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FORMULATION AND EVALUATION OF ONCE-DAILY SUSTAINED RELEASE ACECLOFENAC DENDROPTHOE FALCATA GUM MATRIX TABLETS

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ABSTRACT

The main aim of the present investigation was to develop matrix tablets of aceclofenac with dendropthoe falcata gum and to study its functionality as a matrix forming agent for once daily sustained release tablet formulations. Physicochemical properties of dried powdered dendropthoe falcata gum were studied. Various formulations of aceclofenac dendropthoe falcate gum were prepared. The formulated tablets found to have better uniformity of weight and drug content with low sd values. The swelling behavior and release rate characteristics were studied. The dissolution study proved that the dried dendropthoe falcata gum can be used as a matrix forming material for making once daily sustained release matrix tablets.

Key words: Aceclofenac, Dendropthoe falcata, matrix tablets, once daily sustained release.

INTRODUCTION

Aceclofenac is a potent non-steroidal anti-inflammatory drug, which is a commonly prescribed drug for the treatment of patients suffering with pain, rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. [1] It is a weak acid (pka = 4.7) practically insoluble in water and acidic environment but highly permeable (class 2) according to the

biopharmaceutical classification system (BCS). The oral absorption is uniform, rapid and complete with a bioavailability of nearly 100% and an elimination half-life of 2–4 h.[2] Aceclofenac is reported to have a short biological half-life (3.4 ± 0.7 h) requiring it to be administered in 100mg twice daily. Hence we have selected aceclofenac for the development of once daily sustained release matrix tablets. The pharmacokinetics and dosage schedule supports once daily sustained release formulations for Aceclofenac for better control of pain, enhance clinical efficacy and patient compliance. Dendrophthoe falcata (Loranthaceae) commonly known as 'Vanda' in Marathi is dried as well as fresh stem parasitic on magnifera indica. It is an evergreen shrub with bark smooth grey, leaves opposite unequal, thick 1.6-25.4 cm long, flowers single, orange-red or scarlet softly pubescent, berries soft ovoid-oblong, 1.3 cm diameter and indigenous to India, Sri lanka, Thailand, Indo-china and Australia. The aerial parts are used in wounds, menstrual troubles, asthma, psychic disorders, pulmonary tuberculosis, consumption and mania by the tribal of India. Leaf paste is used in skin diseases .[3] Its paste is applied on boils, setting dislocated bones and extracting pus. The plant has been scientifically proved to have antilithiatic, diuretic, cytotoxic and immunomodulatory activities.[4-5] The obtained gum is evaluated for various parameters. The objective of present investigation is to design and evaluate once daily sustained release tablets of Aceclofenac using Dendropthoe falcata gum as release retardant.

MATERIALS AND METHODS

Materials

Aceclofenac was obtained as a gift sample from Blue cross company, Nasik, India. Dendropthoe falcate gum was collected from Chandwad region, Nasik, India. Microcrystalline cellulose (Avicel) and Magnesium stearate were purchased from Loba Chemie Mumbai, India. All chemicals used were of analytical reagent grade and double distilled water was used throughout the experiments.

Methods

Purification of dendrophthoe falcata gum

The gum was collected from the dendropthoe falcata tree in Nashik (Chandwad) region. The gum was well dried. The dried gum was powdered in mortar and pass through sieve number

80. The dendropthoe falcata gum was solubilized in distilled water. The concentrated solution was precipitated in ethanol. The precipitate was separated and dried at 60^0C. The dried gum was powdered and stored in tightly closed container.

Standardization of dendrophthoe falcata gum

The gum was standardized for following properties;

Loss on drying

The 5 gm gum was dried at 100 ± 5^0C till the constant weight of gum was obtained.

Ash value:

1 gm of gum was accurately weighed and evenly distributed it in the crucible. It was dried at 105^oC for 1 hour and ignited in muffle furnace at 600 ± 25^0C.

pH

Dendropthoe falcata gum was analyzed for 2-8%w/w gum solutions.

