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Research Article

FORMULATION, EVALUATION AND COMPARISON OF SUSTAINED RELEASE MATRIX TABLETS OF DICLOFENAC SODIUM USING TAMARIND GUM AS RELEASE MODIFIER

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ABSTRACT

Background and purpose of study: In the present investigation, an attempt was made to increase therapeutic effectiveness, reduce dose frequency and improvement in patient compliance, by developing sustained release matrix tablets of Diclofenac sodium using tamarind gum as release modifier. **Methods:** Six batches of sustained release matrix tablets of Diclofenac sodium were prepared by using different drug: polymer ratios viz. 1:1, 1:1.5, 1:2, 1:2.5, 1:3, and 1:3.5 for tamarind gum. Tamarind gum was used as matrix forming material, while microcrystalline cellulose was used as filler to maintain the tablet weight. Infrared spectroscopy was used to investigate the interaction between drug and polymer. The tablets were analyzed to determine their hardness, friability, weight variation, and an *In-vitro* release of drug was performed in phosphate buffer saline (PBS) pH 7.4 for twenty four hours. Swelling study was also carried out to study dispersibility of gums at different concentrations. **Results:** All the physical characters of the fabricated tablet were within acceptable limits. No interaction between drug and polymer was confirmed by infrared spectrum. Concentration dependent swelling of tamarind gum shows dispersibility of gum at particular manner to release drug. A better sustained drug release (98.7%) was obtained with the matrix tablet (Batch F) of the tamarind gum. C**onclusion:** It is cleared that the drug release from matrix tablets prepared by using tamarind gum can be sustained for more than 12 hrs and release of drug vary with concentration of polymer in matrix tablets.

Key words: Sustained release matrix tablet, Gum acacia, Tamarind gum, Diclofenac sodium.

INTRODUCTION

Drug products designed to reduce the frequency of dosing by modifying the rate of drug absorption have been available for many years[1]. Regular research is going on for the use of natural occurring biocompatible polymeric material in designing of dosage form for oral controlled release administration. Natural gums are biodegradable and nontoxic, which hydrate and swell on contact with aqueous media, so these have been used for the preparation of dosage form[2]. Plant polysaccharide, has been shown to be useful for the construction of drug delivery systems for specific drug delivery[3]. Tamarind gum was xyloglycon present in tamarind seed. It is a hydrophilic polymer and had been limited for use as gelling, thickening, suspending and emulsifying agents[4, 5]. It possesses properties like high viscosity, broad pH tolerance and adhesivity[6, 7]. In addition to these other important properties of TSP have been identified recently. They include non- carcinogenicity mucoadhesivity, biocompatibility, high drug holding capacity and high thermal stability[8, 9, 10, 11]. This led to its application as excipient in hydrophilic drug delivery system. High patient compliance and flexibility in developing dosage forms made the oral drug delivery systems the most convenient mode of drug administration compared to other dosage forms. Of these, matrix systems have gained widespread importance. In the present study matrix tablet of Diclofenac sodium was prepared. The basic idea behind the development of such a system is to maintain a constant level of drug in the blood plasma in spite of the fact that the drug does not undergo disintegration. This type of system is quite useful where a sustained effect is required over a long period of time Diclofenac sodium is sodium2-[(2, 6-dichlorophenyl)-amino] phenyl acetate Diclofenac is an acidic nonsteroidal antiinflamatory drug (NSAID) with analgesic property. Diclofenac is used to trat pain, dysmenorrhea, ocular inflammation, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis and actinic keratosis[12, 13]. The present investigation was done with an aimed to formulate sustained release matrix system using tamarind gum.

