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Fabrication and Evaluation of Montelukastsodium *Sustained Release Matrix Tablets Using Hibiscusrosa-sinensis Leaves Mucilage*

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Abstract

The main target of the present investigation was to prepare Montelukast sodium matrix tablets by using *Hibiscus rosa-sinensis* leaves mucilage for its release retardant bustle. *Hibiscus rosa-sinensis* leaves were characterized for physicochemical assets. Diverse matrix tablets were prepared by wet granulation technique. The prepared matrix tablets found to have good pre-compression and post compression parameters. The swelling performance, release rate features and the *in vitro* dissolution study displayed that the dried *Hibiscus rosa-sinensis* leaves mucilage can be used as a matrix former in tablets. The drug release kinetics from optimized F-5 formulation showed zero order release. The study concludes that *Hibiscus rosa-sinensis* leaves mucilage can be used as aproficient matrix forming polymer, to retard the release of Montelukast from the tablets.

Keywords: Montelukast sodium, *Hibiscus rosa-sinensis*, matrix tablets, sustained release

Contents

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1. Introduction

Hibiscus rosa-sinensis, (*Malvaceae* family) (China rose) has glossy dark green leaves which gives a good quantity of mucilage upon wetting with water [1]. Montelukast sodium is a leukotriene receptor antagonist (LTRA) prescribed in the treatment of asthma and to get rid of seasonal allergies. Its bioavailability is 63% [2]. In this work a sustained release matrix tablets were prepared with good patient acceptance and reduced side effects [3]. Monteluka stsustained release tablets were prepared by using *Hibiscus rosa-sinensis* leaves mucilage.

2. Materials and Methods

Montelukastsodium was obtained as a gift sample from Dr. Reddy's laboratories, Hyderabad, India.*Hibiscus rosa-sinensis*leaves were collected from medicinal garden of Balaji College of Pharmacy, Ananthapuramu, India. The plant was authenticated at department ofPharmacognosy, Balaji College of Pharmacy, Ananthapuramu, India. Micro crystalline cellulose, talc and Magnesium stearate wereprocured from SD Fine chemicals, Mumbai, India. All other chemicals used were of AR grade. Double distilled water was used throughout the experiments.

Extraction of mucilage

The fresh *Hibiscus rosa-sinensis* leaves were collected and washed with water. The leaves 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. Acetone (in the quantities of 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 a desiccator at 30 °C & 45% relative humidity till use [4]. This mucilage was tested for flow properties and shown in Table 1. All values were found to be satisfactory.

Table 1: Flow properties of dried *Hibiscus rosa-sinensis* leave mucilage

Formulations	Angle of Repose (¯)	Compressibility Index (%)	Hauser's Ratio
F1	25.89±0.20	15.21±0.01	1.125±0.02
F2	24.28±0.98	21.25±0.05	1.025±0.01
F3	23.54±0.62	18.69±0.02	1.095±0.01
F4	24.25±1.35	17.58±0.05	1.055±0.02
F5	25.11±0.67	16.25±0.11	1.094±0.01
All values mentioned as mean ±SD; Number of trials (n)=3			

Preparation of matrix tablets

The matrix tablets of Montelukast with *Hibiscus rosa-sinensis* leaves mucilage were prepared by using different drug: mucilage ratios [4]. The compositions of formulations were represented in Table 2.

Table 2: Formulae of matrix tablets

Ingredients (mg)	Formulations					
	F-1	F-2	F-3	F-4	F-5	F-6
Montelukast sodium	10	10	10	10	10	10
Hibiscus rosa-sinensis leaves mucilage (dried)	10	15	20	25	30	35
Micro crystalline cellulose (Avicel)	120	115	110	105	100	95
Magnesium stearate	5	5	5	5	5	5
Talc	5	5	5	5	5	5
Total weight of tablet	150	150	150	150	150	150

Evaluation

Drug excipient compatibility study

This was performed by FTIR studies.

Flow Properties

Angle of Repose: The angle of repose was calculated using the following equation [5]

$$\theta = \tan^{-1}(h/r)$$

Where h and r are the height and radius of the powder pile respectively

Bulk Density

Both loose bulk density (LBD) and tapped bulk density (TBD) were calculated using the following formulas [6].

