INTERNATIONAL JOURNAL OF PHARMACEUTICAL, CHEMICAL AND BIOLOGICAL SCIENCES

Available online at www.ijpcbs.com

Research Article

FORMULATION AND EVALUATION OF DICLOFENAC SODIUM MATRIX TABLETS USING *ABELMOSCHUS ESCULENTUS* MUCILAGE AS A POLYMER

A. Seetha Devi, MD. Tabasum*, T. Harika, VL. Anusha, B. Viswanath and Sanikommu Baji Reddy

Department of Pharmaceutical Technology, Hindu College of Pharmacy, Amaravathi road, Guntur, Andhra Pradesh, India.

ABSTRACT

The aim of this work was preparation and evaluation of diclofenac sodium controlled release matrix tablets using various proportions of natural polymer *Abelmoschus esculentus* mucilage powder (i.e;Drug:Polymer ratio-1:0.25,1:0.5,1:1,1:1.5,1:2) as release controlling factor by Wet Granulation method. The tablets were evaluated for various parameters like friability, weight variation, hardness, drug time, content uniformity. *In vitro* drug release characteristics of dosage form was evaluated in 6.8 pH phosphate buffer. All the formulations followed zero order kinetics along with diffusion mechanisms. From *In vitro* release data, formulation F4 containing Drug:Polymer (1:1.5) showed maximum drug release of 99.8% . All the formulations F1 to F5 undergo Non-Fickian diffusion or Enomalous diffusion mechanism. Analysis of drug release rate from matrix system indicated drug was release by super case-II transport mechanism.

Keywords: Diclofenac sodium, *Abelmoschus esculentus* (A.E) mucilage powder, Super case –II.

INTRODUCTION

Controlled release drug delivery systems significantly improved therapeutic efficacy especially as matrix systems which is the innumerable method used to develop a rate controlled formulation.[1] A matrix system can be better defined as a well mixed system comprising of one or more drugs with gelling agent i.e; hydrophilic polymers. Various materials like waxes, hydrophilic polymers, hydrophobic polymers and Gums have been employed in the formulation of matrix tablets. The present work is an attempt to extract and investigate the controlling property of polymer of natural origin i.e; *Abelmoschus esculentus,* grown as a vegetable crop in tropic, subtropic and warmer area of the temperature zones. The reason for choosing a natural polymer is due to disintegrating property, non toxicity, low cost, free availability, eco-friendly, potentially degradable and compatible. Diclofenac sodium is an effective anti-inflammatory, analgesic and antipyretic catergorized under NSAIDs'[2]. Diclofenac sodium 2-[(2, 6-dichlorophenyl) amino] benzene acetic acid sodium salt is a benzene acetic acid derivative with potent analgesic and anti inflammatory properties. It is used for inflammatory mediator such as inhibition of leucocyte migration. Cycloxygenase (COX-1, COX-2) activity leading to inhibition of prostaglandins synthesis. Antipyretic effects may be due to the action on the hypothalamus, resulting in peripheral dilation, increased cutaneous blood flow and subsequent heat dissipation.[4] It has biological half-life of 1.2 -2hrs so it is rapidly eliminated from the system. But major problem is it causes GI irritation, peptic ulceration with bleeding was present in large doses in GI tract. So Diclofenac sodium is a suitable for oral controlled release tablets and it would be a great advantage to slow down its release in GI, where therapeutic action can be prolonged and side effects may be minimized. Diclofenac is practically insoluble in water. For poorly soluble orally administered drugs, the rate of absorption is often controlled by the rate of dissolution.[2, 3]

MATERIALS AND METHODS

Diclofenac sodium (Aurabindo pharmaceuticals, Hyderabad; *Abelmoschus esculentus* was procured from local market. All the other ingradients used were of analytical grade and

were purchased from S.D Fine chemicals,Ltd; Mumbai, India.