MATERIALS AND METHODS

Isolation of gum from tamarind Seed

The crushed seeds of *Tamarindus indica* were soaked in water for 24 h, boiled for 1 h, and kept aside for 2 h for the release of gum into water. The soaked seeds were taken and squeezed in a muslin bag to remove marc from the filtrate. Then, to the filtrate, equal quantity of absolute ethyl alcohol was added to precipitate the gum. The gum was separated by filtration. The marc was not discarded but it was sent for multiple extractions with decreasing quantity of extracting solvent, i.e., water with the increase of number of extractions. The isolation was continued until the material was free of gum. The separated gum was dried in hot air oven at temperature 40°C. The dried gum was powdered and stored in airtight containers at room temperature[14, 15, 16].

Procurement of drug and other excipients

Diclofenac sodium was obtained as gift sample from Alchem Laboratories, Baddi India. Microcrystalline cellulose was procured from RANKEM Limited, New Delhi, India.

Infrared study of excipients

Infrared study was carried out with aim to investigate either excipients interact with each other or not. An infrared spectrum of each excipient is characteristics for it and if any change in peak is observed, shows interaction between excipients (Figure 1, Figure 2 and Figure 3).

Preparation of SR matrix tablets

According to Table 1 sustained release matrix tablets of Diclofenac sodium were prepared by using different drug: polymer ratios viz. 1:1, 1:1.5, 1:2, 1:2.5, 1:3, 1:3.5 for various batches Batch A, Batch B, Batch C, Batch D, Batch E and Batch F respectively. Tamarind gum was used as matrix forming material, while microcrystalline cellulose was used as filler to maintain the tablet weight. All ingredients were passed through a # 20 sieve, weighed and blended. The granules (which were obtained after wet granulation) were compressed by a direct compression technique, using KBr press, with the help of 8mm flat faced punches[17, 18].

Evaluation of fabricated matrix tablets

Weight variation

All prepared matrix tablets were evaluated for weight variation as per USP XXIV monograph. Twenty tablets of each batch were used to evaluate weight variation among tablets and standard deviation was calculated[19, 20].

Friability

Table 1: Formulation composition of tamarind gum matrix tablets

Ingredients	Formulations					
	Batch A	Batch B	Batch C	Batch D	Batch E	Batch F
Diclofenac sodium	50mg	50mg	50mg	50mg	50mg	50mg
Tamarind gum	50mg	75mg	100mg	125mg	150mg	175mg
Microcrystalline cellulose	200mg	175mg	150mg	125mg	100mg	75mg
Total weight	300mg	300mg	300mg	300mg	300mg	300mg

Table 2: Various evaluation parameters for fabricated tamarind gum tablets

Parameter	Tamarind Gum					
	Batch A	Batch B	Batch C	Batch D	Batch E	Batch F
Weight variation(gm)	0.299±0.01	0.300±0.01	0.291±0.01	0.293±0.01	0.298±0.01	0.293±0.01
Friability (%)	0.05±0.01	0.03±0.01	0.03±0.01	0.03±0.01	0.02±0.01	0.02±0.01
Hardness (N)	20.24± 0.12	20.27±0.15	20.40±0.1	20.53±0.06	20.77±0.06	20.80±0.1
Thickness(mm)	3.623±0.01	3.727±0.02	3.790±0.03	3.677±0.18	3.777±0.19	3.707±0.05

