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Research Article

Formulation, In Vitro Evaluation and Comparison of Sustained Release Matrix Tablets of Diclofenac Sodium using Okra Gum as Release Modifier

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ABSTRACT

In the present investigation, an attempt was made to formulate sustained release matrix tablets of Diclofenac sodium using Gum acacia and Okra gum as release modifier. 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 both gum acacia and Okra gum. The tablets were analyzed for their hardness, friability, weight variation, and an In-vitro release 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. The physical characters of the fabricated tablet were within acceptable limits. Gum acacia showed better swelling than Okra gum. A better sustained drug release (98.7%) was obtained with the matrix tablet (Batch F) of the Okra gum. Results showed that the drug release from matrix tablets prepared by using natural polymers can be sustained for more than 12 hrs and the drug release vary with concentration of polymer in matrix tablets.

Keywords: Sustained release matrix tablet, Gum acacia, Okra gum, Diclofenac sodium, swelling index.

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]. Gum acacia is often used as plasticizer and tablet binder. The gum acacia has been recognized as an acidic polysaccharide containing D-galactose, L-arabinose, L-rhamnose and D-glucuronic acid[4]. Okra gum was Polysacharide present in Okra pods. Both of these are hydrophilic polymer and had been limited for use as gelling, thickening, suspending and emulsifying agents . Diclofenac sodium is sodium 2-[(2, 6-dichlorophenyl)-amino] phenyl acetate. Diclofenac is an acetic acid nonsteroidal antiinflammatory drug (NSAID) with analgesic property. Diclofenac is used to treat pain, dysmenorrhea, ocular inflammation, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and actinic keratosis[9,10]. The present investigation is aimed to formulate the matrix tablet of Diclofenac sodium with tamarind gum and gum acacia using no other varying parameter.

MATERIAL AND METHODS

Isolation of Okra gum from Okra pods

The Lady's finger/bendy was procured from local market and was shade dried this was then powdered by crushing and grinding. Lady's

finger/bhendi was dried in an oven at 37°c for drying and it was powdered for 5 min in a mechanical blender and passed through sieve no. 120 to get fine powder. It was then soaked in distilled water for 24 hours in a RB flask. It was boiled for 1 hour under reflux with occasional stirring and kept aside for 2 hours for release of mucilage into water. The material was filtered through muslin bag, hot distilled water was added through the sides of the marc and squeezed well in order to remove mucilage completely. Equal volume of ethanol was added to the filtrate to precipitate the mucilage and kept inside refrigerator for a day to effect settling. It was filtered and dried completely in an incubator at 37˚c, powdered, sieved and weighed. It was subjected to chemical tests to confirm its identity.

Procurement of drug and other excipients

Diclofenac sodium was obtained as gift sample from Alchem Laboratories, Baddi India. The Pharmacopoeial grade of gum acacia was obtained from RFCL Limited, New Delhi, India and microcrystalline cellulose was procured from RANKEM Limited, New Delhi, India.

Preparation of SR matrix tablets

According to Table 1 and Table 2 sustained release (SR) 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. Okra gum and gum acacia were 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 (IR Press), with the help of 8mm flat faced punches[14, 15].

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[16, 17].

Friability

Tablets of all batches were used to evaluate friability as per USP XXIV monograph. Friability testing was done by Roche friabilator with triplicate readings[16, 17].

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[16,17].

Thickness

Thickness was measured by vernier caliper as per USP XXIV monograph. The readings were carried out in triplicate and average value was noted[16,17.]

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 [18,19].

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;

$$S.I = \{(Mt-Mo) / Mo\} X 100,$$

Where, S.I = swelling index, Mt = weight of tablet at time t (h) and Mo = weight of tablet at zero time[20, 21].

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[22,23].

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 and Table 3, 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[16, 17].Sustained drug release was displayed by all formulations in phosphate buffer (pH 7.4). Figure 1 and Figure 2 showed the swelling characteristics of gum acacia and Okra gum respectively. The swelling index was calculated with respect to time. As time increases, the swelling index was increased, because weight gain by tablet was increased proportionally with rate of hydration up to certain limit. 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[20, 21].

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[22-26].

The in vitro release of Diclofenac sodium from gum acacia and Okra gum were showed in Figure 3 and Figure 4 respectively. From the findings, obtained so far it can be concluded that Batch F of Okra 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 Okra gum which is a natural polymer can be used as a promising drug release retardent in comparision to the estabilised gum acacia in a particular cocentration range.

Table 1: Formulation composition of matrix tablets

Ingredients	Formulations					
	Batch A	Batch B	Batch C	Batch D	Batch E	Batch F
Diclofenac Sodium	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg
Polymer [a]	50 mg	75 mg	100 mg	125 mg	150 mg	175 mg
Microcrystalline cellulose	200 mg	175 mg	150 mg	125 mg	100 mg	75 mg
Total weight	300 mg	300mg	300mg	300 mg	300 mg	300 mg

a gum acacia and Okra gum for their respective batches.