Isolation of Abelmoschus esculentus mucilage[2]

Fresh A.E fruits were collected and washed with water to remove dirt and debris. Incisions were made on the fruits & left over night. The fruits were crushed and soaked in water for 5- 6hrs for 30min and left to withstand for 1hr to allow complete release of the mucilage into the water. The mucilage was extracted using a multilayer muslin cloth bag to remove marc from the solution. Acetone (3times the volume of filtrate) was added to precipitate the mucilage. The mucilage was separated, dried in an oven at 40°c for 10min, collected, ground, passed through a # 80 sieve and stored in a desiccators at 30°c and 45% relative humidity before use.

Preparation of diclofenac sodium matrix tablets

Matrix tablets each containing 100mg of Diclofenac sodium were prepared by Wet-Granulation method using A.E mucilage. The tablets prepared were as per the formulae given in the Table 1. Diclofenac sodium, Diluents (lactose) and polymer (*Abelmochus esculentus* mucilage powder) in various ratios like 0.25%, 0.5%, 1.1%, 1.5% and 2% were taken accurately and blended thoroughly. The blend was moistened with distilled water to get damp mass. The damp mass was then passed through sieve no 12 and the granular mass obtained were dried in hot air oven at 60° c for 1hr.The dried granules were passed through sieve no 16 to get free flowing and uniform sized granules. The granules were lubricated with 2% talc and 2% magnesium stearate were added which is previously passed through sieve no 100. The resulting mixture was compressed by Cadmac 16 station tablet punching machine to a hardness of 7.5-8 kg/sq.cm using flat punches.

EVALUATION OF TABLETS [5, 6]

Precompression parameters

Angle of repose: Angle of Repose (θ) is the maximum angle between the surface of a pile of powder and horizontal plane. It is determined by using funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone heighty (h) was obtained. The radius of the heap (r) was measured as angle of repose (θ) was calculated using the formula:

$$\theta = \tan^{-1}(h/r)$$

Bulk density: Apparent bulk density (p_b) was determined by pouring the blend in to a graduated cylinder. The bulk volume (v_b) and weight of the powder (M) was calculated using the formula:

$$Pb = M/V_b$$

Tapped density: The measuring cylinder containing a known mass of blend was tapped for a fixed time. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (Pt) was calculated by using formula:

$$Pt = M/Vt$$

Compressibility index: The simplest way for measuring of free flow of powder was compressibility, an indication of the ease with which a material can be induced to flow was given by compressibility index (I).

$$I = (Vo-Vt/Vo) \times 100$$

Where, Vo is the bulk volume and Vt is tapped volume.

Hausner's ratio: Hausner's ratio was an indirect index of ease of powder flow. It was calculated by:

$$\text{Hausner ratio} = Pt/Pd$$

Where, Pt is tapped density and P_d is bulk density lower hausner's ratio(<1.25) indicates better flow properties than higher ones (> 1.25)

Post compression parameters

Weight variation: Twenty tablets were selected random and weighed individually. The individual weights were compared with average weight for determination of weight variation.

Friability: Twenty tablets from each batch were selected randomly and weighed. These preweighted tablets were subjected to friability testing using Roche friabilator for 100 revolutions. The tablets in the fibrilator undergo both abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at height of 6 inches in each revolution. Tablets were removed, de-dusted and weighed again. Following formula was used to calculate the friability.

$$F = (1-W_0 - W)\ 100$$

Where, W_0 is weight of the tablets before and W is weight of the tablets after test.

Hardness: Five tablets from each batch were selected and hardness was measured using Monesanto hardness tester to find the average tablet hardness or crushing strength.

Content uniformity: Five tablets were selected randomly and powdered. A quantity of this powder corresponding to 100 mg of Diclofenac sodium was dissolved in 100 mL of pH 6.8 phosphate buffer stirred for 60 min and filtered. 1mL of the filtrate was diluted to 100 mL with pH 6.8 phosphate buffer. Absorbance of this solution was measured at 276 nm using pH 6.8 phosphate buffer as blank and content of Diclofenac sodium was estimated.