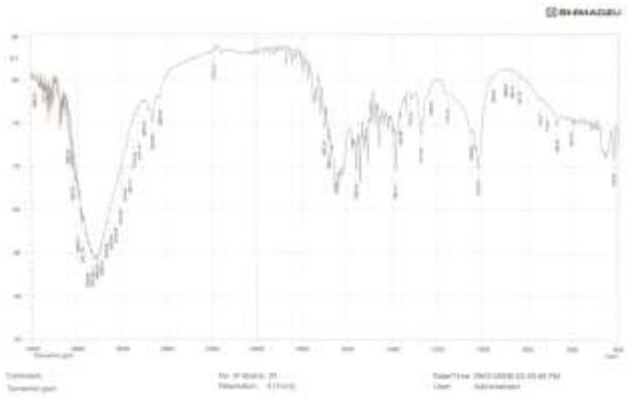

Figure 1: Infrared spectra of tamarind gum

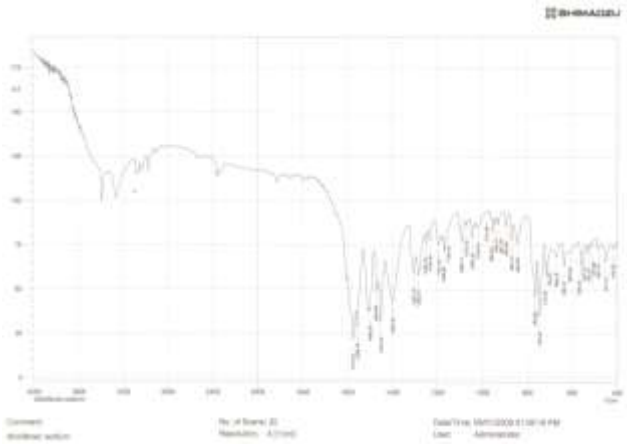

Figure 2: Infrared spectra of diclofenac sodium

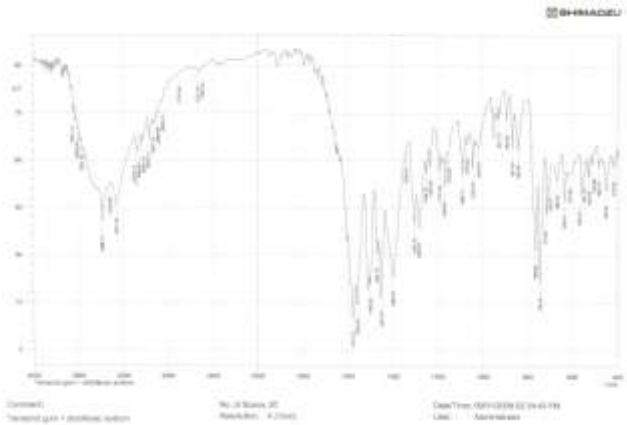

Figure 3: Infrared spectra of mixture of tamarind gum and diclofenac sodium

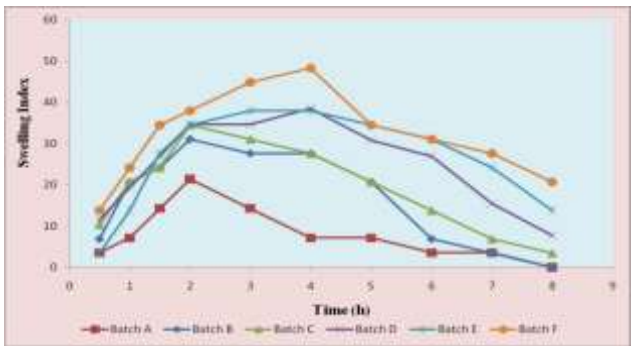

Figure 4: Swelling index profile of tablets containing tamarind gum as polymer

Figure 5: Different stages of swelling of a tablet

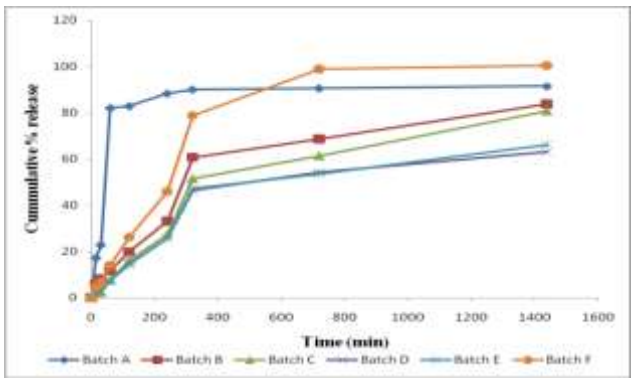

Figure 6: Drug release profile using tamarind gum as polymer

Tablets of all batches were used to evaluate friability as per USP XXIV monograph. Friability testing was done by Roche friabilator with triplicate readings[19, 20].

