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Plantago Ovata Mucilage: A Natural Release Rate Retardant In Aceclofenac Tablet Formulation

B. V. Basavaraj*[1], P. Anusha[1], S. Bharath[1], R. Deveswaran[1],V. Madhavan[2]

1. Department of Pharmaceutics,M.S. Ramaiah College of Pharmacy, M.S.R.I.T Post, M.S.R. Nagar, Bangalore 560-054

2. Department of Pharmacognosy,M.S. Ramaiah College of Pharmacy, M.S.R.I.T Post, M.S.R. Nagar, Bangalore 560-054

ABSTRACT

In the present work, an attempt has been made to study the sustaining release property of isolated mucilage powder of *Plantago ovata* by formulating the sustained release tablets of aceclofenac and comparing its efficiency with hydrophilic matrix polymer HPMC K4 M. The drug compatibility with mucilage was checked by FTIR studies and found to be intact and stable. The results of pre-compression studies revealed that they were within prescribed limits that indicate good flowing property. All the formulations were found to be within the acceptable limits of official weight variation test. In all the formulations, friability was less than 1 % indicating good mechanical resistance of tablets. Drug content was found to be within acceptable limits. The formulations were also evaluated for hardness, thickness and dissolution profile. The data of drug dissolution was fitted into kinetic models which revealed that all the formulations followed *Peppas* release kinetics. The results revealed that the formulation F4 showed sustained drug release up to 12 hours. It also revealed that the isolated mucilage powder of *Plantago ovata* showed better sustained release over HPMC K4 M. In conclusion, *Plantago ovata* mucilage, obtained from natural source could be used as a reliable alternative over the synthetic polymers used for sustained release formulations.

Key words: Aceclofenac, *Plantago ovata* mucilage, HPMC K4 M, Release retardant

*Corresponding Author Email: bvbasu@rediffmail.com

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INTRODUCTION:

Over the past two decades, sustained release dosage forms have made significant progress in terms of clinical efficacy and patient compliance as conventional formulations are required to be administered in multiple doses for the treatment of chronic conditions and therefore have several disadvantages. Matrix tablets composed of drug and polymer as release retardant offer the simplest approach in designing a sustained release system1. Aceclofenac, a newer derivative of the diclofenac group of non-steroidal anti-inflammatory drug (NSAID) has analgesic and anti-inflammatory activities and is considered to be the first-line drug in the symptomatic treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. It directly blocks the prostaglandin synthesis. The short biological half-life (about 4 h) and dosing frequency make aceclofenac an ideal candidate for sustained release2,3. The development of novel dosage form of drug delivery systems has resulted in a need for new excipients to support the desired properties. In novel drug delivery systems, polymer plays a vital role. Development of new excipients is time consuming, involves tedious procedures and is highly expensive. Instead, identification of new uses for the existing substances is relatively inexpensive and less time consuming4. There has been ever increasing demand for plant based products as excipients. The use of natural polymers and their semi-synthetic derivatives in drug delivery continues to be an area of active research despite the advent of synthetic polymers. Natural polymers remain attractive primarily because they are inexpensive, readily available, capable of multitude of chemical modifications and potentially degradable and compatible due to their origin5. The various natural polysaccharides used in drug delivery application include xanthan gum, locust bean gum and guar gum6. Another natural polysaccharide, *Plantago ovata* mucilage obtained from the seeds of *Plantago ovata* possesses property like high swelling index. It can be used as disintegrant, suspending agent, sustaining agent and as emulsifying agent.

MATERIALS AND METHODS

Materials

Aceclofenac was procured from a reliable source. *Plantago ovata* seeds were purchased from local market. All other excipients used were of analytical grade.

Methods

Isolation of mucilage

Plantago ovata seeds were used for the isolation of mucilage. The seeds were soaked in distilled water (20 – 30 times) for 48 h and then boiled for few minutes for complete release of mucilage into water. The mucilage was collected by squeezing in a muslin cloth to remove marc. Then

three volumes of ethanol were added to the collected material in order to precipitate the mucilage[7]. The mucilage was separated and dried in oven at a temperature less than 60º C, powdered, sieved (# 80 meshes), weighed and stored in desiccator until further use[8].

Characterization of the mucilage

Phytochemical Examination

Preliminary tests were performed to confirm the nature of mucilage obtained. The tests were performed for the determination of presence of carbohydrates (Molisch's test), mucilage (Ruthenium red test) and starch (Iodine test)[9].

Physicochemical properties of the mucilage

The physicochemical properties such as swelling index, loss on drying, total ash, bulk and tapped density, viscosity, melting point were determined according to official methods[10,11].