Drug-excipient compatibility studies

Infrared (IR) spectroscopy was conducted using a FTIR 8400S spectrophotometer (Shimadzu, Tokyo, Japan) and the spectrum was recorded in the wavelength region of 4000 to 400cm^{-1}.[6] The procedure consisted of dispersing a sample (drug alone or mixture of drug and excipients) in KBr and compressing into discs by applying a pressure of 5 tons for 5 min in a hydraulic press. The pellet was placed in the light path and the spectrum was obtained.

Preparation of matrix tablets

Once daily sustained release matrix tablets of Aceclofenac with Dendropthoe falcata gum were prepared by using different drug: gum ratios viz. 1:0.250, 1:0.375, 1:0.500, 1:0.675 and 1:0.750. Different tablet formulations were prepared by direct compression technique and the formulations were named as AP-1, AP-2, AP-3, AP-4 and AP-5 respectively as shown in Table 1. All the powders were passed through mesh #80. Talc and magnesium stearate were finally added as glidant and lubricants. The drug and powdered gum were compressed (11mm diameter, biconvex punches) using a Rimek Minipress 2D tablet compression machine (Karnavati Engg.Ltd.). Prior to the compression, the powdered gum was evaluated for several tests.

Table 1: Formulation Design.

Ingredients (mg)	Formulations				
	AP-1	AP-2	AP-3	AP-4	AP-5
Aceclofenac	200	200	200	200	200
Dendropthoe falcate Gum (dried)	50	75	100	125	150
MCC (Avicel)	245	220	195	170	145
Magnesium stearate	5	5	5	5	5
Total weight of tablet	500	500	500	500	500

EVALUATION OF TABLETS

Thickness

The thickness of the tablets was determined using a Vernier caliper (Vashishat, Ambala Cantt.,Haryana, India). Five tablets from each batch were used and average values were calculated.

Uniformity of Weight

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance (Shimadzu corporation D455003609, Japan) and the test was performed according to the official metho. [7]

Hardness and Friability

For each formulation, the hardness and friability of tablets equivalent to 6.5 g were determined using the Monsanto hardness tester (Rolex, Chandigarh, India) and the Roche friabilator (Electrolab friabilator EF-1W, Mumbai, India), respectively. [8]

Drug Content

An accurately weighed amount of powdered matrix tablets (500 mg) was extracted with water and the solution was filtered through Whatmann filter paper. The absorbance was measured at 275 nm after suitable dilution.

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.[9]

S.I = {(Mt-M0) / M0} X 100

Where, S.I = swelling index,

Mt = weight of tablet at time 't' and

Mo = weight of tablet at time t = 0.

Dissolution studies

The in vitro dissolution study was carried out using USP Type 2 dissolution apparatus (Electrolab TDT-08L, Mumbai, India). The study was carried out in 900 mL of 1% SLS in 0.1N HCl for first 2 hours and then 900 mL of phosphate buffer (pH 6.8) from 3 to 12 h. The dissolution medium was kept in thermostatically controlled water bath, maintained at 37±0.5^{0}C. The paddle was lowered so that the lower end of the stirrer was 25 mm above from the base of the beaker. The pre-weighed tablet was then introduced into the dissolution jar and the paddle was rotated at 75 rpm. At different time intervals, 5 ml sample was withdrawn and analyzed spectrophotometrically at 275 nm for the drug release. At each time of withdrawal, 5 mL of fresh corresponding medium was replaced into the dissolution flask.[10]

RESULTS AND DISCUSSION

Physicochemical properties of dried powdered dendropthoe falcata gum were studied. The loss on drying was found to be less than ≤ 7% w/w. Percentage ash content was found to be less than 7.5%w/w. pH found to be in the range of 6.5 to 5.5.