In vitro drug release/Dissolution studies

The tablet samples were subjected to in-vitro dissolution studies using USP Type 2 dissolution apparatus at 37±2°C and 50 rpm speed. As per the official recommendation of USFDA, 900 ml of 0.1 N Hcl (2hrs) and pH 6.8 Phosphate buffer (next 8hrs) was used as dissolution medium. Aliquot equal to 5 ml was withdrawn at specific time intervals and. The dissolution media volume was complimented with fresh and equal volume of blank media (0.1 N Hcl). The aliquots were filtered and scanned with appropriate dilution and amount of Diclofenac sodium released from the tablet samples was determined spectrophotometrically at a wavelength of 276 nm (Table 4) by comparing with the standard calibration curve.

Release kinetics

In order to establish the mechanism of drug release the *in-vitro* drug release data was fitted to four popular exponential equations (zero order, first order, Higuchi, and koresmayer peppas).The drug release of all the formulations was found to be followed zero order kinetics as correlation coefficient(**r^2)**values are higher than that of first order kinetics as shown in Table 5. By incorporating the release data in Higuchi and erosion models, the r^2 values of Higuchi model were found to be slightly greater than Erosion model. So this indicates drug release from Matrix tablets followed diffusion mechanism. To further confirm the exact mechanism of drug release the data was incorporated into Koresmayer peppas model and the mechanism of drug release was indicated according to the value of release exponent (n).

RESULTS AND DISCUSSION

All the tablets were prepared by wet granulation method and the compositions of all the formulations was given in (Table 1) the Formulations F1 to F5, were made by taking different proportions (i.e;D:P ratio are 1:0.25,1;0.5,1:1,1:1.5,1:20) of A.E mucilage. In all the formulations, 100 mg of Diclofenac sodium was incorporated and final weight was made up to 500 mg. The granules of different formulations were evaluated for angle of repose, bulk density, tapped density, compressibility index and hausner's ratio. The results are shown in (Table 2). Angle of repose values ranged from 19.7°-25.4°indicates good flow property of granules. The free flowing properties of granules were further confirmed by determining carr's index and hausners ratio. The carr's index values and hausner's ratio values were ranged from 19.7-24.2 and 1.19-1.24. The values of bulk density ranged from 0.496-0.576 gm/cm^3 and the values of tapped density range from 0.63-0.665 gm/cm^3 were found to be within the limits as per USP. Tablets of all the formulations were subjected to many in-process evaluation parameters such as physical appearance, content uniformity, weight variation hardness and friability tests are shown in the (Table 3). All the tablets were round in shape with no visible cracks and having smooth appearance. The average percentage weight variation of 20 tablets from the average was remained within ±0.1%.This weight variation test revealed that the tablets were within the range of pharmacopoeial limit. Drug content of all batches of tablets were within the range of 98.2 to 99.8% indicating good uniformity among different formulations of the tablets. All the formulations showed reasonably good hardness values ranged from 6.9 to 8.01 kg/cm^2. Further, to strengthen these values friability values are also considered. The percentage weight loss of all the formulations was less than 0.8%.This indicates that all the tablets withstand the mechanical shocks during handling. Among all the formulations F4 showed maximum drug release of 99.8±2.9%. The *in-vitro* drug release data was fitted to four popular exponential equations (zero order, first order, higuchi and koresmayer peppas).The drug release of all the formulations was found to be followed zero order kinetics as correlation coefficient (**r^2)** values are higher than that of first order kinetics. By incorporating the release data in higuchi and erosion models, the r^2 values of Higuchi model were found to be slightly greater than Erosion model. So this indicates drug release from Matrix tablets followed diffusion mechanism. To further confirm the exact mechanism of drug release the data was incorporated into koresmayer peppas model and the mechanism of drug release was indicated according to the value of

release exponent (n). The release exponent values 'n' values of F1 – F5 were 0.91 to 0.94 (i.e., between 0.5 – 1). So it indicates all the formulations F1 to F5 undergo Non-Fickian diffusion or Enomalous diffusion mechanism.