Differential Scanning Calorimetry Analysis

The thermal properties of the mucilage were characterized using DSC. The DSC curve of mucilage was generated by differential scanning colorimeter. Sample of about 5 mg were placed in 50 µl perforated alluminium pans and sealed. Heat runs for each sample were set from 5-300° C using nitrogen as purging gas.

Formulation of Aceclofenac tablets

The sustained release tablets of aceclofenac were prepared by aqueous wet granulation method. *Plantago ovata* mucilage powder and HPMC at various concentrations were used as release retardants, di calcium phosphate as a diluent, PVP as a binder, Sodium saccharin as sweetener, Vanillin as flavouring agent, purified talc as lubricant and magnesium stearate as glidant. Proportion of excipients with drug is as given in Table 1. All the ingredients were sifted through sieve no. 60. The drug was mixed with di calcium phosphate, PVP, sodium saccharin and vanillin. The granules were prepared by adding the heated solution of mucilage (by varying concentrations of 4, 6, 8, 10 % w/v) in water. The same is repeated with HPMC K4 M solution of 10 % w/v concentration. Finally, the granules were dried and sieved. They are further blended with talc and magnesium stearate prior to compression. The granules were then compressed into tablets using 8 mm round concave punches in rotary punching machine (Rimek RSB-4 mini press, Cadmach, Ahmedabad).

Table 1: Phytochemical Tests on the Isolated Mucilage Powder of *Plantago Ovata*

S. No	Identification tests	Name of the test	Observations
1	Tests for carbohydrates	Molisch's test	**+ ve**
2	Tests for mucilage	Ruthenium Red test	**+ ve**
3	Tests for starch	Iodine test	**- ve**

Preformulation studies

Compatibility studies

Drug-mucilage compatibility was studied by IR spectral studies. The IR spectrum of Aceclofenac and the physical mixture of pure drug sample and isolated mucilage powder were recorded using FTIR spectrophotometer (FTIR 8400 S, Shimadzu, Japan). The substance to be examined was triturated with finely powdered and dried KBr. The grinded mixture was then placed in the sample cell and the reflectance spectrum was examined. The spectra were recorded over the scanning range of 4000-400cm^{-1}.

Evaluation of the Tablet formulations

Pre-compression parameters

The granules were studied for various micromeritic properties such as angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio[12,13].

Post-compression parameters

The tablets were evaluated for weight variation and thickness. Hardness and friability of the tablets were determined by using Monsanto hardness tester and Roche Friabilator at 25 rpm for 4 min, respectively.

Determination of Drug content

Twenty tablets were weighed and powdered. An amount of the powder equivalent to average weight of the tablets was weighed and dissolved in 100 ml of phosphate buffer, pH 7.4 filtered, diluted suitably and estimated for the drug content at 273 nm using UV-Visible spectrophotometer (UV 1700 - Shimadzu, Japan)[14,15].

***In-vitro* dissolution studies**

In- vitro drug release studies of all the formulations were carried out using multi basket tablet dissolution test apparatus (Lab India, DS 8000, Navi Mumbai) at 50 rpm. Phosphate buffer, pH 7.4 was used as the dissolution medium with temperature maintained at 37±1° C. Samples of 5ml were withdrawn at different time intervals and replaced with the same volume of fresh buffer to maintain sink conditions. The withdrawn samples were diluted suitably and analyzed at 273 nm using UV-Visible spectrophotometer against phosphate buffer, pH 7.4 as blank.

Kinetic treatment of dissolution data

The dissolution data of all the formulations were fitted into the kinetic models of zero-order, first order, Higuchi, Korsmeyer-Peppas and Hixson-Crowell in order to describe the release mechanism of the drug[16].

RESULTS AND DISCUSSION

The isolation method yielded 17 % of mucilage powder from the seeds of *Plantago ovata*. The phytochemical examination of the mucilage confirmed the presence of carbohydrates, absence of starch and the obtained substance was mucilage (Table 1). The physicochemical properties of the mucilage were detailed in Table 2. DSC thermogram of the mucilage showed an exothermic peak at 301.05° C corresponding to its melting point (Figure 1) with slight stretching owing to hydration of the mucilage as well as evaporation of water.

Table 2: Physicochemical Characterization of the Isolated Mucilage Powder

Parameter	Results
Swelling index	86
pH	6.26
Angle of repose	33°
Bulk density (g/cc)	0.634
Tapped density (g/cc)	0.73
Carr's index	13.05
Hausner's ratio	1.150
Viscosity at 100 rpm (cP)	8.33
Specific gravity	1.005
Melting point (° C)	296
Loss on drying (%)	9
Total ash (%)	3

