



Fabrication and Characterization of Diclofenac Sodium *Hibiscus rosa-sinensis* leaves Mucilage Sustained Release Matrix Tablets

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Abstract

The main objective of the present study was to develop matrix tablets of Diclofenac sodium with *Hibiscus rosa-sinensis* leaves mucilage and to study its functionality as a matrix forming material for sustained release tablet formulations. Physicochemical properties of dried, powdered mucilage of *Hibiscus rosa-sinensis* leaves were studied. Various formulations of Diclofenac sodium *Hibiscus rosa-sinensis* leaves mucilage were prepared. The formulated matrix tablets found to have better uniformity of weight and drug content with low SD values. The swelling behavior, release rate characteristics and the dissolution study proved that the dried *Hibiscus rosa-sinensis* leaves mucilage can be used as a matrix forming material for making Sustained release matrix tablets. The drug release from selected DHR-5 formulation was by zero order kinetics. Thus, *Hibiscus rosa-sinensis* leaves mucilage can be used as an effective matrix former, to sustain the release of Diclofenac sodium.

Key words: Diclofenac sodium, *Hibiscus rosa-sinensis*, matrix tablets, sustained release.

Introduction

Hibiscus rosa sinensis, (*Malvaceae* family) commonly known as China rose is popular landscape shrub, creates a bold effect with its medium-textured, glossy dark green leaves and with 4-6 inch wide and up to 8 inch long, showy flowers, produced throughout the year and grows up to 7-12 feet [1].

Diclofenac sodium is a Non-Steroidal Anti Inflammatory agent, which is widely used in the long-term therapy for rheumatoid arthritis. The biological half-life of Diclofenac sodium is about 1-2 h; therefore it requires multiple dosing to maintain therapeutic drug blood level. The most frequent side effects of Diclofenac sodium on long-term administration are

gastrointestinal disturbances, peptic ulceration and gastrointestinal bleeding. Diclofenac sodium is poorly soluble in water and acidic pH (1-3) but is rapidly soluble in alkaline pH (5-8) [2]. Hence an attempt was made to formulate a sustained release dosage form containing solid dispersion of Diclofenac sodium for immediate release and beads of Diclofenac sodium for controlled release, which eliminates the need of multiple dosing there by increasing patient compliance and decreasing the occurrence of adverse effects [3]. The objective of present investigation is to design and evaluate sustained release tablets of Diclofenac sodium using *Hibiscus rosa-sinensis* leaves mucilage as release retardant.

Materials and Methods

Materials:

Diclofenac sodium was obtained as a gift sample from Waksman Selman Laboratories, Anantapur, India. *Hibiscus rosa-sinensis* leaves were collected from plants growing in local areas of Anantapur, India. The plant was authenticated at the Botany Department of Sri Krishnadevaraya University, Anantapur, India. Micro crystalline cellulose (Avicel) and Magnesium stearate were procured from SD Fine chemicals (Mumbai, India). All other chemicals used were of analytical reagent grade. Double distilled water was used throughout the experiment.

Methods

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 minutes 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 quantity 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 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

Parameters	Value
Bulk density (g/ml)	0.58
Tapped density (g/ml)	0.79
Carr's index (%)	26.58
Hausner's ratio	1.25
Angle of repose (°)	27.83
Number of experiments (n)=3	

Preparation of Sustained release matrix tablets

Sustained release matrix tablets of Diclofenac sodium with *Hibiscus rosa-sinensis* leaves mucilage were prepared by using different drug: mucilage ratios viz. 1:0.2, 1:0.4, 1:0.6, 1:0.8 and 1:1.0. *Hibiscus rosa-sinensis* leaves mucilage was used as matrix forming material while microcrystalline cellulose as a diluent and Magnesium stearate as a lubricant. All ingredients used were passed through a # 100 sieve, weighed and blended [5]. The granules were prepared by wet granulation technique and compressed by using 10 mm flat faced punches. The compositions of formulations were represented in Table 2.

Table 2: Formulae of matrix tablets

Ingredients (mg)	Formulations				
	DHR-1	DHR-2	DHR-3	DHR-4	DHR-5
Diclofenac sodium	100	100	100	100	100
<i>Hibiscus rosa-sinensis</i> leaves mucilage (dried)	20	40	60	80	100
Micro crystalline cellulose (Avicel)	125	105	85	65	45
Magnesium stearate	5	5	5	5	5
Total weight of tablet	250	250	250	250	250

The physicochemical properties of formulated matrix tablets viz., thickness, hardness and friability were found to be satisfactory [6-10]. And these tablets have uniformity of drug content [11] which was represented in Table 3.