Table 2: Various evaluation parameters for fabricated gum acacia tablets

Ingredients	Gum acacia					
Parameter	Batch A	Batch B	Batch C	Batch D	Batch E	Batch F
Weight variation(gm)	0.301 ±0.01	0.293±0.02	0.299±0.01	0.298±0.01	0.301±0.01	0.302±0.01
Friability (%)	0.03±0.01	0.02±0.01	0.02±0.01	0.02±0.01	0.01±0.01	0.01±0.01
Hardness (N)	20.07± 0.06	20.20± 0.0	20.37±0.06	20.53±0.06	20.63± 0.06	20.83±0.06
Thickness(mm)	3.503±0.02	3.560±0.08	3.740±0.04	3.683±0.03	3.777±0.04	4.04±0.07

Table 3: Various evaluation parameters for fabricated Okra gum tablets

Ingredients	Okra gum					
Parameter	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	0.04±0.01	0.03±0.01	0.02±0.01	0.05±0.01	0.05±0.01
Hardness (N)	20.24 ± 0.06	20.16 ± 0.0	20.41±0.06	20.24±0.06	20.21± 0.06	20.23±0.06
Thickness(mm)	3.623±0.02	3.421±0.08	3.140±0.04	3.289±0.03	3.414±0.04	4.310±0.07

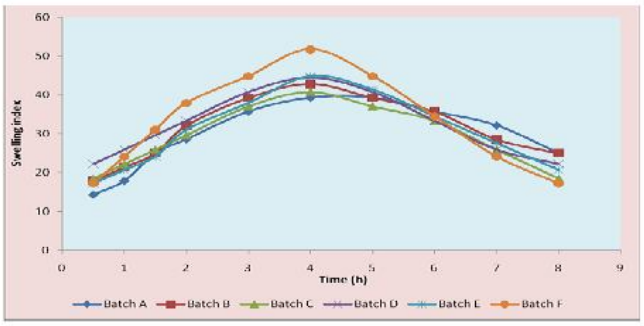

Fig. 1: Swelling Index profile of tablet containing gum acacia as polymer

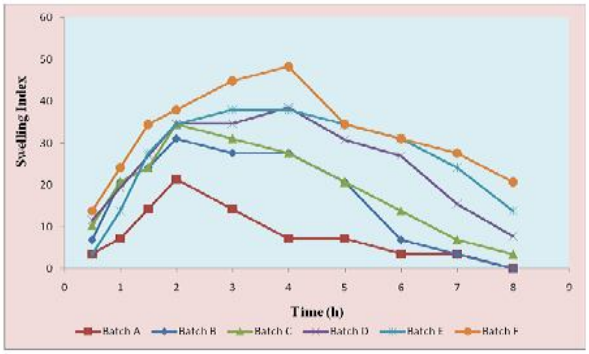

Fig. 2: Swelling index profile of tablets containing Okra gum as polymer

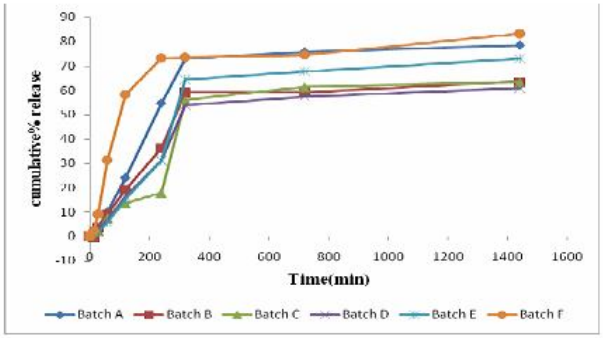

Fig. 3: Drug release profile of tablets containing gum acacia as polymer

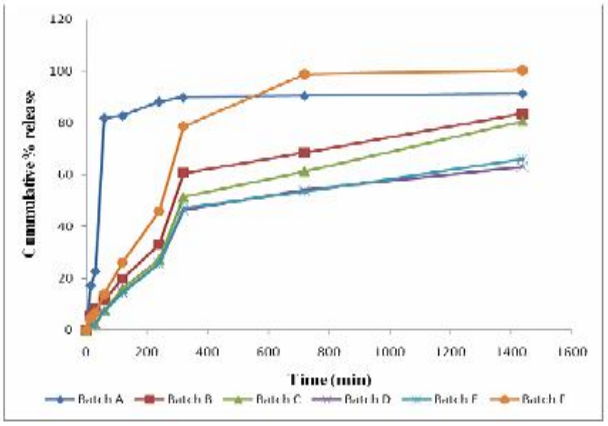

Fig. 4: Drug release profile of tablets containing Okra gum as polymer

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