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Full Length Research Paper

FORMULATION AND OPTIMIZATION OF SUSTAINED RELEASE MATRIX TABLETS OF DICLOFENAC SODIUM USING PECTIN AS RELEASE MODIFIER

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ABSTRACT

Purpose: *In the present investigation, an attempt was made to increase therapeutic effectiveness, reduction in dosing frequency and thus improving patient compliance, by developing sustained release matrix tablets of Diclofenac sodium using pectin as release modifier.*

Method: *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 pectin. Pectin was used as matrix forming material, while microcrystalline cellulose was used as filler to maintain the tablet weight. The tablets were analyzed to determine their hardness, friability, weight variation, and an In-vitro release of drug was performed in phosphate buffer saline pH 7.4 for twenty four hours. Swelling study was also carried out to study dispersibility of pectin at different concentrations.*

Results: *All the physical characters of fabricated tablet were within acceptable limits. As the concentration of pectin increases, swelling index also increased. Table showed better release retardant in a specific concentration range.*

Conclusions: *It is clear through the dissolution studies that the release profile of Diclofenac sodium from matrix tablets prepared using pectin was retarded approximately 24 h. Thus pectin stands as a potential candidate for sustained release formulation.*

Key Words: *Diclofenac sodium, pectin, sustained release matrix tablets.*

INTRODUCTION:

In recent years the basic aim in the designing of drug products is to reduce the frequency of dosing by modifying the rate of drug absorption [1]. Regular research is going on in field of use of natural occurring biocompatible polymeric material in designing of dosage form for oral controlled release administration [2, 3]. Hydrophilic swellable polymers are widely used to control the release of drugs from matrix formulations [4, 5]. Natural polymers are biodegradable and nontoxic, which hydrate and swell on contact with aqueous media, and these have been used for the preparation of dosage form. Pectin, including high and low ester content and

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amidated pectin, are used in food all over the world. It is an edible plant polysaccharide and has been shown to be useful for the construction of drug delivery systems for targeted drug delivery [6-9]. Pectin is a hydrophilic polymer, which until recently had been limited for use in gelation, thickening, suspending and as emulsifying agent.

It is essential to develop cost-effective and less tedious procedures for preparation of sustained release formulations on the industrial scale. The most commonly used method for fabricating drugs in a controlled-release formulation is by incorporating them into a matrix containing a hydrophilic rate controlling polymer. Matrix systems are widely used in oral controlled drug delivery because of their flexibility (which results in obtaining desirable drug release profile), cost effectiveness and broad regulatory acceptance [10, 11]. Diclofenac Sodium is sodium 2-[(2, 6-dichlorophenyl)-amino] phenyl acetate and is an acetic acid nonsteroidal antiinflammatory drug (NSAID) with analgesic and antipyretic properties. It is used to treat, dysmenorrhea, ocular inflammation, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and actinic keratosis [12, 13]. The present investigation is aimed to formulate the sustained release matrix tablet of Diclofenac sodium with different concentration of pectin, using no other varying parameter.

MATERIAL AND METHODS:

Diclofenac Sodium was obtained as gift sample from Alchem Laboratories, Baddi, Himanchal Pradesh, India. The Pharmacopoeial grade of Pectin was obtained from RFCL limited, New Delhi. All materials used were of analytical grade, and procured from commercial sources.

Preparation of sustained release matrix tablets:

According to Table1 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 P1, Batch P2, Batch P3, Batch P4, Batch P5 and Batch P6 respectively. Pectin 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 [14, 15].

Table 1*:* Formulation composition of Pectin matrix tablets.

Ingredients	Formulations					
	Batch P1	Batch P2	Batch P3	Batch P4	Batch P5	Batch P6
Diclofenac sodium	50mg	50mg	50mg	50mg	50mg	50mg
Polymer	50mg	75mg	100mg	125mg	150mg	175mg
Microcrystalline cellulose	200mg	175mg	150mg	125mg	100mg	75mg
Total weight	300mg	300mg	300mg	300mg	300mg	300mg

Infrared study: All the ingredients were studied for compatibility between them. For that purpose infrared spectra of individual ingredients were compared with infrared spectra of blended powder.

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 weighed and transferred into a 100 ml volumetric flask. Initially, 10 ml of phosphate buffer (pH7.4) 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, dried with tissue paper, and weighed. Then for every 1 h, weight of the tablet was 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 [20, 21].

In vitro drug release study: *In vitro* drug release was studied using LabIndia dissolution apparatus, with 900 ml of dissolution medium maintained at 37±1°C for 24 h, at 100 rpm. 5ml of sample was withdrawn after every hour, and was replaced by an equal volume of fresh dissolution medium of same pH. Collected samples were analyzed spectrophotometrically. At measured wavelength of 276nm, and cumulative percent drug release was calculated. The study was performed in triplicate and results were recorded [22, 23].