Table 3: Physical properties of matrix tablets

Sl. No	Formulation	Thickness (mm)	Hardness (kg/cm ²)	Friability (%)	Drug content (%)
1	DHR-1	6.4±0.21	6.10±1.25	0.50±0.02	100.1±5.05
2	DHR-2	6.8±0.15	7.50±1.40	0.45±0.05	101.5±5.35
3	DHR-3	6.5±0.41	6.50±1.35	0.50±0.03	99.7±2.50
4	DHR-4	6.3±0.39	5.50±1.45	0.78±0.06	99.9±4.60
5	DHR-5	6.7±0.58	6.5±1.30	0.85±0.07	99.7±5.65

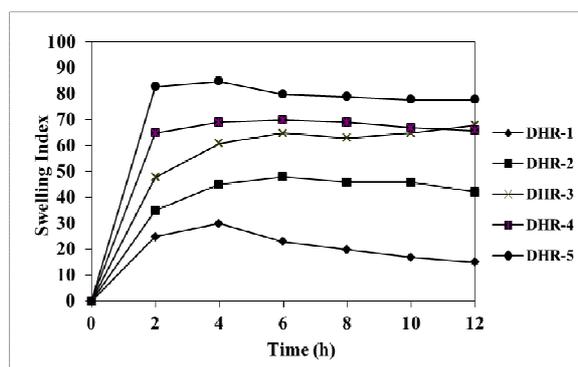
Number of trials (n) = 5

Swelling behavior of sustained release matrix tablets [12]

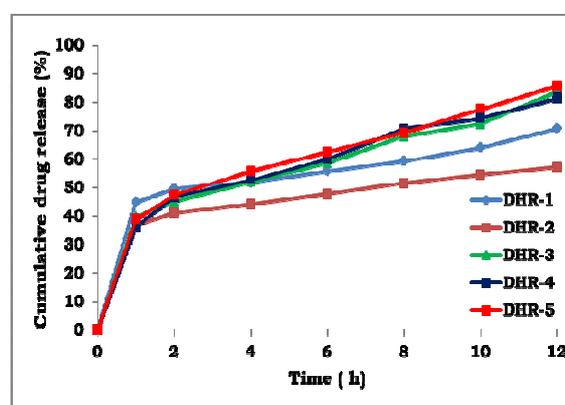
The swelling behavior of formulation DHR-1, DHR-2, DHR-3, DHR-4 and DHR-5 were studied. One tablet from each formulation was kept in a petri dish containing phosphate buffer pH 7.4. For every 2 h, the tablet was withdrawn, kept on tissue paper and weighed. The weighing was continued for every 2 h, till the end of 12 h. The % weight gain by the tablet was calculated by formula.

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

Where, S.I = swelling index, M_t = weight of tablet at the time (t) and M_0 = weight of tablet at time 0. Swelling behavior of Sustained release matrix tablets were represented in Fig.1.

Fig.1. Swelling Index of formulated matrix tablets***In vitro* drug release studies [9]**

Release of Diclofenac sodium from the matrix tablets was studied using a six basket USP XXIII dissolution apparatus taking 900 ml of HCl (pH 1.2) solution for first 2 h and phosphate buffer (pH 7.4) for next 10 h. The dissolution media were maintained at a temperature of $37^{\circ} \pm 0.5^{\circ}\text{C}$. The speed of rotation of basket was maintained 50 rpm. The basket was covered with 100-mesh nylon cloth to prevent the escape of the beads. For the intervals of 30 min the samples were withdrawn, filtered and suitably diluted to determine the absorbance at 276 nm using UV/visible single-beam spectrophotometer-117 (Systronics Corporation, Mumbai, India). The drug release experiments were conducted in triplicate ($n = 3$). The *in vitro* dissolution rates were further tested using pharmacokinetic models. The cumulative % of drug released vs. time (zero order release plot) was shown in Fig. 2.

Fig.2. Zero order release Plot**Results and Discussion**

Matrix tablets, each containing 100 mg of Diclofenac sodium were prepared using dried mucilage of *Hibiscus rosa-sinensis* leaves in various drug: mucilage ratios (1:0.2, 1:0.4, 1:0.6, 1:0.8 and 1:1.0). *In vitro* drug release profile of Diclofenac sodium from formulated matrix tablets were proved that the rate of release was faster in DHR-1 and slower in DHR-5. This result shown that, as the proportion of *Hibiscus rosa-sinensis* leaves mucilage increased, the overall time for release of the drug from the matrix tablet was also increased. Drug releases from matrix tablets were by drug dissolution, drug diffusion or a combination of both.

Conclusion

The present study revealed that *Hibiscus rosa-sinensis* leaves mucilage appears to be suitable for use as a release retardant in the manufacture of sustained release matrix tablets because of its good swelling, good flow rate 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 Diclofenac sodium.

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