flow property of granules was found to be decreased with increase in mucilage concentration. The formulated matrix tablets have hardness 4.4 – 5.2 kg/cm^2, thickness 3.53 to 5.82 mm. Percent weight loss in the friability test was found to be less than 0.1% in all the cases. All the matrix tablets contain Diclofenac sodium within range of 96.4 - 98.9% of the labeled amount. Percentage friability and weight variation passes the test as per standard pharmacopoeial limit. The in-vitro drug release profile of Diclofenac sodium from all the formulations is shown in Fig.1. The results indicated retardant release of drug from all the formulations with increase in the polymer concentration. The cumulative percentage of drug release from prepared formulations after 12 hours were 89.44%, 77.54%, 69.53% for F1, F2 and F3 respectively. The maximum cumulative percentage of drug released from different formulations is given in the following order:

F1 > F2 > F3

The cumulative percentage drug release data obtained were fitted to zero order, first order, Higuchi's and Peppas equations to understand the mechanism of drug release from the matrix tablet. The slopes and the regression co-efficient of determinations R^2 were listed in Table 4. The drug release kinetics of all of the fabricated formulations, F1, F2 and F3 predominantly follows Higuchi pattern of drug release followed by first order, Peppas and then zero order. According to Peppas model, the 'n' value for F1, F2 and F3 was found to be 1.062, 1.062 and 1.071 respectively, which are more than 0.5, indicates that the release approximates non-Fickian diffusion mechanism.

CONCLUSION

The result of the present study demonstrated the isolated *Abelmoschus esculentus'* mucilage can be used as a drug release retardant in the formulation of sustained release dosage forms. The drug release was extended over a period of more than 12 hours. The drug release kinetics of all formulations follows Higuchi pattern and the mechanism of diffusion was observed to be Non-Fickian. Thus *Abelmoschus esculentus'* mucilage could serve as an effective retardant polymer in formulation development of sustained release dosage forms.

Table 1: Formulation of Diclofenac sodium matrix tablets

Ingredients (mg/tablet)	Formulations		
	F1	F2	F3
Diclofenac sodium	100	100	100
Lactose	170	170	170
Binder	100	150	200
Starch	8	8	8
Magnesium sterate	40	40	40

Table 2: Preformulation parameters of Diclofenac sodium granules prepared from *Abelmoschus esculentus'* mucilage

Formulations	Angle of Repose	Loose Bulk Density (g/ml)	Tapped Bulk Density (g/ml)	Compressibility Index (%)
F1	26.5^0	0.28	0.43	34.88
F2	38.65^0	0.37	0.52	28.84
F3	41.9^0	0.45	0.69	35.11

Table 3: Evaluation data for physical parameters of matrix tablets

Parameter	F1	F2	F3
Weight variation (%)	0.028	0.013	0.011
Friability (%)	0.49	0.38	0.32
Hardness (kg/cm^2)	4.4	4.7	5.2
Disintegration (min)	4	11	26
Assay or content uniformity (%)	96.4	97.5	98.9

Table 4: In Vitro release kinetics of matrix tablets of Diclofenac sodium

Formulation code	Zero order		First order		Highuchi model	Peppas model	
	R^2	Slope	R^2	Slope	R^2	R^2	Slope
F1	0.989	7.53	0.746	0.121	0.909	0.991	1.602
F2	0.99	6.742	0.741	0.12	0.94	0.995	1.602
F3	0.922	5.931	0.82	0.313	0.903	0.939	1.071

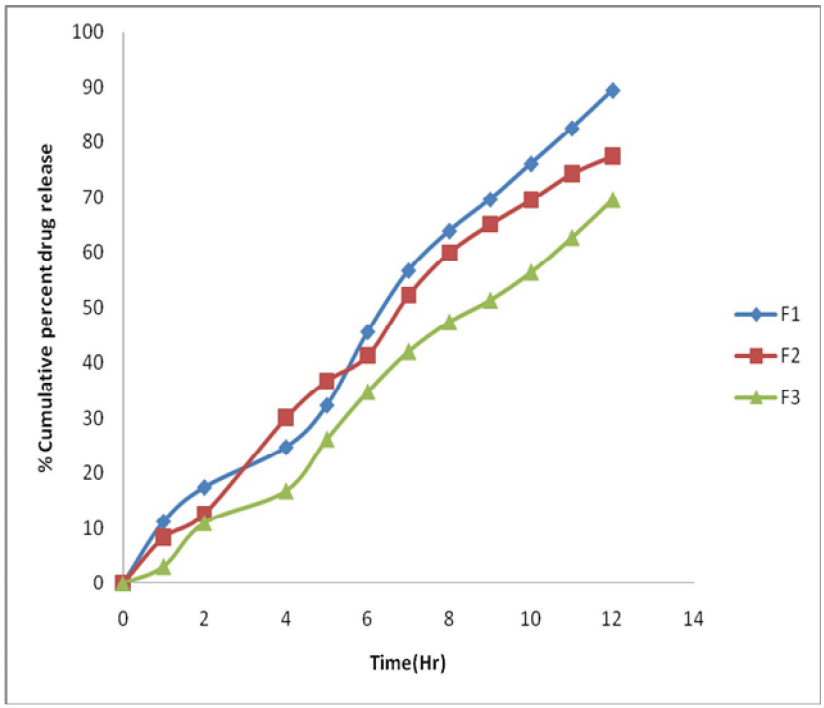

Fig. 1: In-vitro release profile of Diclofenac sodium matrix tablet (F1 to F3)

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