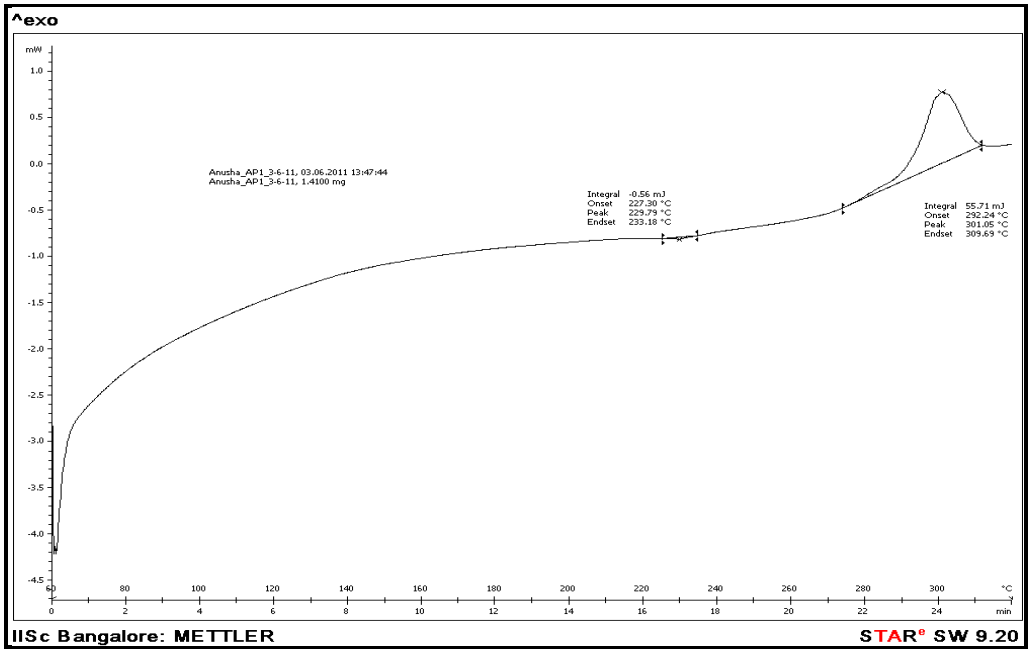

Figure 1: DSC Thermogram of *Plantago ovata* mucilage powder

Sustained release tablets each containing 200 mg of aceclofenac were prepared employing mucilage powder of *Plantago ovata* and HPMC K4 M at various concentrations using aqueous

wet granulation method (Table 3). The drug excipient interaction was studied by FTIR spectroscopy revealed that the drug was stable and intact in the mixture as there was no shift in the principle peaks of pure drug (Figure 2).

TABLE 3: Composition of Different Batches of Aceclofenac Tablets

S. No	Ingredients	F1	F2	F3	F4	F5
1	Aceclofenac	200	200	200	200	200
2	Di calcium phosphate	127	127	127	127	127
3	*Plantago ovata* mucilage (% w/v)	4	6	8	10	-
4	HPMC (% w/v)	-	-	-	-	10
5	Poly vinyl pyrollidone	15	15	15	15	15
6	Sodium saccharin	2	2	2	2	2
7	Vanillin	2	2	2	2	2
8	Magnesium stearate	2	2	2	2	2
9	Talc	2	2	2	2	2
Total tablet weight (mg)		350	350	350	350	350