Table 1: Formulation of Diclofenac Sodium Matrix Tablets

Ingredients	F1 (mg) D:P(1:0.25)	F2 (mg) D:P(1:0.5)	F3 (mg) D:P(1:1)	F4 (mg) D:P(1:1.5)	F5(mg) D:P(1:2)
Diclofenac sodium	100	100	100	100	100
A.E mucilage	25	50	100	150	200
Talc	10	10	10	10	10
Mg stearate	10	10	10	10	10
Lactose	355	330	280	230	180
TOTAL WEIGHT	**500**	**500**	**500**	**500**	**500**

Table 2: Pre-Compression Parameters

Formulation	Angle of repose (°)†	Bulk Density (g/mL) †	Tapped Density (g/mL) †	Carr's Index (%)†	Hausner's ratio †
F1	22.4±0.6	0.525±0.06	0.65±0.04	24.2±0.86	1.24±0.01
F2	19.7±0.7	0.552±0.05	0.665±0.03	20.1±0.36	1.20±0.01
F3	23.6±0.3	0.576±0.04	0.645±0.04	19.7±0.35	1.19±0.02
F4	25.4±0.5	0.496±0.03	0.63±0.05	21.4±1.09	1.21±0.02
F5	22.6±0.2	0.536±0.04	0.65±0.06	23.4±0.42	1.23±0.01

Table 3: Post- Compression Parameters

Formulation	Hardness (Kg/cm^3)	Weight variation	Friability (%)	Drug content (%)
F1	7.6±1.1	499±0.12	0.56	99.7±1.2
F2	6.9 ± 0.82	498±0.3	0.72	98.2±1.0
F3	8.01 ± 0.51	498±0.22	0.65	99.8±0.7
F4	7.4 ± 0.76	499±0.41	0.79	98.9±1.1
F5	7.1 ± 0.22	498±0.9	0.67	99.2±0.8

Table 4: *In Vitro* Dissolution Studies of Diclofenac sodium

Time (hrs)	Cumulative percentage of diclofenac sodium released				
	F1	F2	F3	F4	F5
0	0	0	0	0	0
0.5	10.2±1.2	9.5±1.1	9.1±1.0	7.9±0.5	7.1±0.4
1	14.1±1.5	13.2±1.3	12.1±1.2	10.8±1.5	9.9±1.4
2	25.5±1.9	22.1±1.7	19.2±1.6	17.1±1.8	15.9±1.6
3	39.4±2.3	35.6±2.1	30.4±2.0	26.5±1.9	22.3±1.5
4	56.2±3.9	50.4±3.5	45.3±3.0	40.3±3.2	35.6±2.1
5	75.7±3.7	70.3±3.5	64.9±1.6	57.6±3.9	46.7±3.6
6	89.6±2.7	82.7±2.2	76.5±3.8	69.1±1.9	56.4±3.9
7	100	94.1±2.1	84.6±2.4	80.4±2.0	65.2±1.5
8		100	94.4±2.2	88.6±2.6	74.3±3.6
9			100	96.7±2.5	80.1±2.0
10				**99.8±2.9**	86.5±2.6

Table 5: Release Kinetics of Diclofenac Sodium Matrix Tablets

Formulations	Zero order	First order	Higuchi	Peppas (n)
F1(1:0.25)	0.9944	0.8863	0.9076	0.9177
F2(1:0.5)	0.991	0.869	0.9142	0.9161
F3(1:1)	0.9878	0.89	0.9184	0.9146
F4(1:1.5)	0.9871	0.744	0.9199	0.940
F5(1:2)	0.9937	0.9517	0.921	0.9186