Hardness

Hardness of all batches was determined using Digital Force Gauge (Model:EL=500N, Electrolab). The test was carried out in triplicate for all batches as per USP XXIV monograph for uncoated tablets[19, 20].

Thickness

Thickness was measured by vernier caliper as per USP XXIV monograph. The readings were carried out in triplicate and average value was noted[19, 20].

Drug content

The tablets were powdered, and 50 mg equivalent weight of Diclofenac sodium in tablet powder was accurately weighted and transferred into a 100 ml volumetric flask. Initially, 10 ml of phosphate buffer (pH6.6) was added and shaken for 10 min. then, the volume was made up to 100 ml with buffer. Subsequently, the solution in volumetric flask was filtered, and 1 ml of the filtrate was diluted and analyzed at 276 nm using UV-visible spectrophotometer (Shimadzu UV-2450, Japan). The drug content of the each sample was estimated from their standard curve [21, 22.]

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 all formulation was studied. One tablet from each formulation was kept in a petridish containing pH 7.4 phosphate buffer. At the end of 0.5 h and 1 h, the tablet was withdrawn, soaked with tissue paper, and weighed. Then for every 1 h, weights of the tablet were noted, and the process was continued till the end of 8 h. Percentage weight gain by the tablet was calculated by formula;

$$S.I = \{(M_t - M_o) / M_o\} X 100,$$

Where, S.I = swelling index, M_t = weight of tablet at time t (h) and M_o = weight of tablet at zero time[23, 24].

***In vitro* drug release study**

In vitro drug release was studied using Lab India Dissolution Apparatus, with 900 ml of dissolution medium (phosphate buffer pH 7.4) maintained at 37±1°C for 24 h, at 50 rpm. 5ml of sample was withdrawn after every hour, and was replaced by an equal volume of fresh dissolution medium of same pH (phosphate buffer pH 7.4). Collected samples were analyzed spectrophotometrically at measured wavelength of 276nm, and cumulative percent drug release was calculated[25, 26].

The data obtained in the in-vitro dissolution study is grouped according to two modes of data treatment as follows:

1. Percentage drug released Vs time (h).

2. Cumulative percentage drug released Vs time (h)

In these two methods, drug release profile can be better studied using cumulative percentage drug release Vs time (h) plot.

RESULTS AND DISCUSSION

Infrared spectra of drug and polymers were used to study the compatibility between them. No change in peak shows that there was no interaction between drug and polymers.

As per the Table 2, the formulated matrix tablets met the Pharmacopoeial requirement of uniformity of weight. All the tablets confirmed to the requirement of assay, as per USP. Hardness, percentage friability and thickness were all within acceptable limits[19, 20].

Sustained drug release was displayed by all formulations in phosphate buffer (pH 7.4). Figure 4 showed the swelling characteristics of tamarind gum. The swelling index was calculated with respect to time (Figure 4). As time increases, the swelling index was increased, because weight gain by tablet was increased proportionally with rate of hydration up to certain limit (Figure 5). Later on, it decreases gradually due to dissolution of outermost gelled layer of tablet into dissolution medium. The direct relationship was observed between swelling index and polymer concentration, and as polymer concentration increases, swelling index was increased[23, 24].

It has been observed that the cumulative percent drug release decreases with increasing concentration of polymer and swelling index. The reason attributed to this fact is slow erosion of the gelled layer from the tablets containing higher amount of natural polymer. This slow release is because of the formation of a thick gel structure that delays drug release from tablet matrix[25, 26, 27, 28].

The *in vitro* release of Diclofenac sodium from tamarind gum was showed in Figure 6. From the findings, obtained so far it can be concluded that Batch F of tamarind gum in the concentration ratio of 1:2.5 was promising concentration for oral sustained release tablet of Diclofenac sodium.

CONCLUSIONS

Natural polymers when used as release retardent exhibits uniform release over longer period of time. Hence it can be concluded that, the tamarind gum which is a natural polymer can be used as a promising drug release retardent in a particular cocentration range.

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