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

1. % Drug release Vs time in h.
2. Cumulative percentage drug release vs. time in h.

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.

Table 2: Evaluation parameters for fabricated Pectin tablets.

Parameter	Pectin					
	Batch P1	Batch P2	Batch P3	Batch P4	Batch P5	Batch P6
Weight variation(gm)	0.295±0.011	0.292±0.008	0.295±0.009	0.294±0.007	0.297±0.010	0.298±0.008
Friability (%)	0.05±0.009	0.04±0.009	0.04±0.008	0.03±0.009	0.03±0.008	0.02±0.009
Hardness (N)	19.87± 0.058	20.03±0.058	20.13±0.058	20.47 ±0.058	20.67± 0.058	20.87 ±0.058
Thickness(mm)	3.243±0.006	3.487±0.025	3.520±0.040	3.590±0.020	3.823±0.006	4.037±0.121

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). Figure1, Figure2 and Figure3 shows the swelling characteristics of pectin fabricated tablets at different interval.

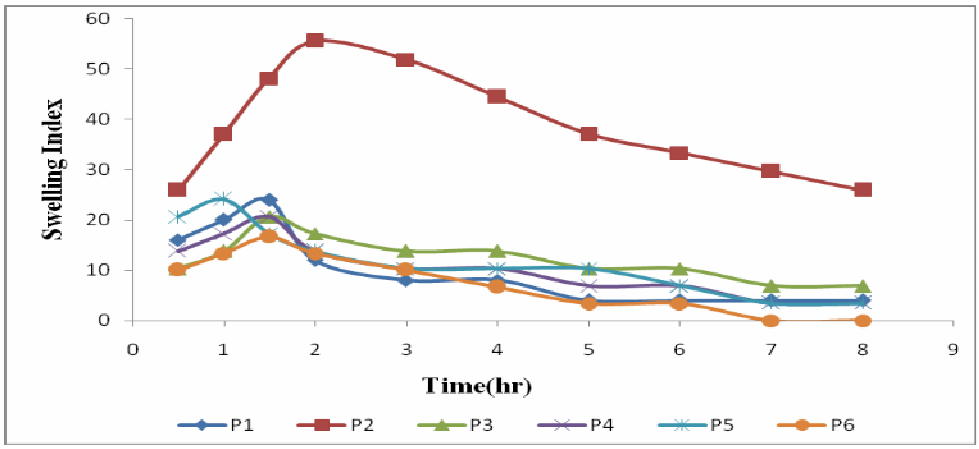

Figure 1: Swelling index profile for pectin based tablets

t= 0 hr t= 2 hr t= 4 hr

Figure 2: Different stages of swelling in tablet

Figure 3: Figure show the dispersion of pectin tablet.

The swelling index was calculated with respect to time. As time increases, the swelling index increased. This was probably 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 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. The slow release supports the fact that the formation of a thick gel structure delays drug release from tablet matrix [24, 25, 26]. The *in vitro* release of Diclofenac sodium from pectin based matrix was showed in Figure 4.

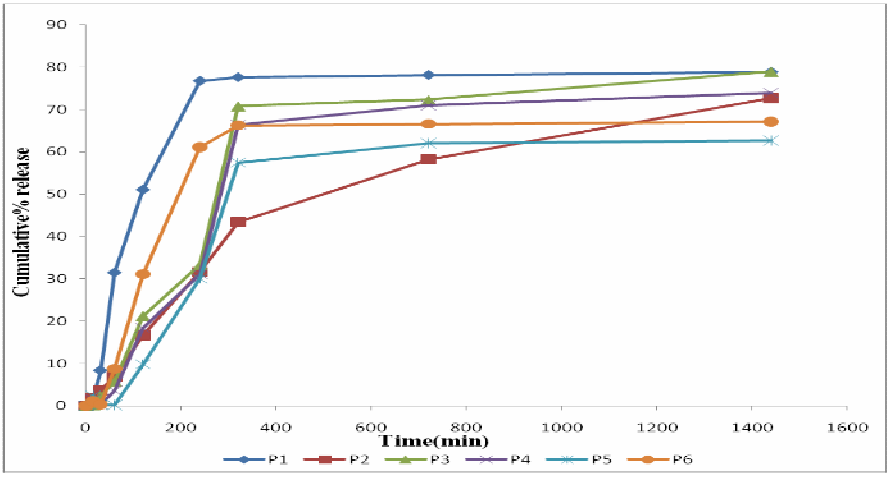

Figure 4: Release profile of pectin matrix tablet.

From the findings, obtained so far it can be concluded that Batch P2 of pectin fabricated tablets in the concentration ratio of 1:1.5 was promising concentration for oral sustained release tablet of Diclofenac sodium.

CONCLUSIONS:

Based on the results obtained, it is possible to design promising oral sustained release matrix tablet containing pectin in a specific range of concentration.

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