LBD = Weight of the Powder/Volume of the packing

TBD = Weight of the powder /Tapped volume of the packing

Compressibility Index

The compressibility index of the gum powder was determined by Carr's compressibility index [6].

$$\text{Carr's Index (\%)} = (\text{TBD} - \text{LBD})/\text{TBD} \times 100$$

The above physical properties of formulated matrix tablets were shown in Table 3.

Evaluation of prepared Tablets

Uniformity in thickness

The thickness of the tablets was determined using a thickness screw gauge (Mitutoyo, New Delhi, India). Five tablets from each batch were used and average values were calculated [7].

Uniformity of Weight

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance (Denver APX-100, Arvada, Colorado) and the test was performed according to the official method [8].

Tablet Hardness

For each formulation, the hardness of 5 tablets were determined [7] using the Monsanto hardness tester (Cadmach, Ahmedabad, India).

Tablet Friability

The loss in weight of tablets during packing and shipping can be determined by friability test. Percentage friability was calculated by using the formula [7].

% Friability = Tablet weight $_{(initial)}$ – Tablet weight $_{(Final)}$/ Tablet weight $_{(initial)}$ X 100

Uniformity in Content

At random 20 tablets were weighed and powdered. The powder equivalent to 100 mg was weighed and dissolved in 100ml of SLS (0.5%) in water. The solution was shaken carefully. The undissolved matter was removed by using Whatmann No.41 filter paper. Then the serial dilutions were carried out and the absorbance was measured at 345.5 nm.

Swelling behavior of Sustained release matrix tablets

The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of formulations AP-1, AP-2, AP-3, AP-4 and AP-5 were studied. One tablet from each formulation was kept in a Petri dish containing pH 7.4 phosphate buffer. At the end of 1 hour, the tablet was withdrawn, kept on tissue paper and weighed then. This procedure was repeated till 12 h. The % weight gain by the tablet was calculated by the following formula [8].

$$S.I = \{(M_t - M_0) / M_0\} \text{ X } 100$$

Where,

S.I = swelling index,

M_t = weight of tablet at time‘t’ and

M_o = weight of tablet at time t = 0. Swelling behavior of sustained release matrix tablets were represented in fig. 1.

***In vitro* drug release studies**

Release of Montelukast from the prepared tablets was done in a six basket USP XXIII dissolution apparatus taking 900 ml of 0.5% SLS in distilled water for next 10 h. The dissolution media were maintained at a temperature of 37±0.5°C. The speed of rotation of basket was maintained at 50 rpm. The samples were withdrawn at 30 min intervals. The samples were filtered and suitably diluted to determine the absorbance at 345.5 nm using UV/ Visible single-beam spectrophotometer (CT-100, Hyderabad, India) [9]. The drug release experiments were conducted in triplicate (n = 3). The *in vitro* dissolution rates were further tested using pharmacokinetic models.

3. Results and Discussion

The FTIR spectrums indicates that there was no incompatibility between drug and the excipient used (Fig.1). Angle of repose, bulk density, carr’s index and Hausner’s ratio indicates the formulation blend had good flow properties (table 3). The matrix tablets, containing 10 mg of Montelukast, were prepared using dried gum of *Hibiscus rosa-sinensis*in various proportions. The prepared tablets were found to have uniformity in thickness, Weight and content.

They also have hardness more than 4kg/cm^2 and the loss in friability was less than 1% indicates that the formulated tablets have good mechanical strength. The wetting time indicates that all the formulated tablets have quick wetting, this may be due to ability of swelling and also capacity of absorption of water (fig.2). The water absorption ratio favors the wetting of the tablet. *In vitro* drug release studies indicates that drug release from matrix tablets were by drug dissolution, drug diffusion or a combination of both. This was obtained after kinetic treatment to the *in vitro* dissolution data (fig 3-7).