*All the ingredients used were taken in mg

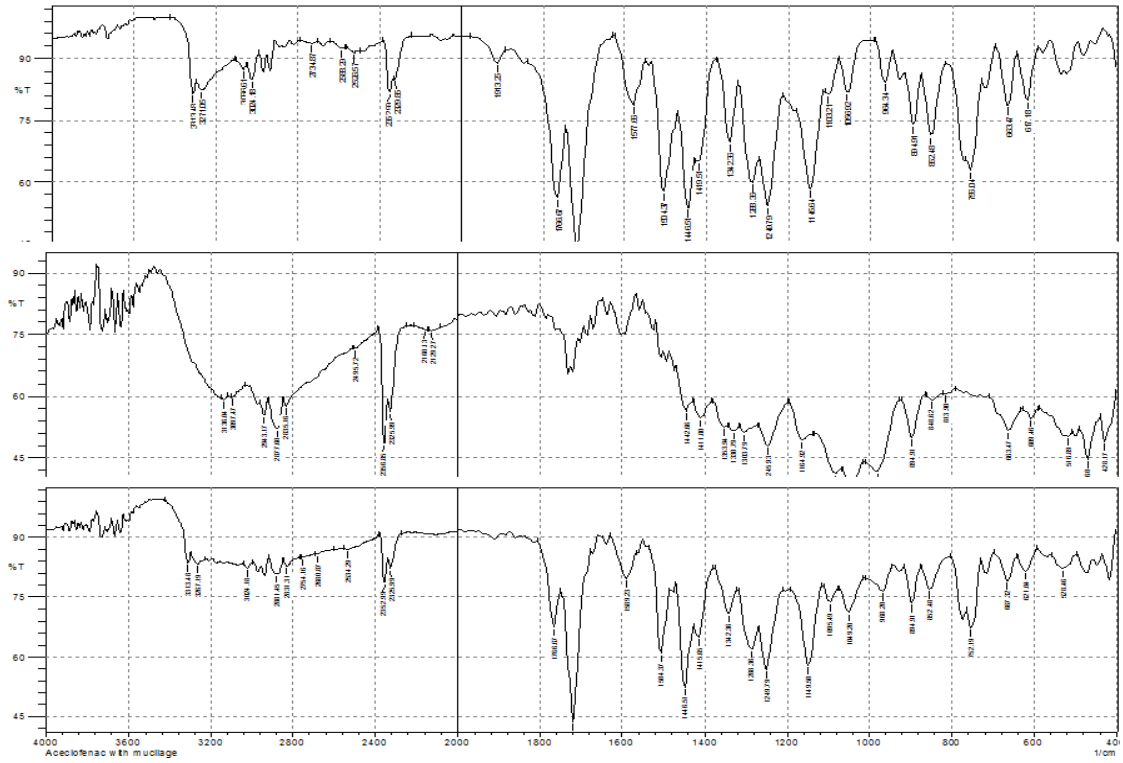

Figure 2: FTIR spectra of drug, mucilage and the physical mixture of drug and mucilage (top to bottom)

The evaluated values of pre-compression parameters were within prescribed limits and indicated good free flowing property as given in (Table 4). The post-compression parameters in all the formulations showed friability less than 1 %, indicated that tablets had a good mechanical resistance. Hardness and thickness of the tablets were found to be in the range of 5 – 6 kg/cm^2

and 4.48 – 4.53 mm respectively (Table 5). Drug content was found to be in the range of 99.23 to 100.21 %.

TABLE 4: Pre-Compression Parameters of Prepared Granules

Formulation Code	Angle of repose	Bulk density (gm/cc)	Tapped density (gm/cc)	Carr's index (%)	Hausner's Ratio
F1	28°	0.56	0.62	9.67	1.10
F2	28°	0.53	0.59	10.17	1.11
F3	27°	0.58	0.64	9.38	1.10
F4	24°	0.57	0.64	10.94	1.12
F5	28°	0.53	0.59	10.17	1.11

Table 5: Post Compression Parameters of Prepared Tablets

Parameter	F1	F2	F3	F4	F5
Weight variation (mg)	350±0.01	351±0.01	350±0.005	349±0.01	350±0.005
Thickness (mm)	4.53	4.48	4.51	4.50	4.49
Hardness (Kg/cm2)	5	5.5	6	6	5
Friability (%)	0.3	0.2	0.1	0.2	0.3
Drug content (%)	99.23	98.94	99.67	99.86	100.21

From the drug release studies, it was evidenced that as the concentration of *Plantago ovata* increases, the drug release decreased and showed sustained activity up to 12 hours and with HPMC K4 M the release was sustained up to 8 hours (Figure 3). The release of drug from all the formulations was found to be followed Peppas kinetics. The formulation F4 followed Peppas release kinetics with the regression coefficient value of 0.9976.

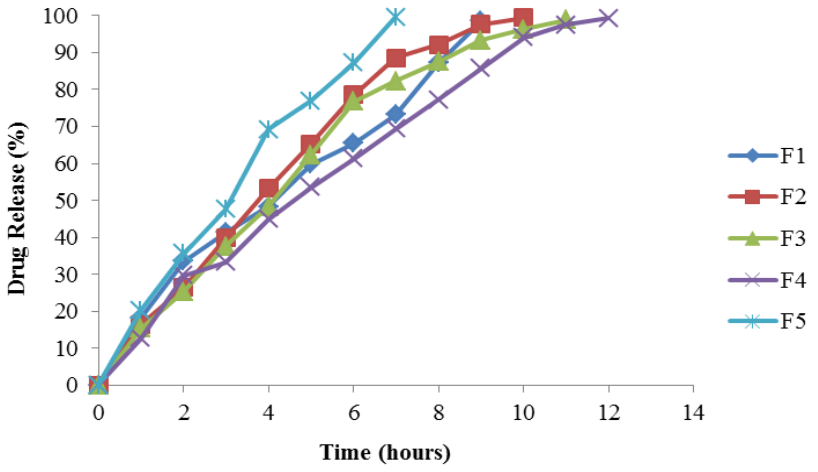

Figure 3: Comparative release profile of all the formulations of Aceclofenac

CONCLUSION

The aceclofenac tablets prepared using *Plantago ovata* mucilage showed appreciable sustained release behaviour up to 12 hours over HPMC K4 M. Thus, it could be employed as a reliable pharmaceutical adjuvant for sustained release formulations.

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