Infrared spectrum of aceclofenac pure drug, infrared spectrum of aceclofenac with dendropthoe falcata were shown in fig. 1 and 2. The graphs indicate there are no negative interactions between drug and matrix material used.

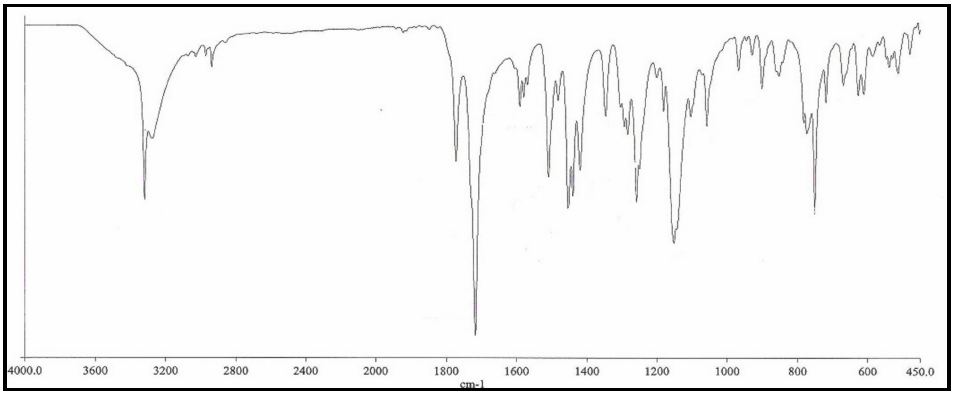

Fig. 1: FTIR spectrum of pure Aceclofenac.

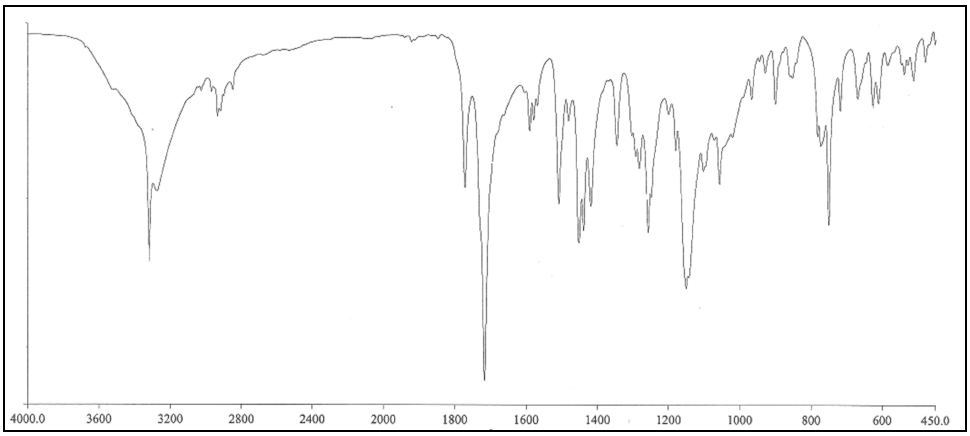

Fig. 2: Mixture of aceclofenac and dendropthoe falcata gum.

Matrix tablets, each containing 200 mg of aceclofenac, were prepared using dried gum of dendropthoe falcata in various drug: gum ratios (1:0.250, 1:0.375, 1:0.500, 1:0.675 and 1:0.750).

Then, the formulated sustained release aceclofenac dendropthoe falcata gum matrix tablets were evaluated for Thickness, hardness, friability and uniformity of content as shown in Table 2. Average thickness was found to be in the range of 6.1-6.3 mm. Hardness of the tablets was found to be in the range of 7.0-7.8 Kg/cm^2. Friability below 1% was an indication of good mechanical resistance of the tablets. The uniformity of drug content was found to be 99% 100% w/w which was within acceptable limits.