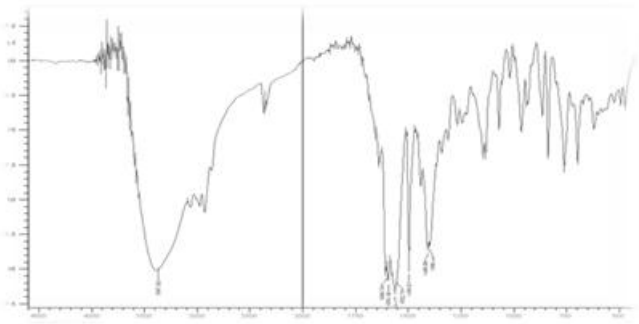

Figure 1: Infrared Spectrum of Montelukast with *Hibiscus rosa-sinensis*gum

Table 3: Physical properties of matrix tablets

Formulation	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)

F-1	4.95±0.05	5.84±0.04	0.22±0.02	100.21±0.36
F-2	4.99±0.01	5.62±0.05	0.62±0.03	99.88±0.62
F-3	4.98±0.02	6.25±0.04	0.44±0.02	99.19±2.25
F-4	5.02±0.05	7.55±0.02	0.32±0.01	99.79±3.36
F-5	5.00±0.08	6.95±0.02	0.26±0.09	99.84±3.28
F-6	5.01±0.04	6.84±0.02	0.19±0.01	99.98±1.64
All values mentioned as men ±SD; Number of trials (n) = 5				

