DESIGNING AND EVALUATION OF DICLOFENAC SODIUM SUSTAINED RELEASE MATRIX TABLETS USING *HIBISCUS ROSA-SINENSIS* LEAVES MUCILAGE

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ABSTRACT

The main objective of the present investigation was to design matrix tablets of Diclofenac sodium using *Hibiscus rosa-sinensis* leaves mucilage and to study its release retardant activity in prepared sustained release formulations. *Hibiscus rosa-sinensis* leaves were evaluated for physicochemical properties. Different matrix tablets of Diclofenac sodium *Hibiscus rosa-sinensis* leaves mucilage were formulated. The matrix tablets found to have better uniformity of weight, hardness, friability and drug content with low deviated values. The swelling behavior, release rate characteristics and the *in- vitro* dissolution study proved that the dried *Hibiscus rosa-sinensis* leaves mucilage can be used as a matrix forming material for preparing sustained release matrix tablets. The kinetics of drug release from selected DHR-5 formulation followed zero order. It was concluded that *Hibiscus rosa-sinensis* leaves mucilage can be used as an effective matrix forming polymer, to sustain the release of Diclofenac sodium from the formulation.

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

INTRODUCTION

Hibiscus rosa-sinensis, (*Malvaceae* family) commonly known as China rose is a 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 drug (NSAIDs), which is commonly 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 has acidic pH (1-3) but is rapidly soluble in alkaline pH (5-8)[2]. Hence an attempt was made to formulate a sustained release formulation with increased patient compliance and decreased signs 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 retarding polymer.

MATERIALS AND METHODS

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 AR (analytical reagent) grade. Double distilled water was used throughout the experiments.

Extraction of mucilage[4]

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 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 a desiccator at 30 °C & 45% relative humidity till use. 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 (^{0})	27.83
Number of experiments (n=3)	

Preparation of matrix tablets[5]

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. 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.

The physicochemical properties of formulated matrix tablets viz., thickness, hardness and friability were found to be satisfactory[6]. And these tablets have uniformity of drug content[7] which was represented in Table 3.

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
Hibiscus rosa-sinensis 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

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[8]

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. At the end of 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.

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

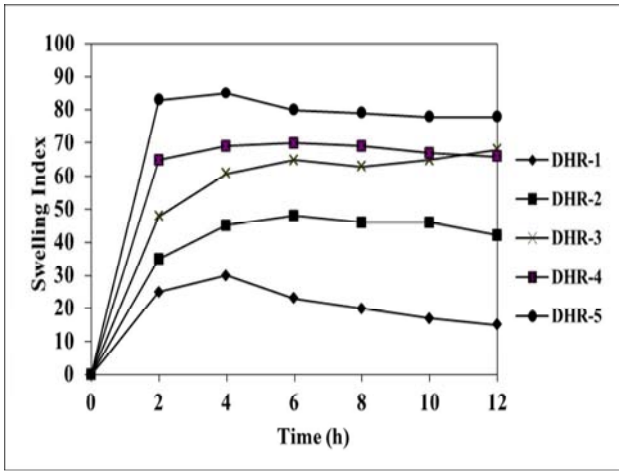
Where, S.I = swelling index, M_t = weight of tablet at the time (t) and

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

***In vitro* drug release studies[9]**

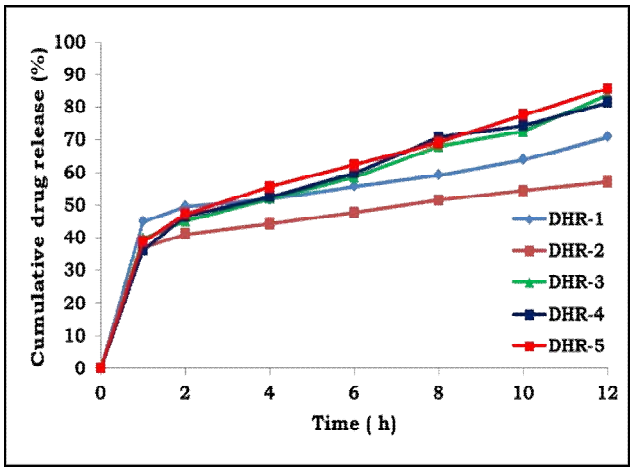
Release of Diclofenac sodium from the matrix tablets was studied using a six basket USP XXIII dissolution apparatus taking 900 mL of HCl (pH 1.2) solution for first 2 h and phosphate buffer (pH 7.4) for next 10 h. The dissolution media were maintained at a temperature of 37° ± 0.5°C. The speed of rotation of basket was maintained at 50 rpm. The basket was covered with 100 mesh nylon cloth to prevent the escape of the beads.

Figure 1. Swelling Index of *formulated* matrix tablets



The samples were withdrawn at 30 min intervals. The samples were 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.

Figure 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 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 Diclofenac sodium.

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