Table 2: Evaluation of tablets*

Formulation	Thickness (mm)	Hardness (Kg/cm2)	Friability (%)	Drug content (%)
AP-1	6.2±0.4	7.0±0.55	0.29±0.08	99.7±0.79
AP-2	6.1±0.2	6.04±0.46	0.43±0.06	100.3±0.58
AP-3	6.3±0.3	6.96±0.55	0.25±0.04	99.9±0.81
AP-4	6.0±0.3	7.76±0.71	0.57±0.07	100.2±0.53
AP-5	6.3±0.2	7.84±0.74	0.78±0.07	99.7±0.72

** Average of three determinations*

The swelling behavior and release rate characteristics were studied. The batch AP-5 has shown highest swelling behavior as compared to other batches as shown in fig.3.

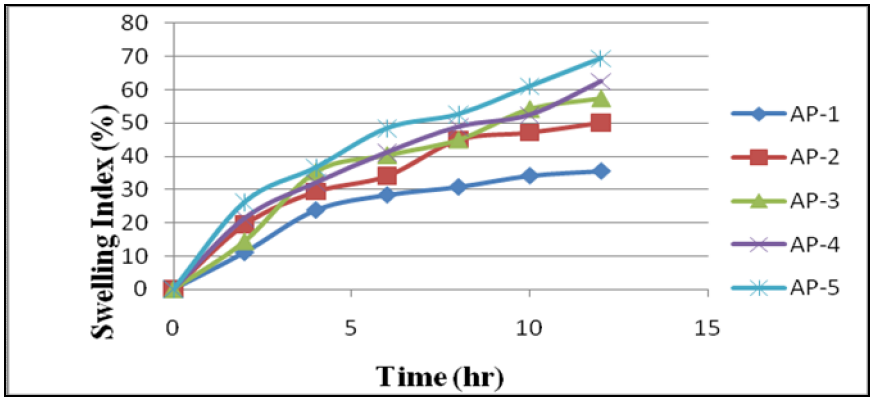

Fig. 3: Swelling Index of Dendropthoe falcata gum Aceclofenac matrix tablets.

Among these formulations, the release rate was increased in the following order: AP-5 > AP-4 > AP-2 > AP-1 > AP-3 as shown in fig.4.

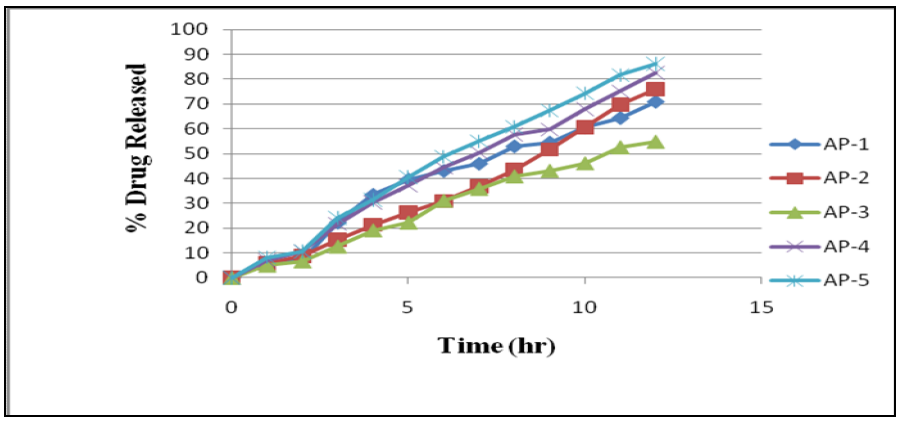

Fig. 4: Zero order release plot of dendropthoe falcata gum aceclofenac matrix tablets

The result has shown that as the proportion of dendropthoe falcata gum increased, the swelling is also increase and the overall time of 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 dendropthoe falcata gum appears to be suitable for use as a release retardant in the manufacture of once daily 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 dendropthoe falcata gum can be used as an excipient for making once daily sustained release matrix tablets.

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