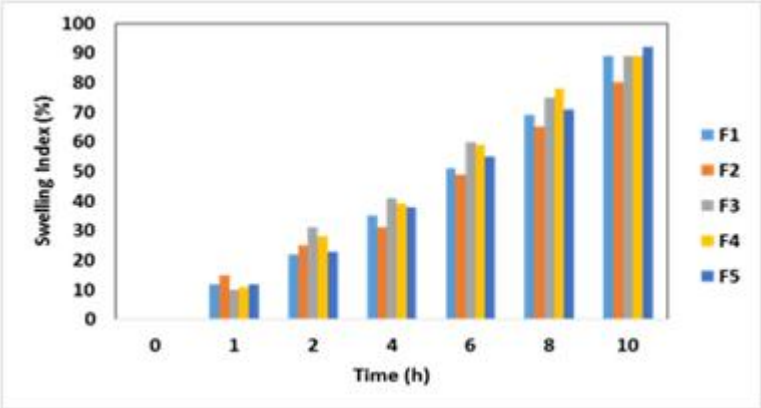

Figure 2: Swelling Index of formulated matrix tablets

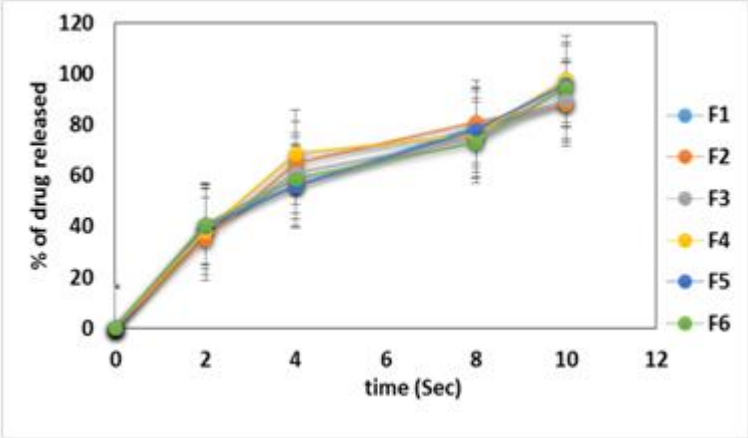

Figure 3: Zero order release Plot of formulated matrix tablets

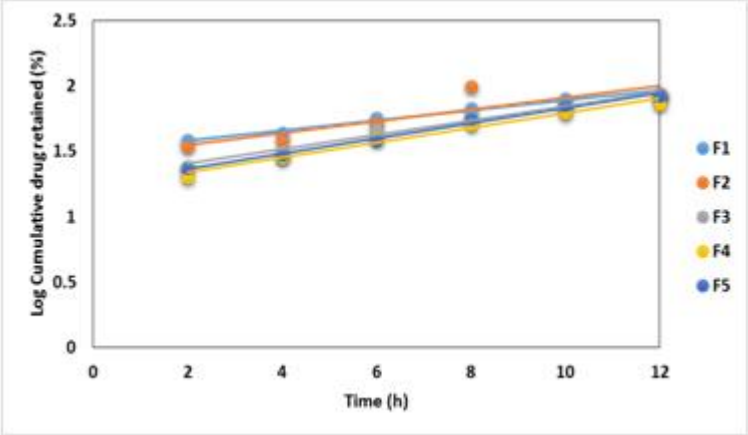

Figure 4: First order release Plot of formulated matrix tablets

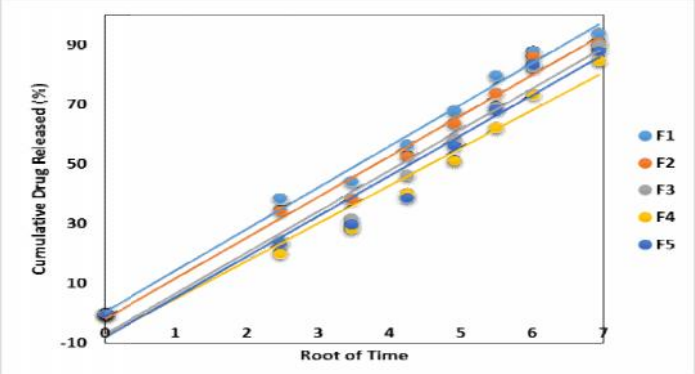

Figure 5: Higuchi Plot of formulated matrix tablets

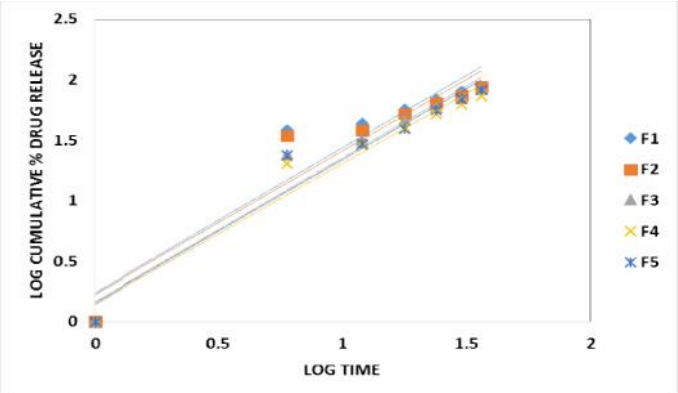

Figure 6: Korsmeyer Peppa's Plot of formulated matrix tablets

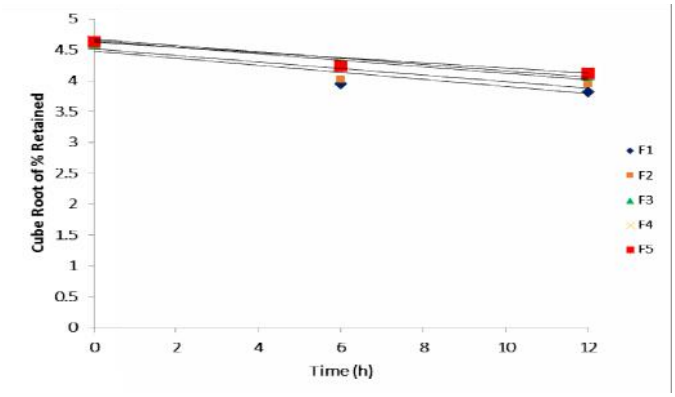

Figure 7: Hixon-Crowell Plot of formulated matrix tablets

4. Conclusion

The present investigation revealed that *Hibiscus rosa-sinensis* leaves mucilage appears to be suitable for use as a release retardant in the formulation of sustained release matrix tablets because of its good swelling, good flow and suitability for matrix formulations. From the dissolution study, it was concluded that dried *Hibiscus rosa-sinensis* mucilage can be used as an excipient for making sustained release matrix tablets of Montelukast.

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