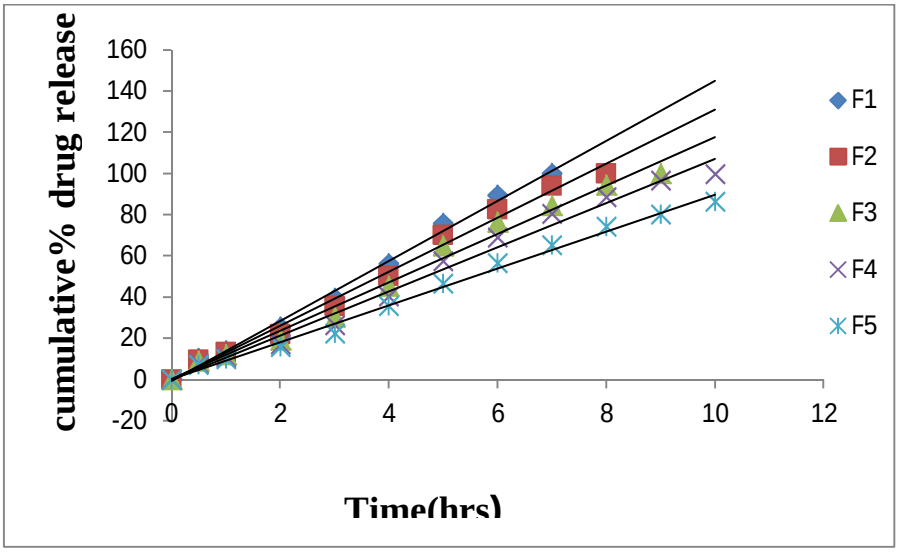

Fig. 1: Zero Order Plot for F1, F2, F3, F4, F5

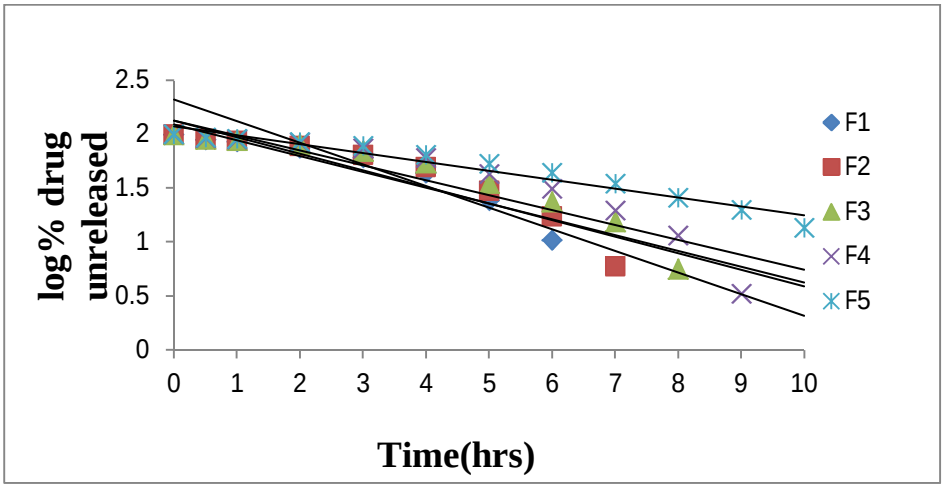

Fig. 2: First Order Plot for F1, F2, F3, F4, F5

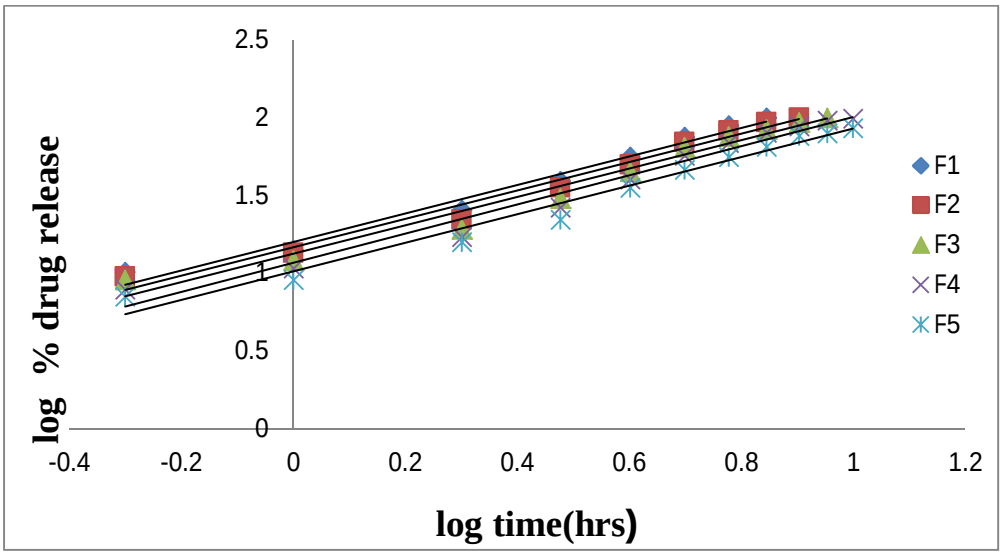

Fig. 3: Koresmayer Peppas Plots F1, F2, F3, F4, F5

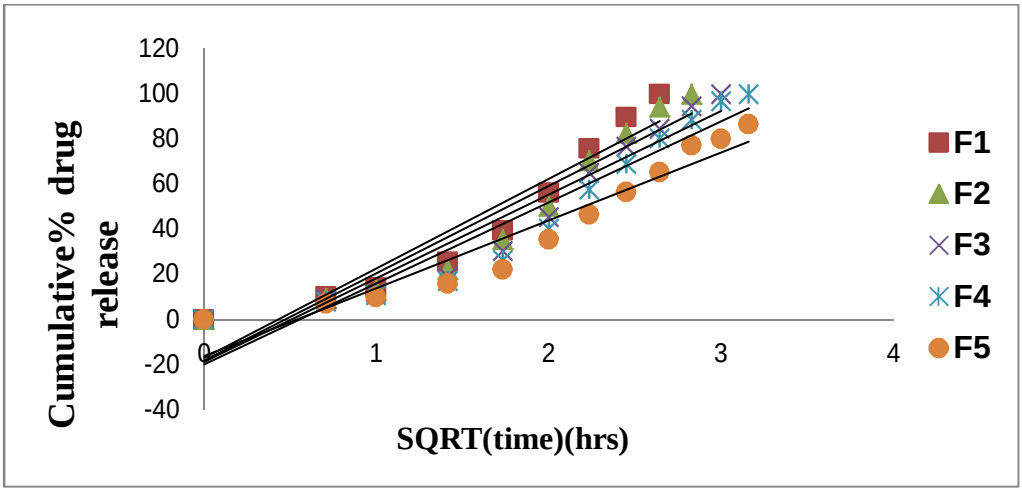

Fig. 4: Higuchi Plot for F1, F2, F3, F4, F5

CONCLUSION

From the present study, it can be concluded that among all the formulations F4 containing 1.5 % A.E. mucilage powder was found to release the drug in a slow, controlled manner with maximum drug release of 99.8% and found to follow Zero order release kinetics with Non – Fickian diffusion mechanism.

REFERENCES

1. Raju Manda. Formulation and *In vitro* evaluation of sustained release Matrix tablets of Aceclofenac by using different natural polymers. Research Journal of Phaarmaceutical biological and chemical sciences. 2010;1(4):279-292.
2. Dhana Lakshmi B. Formulation and Evaluation of Aceclofenac matrix tablets using *Abelmoschus esculentus* mucilage as a polymer. Journal of Advances in Drug Research. 2011;1(2).
3. Ofoefule SI, Chukwu A, Anyakoha N and Ebebe IM. Application of Abelmoschus esculentus in solid dosage formulation I: Use as a binder for a poorly water soluble drug. 2001;63(3):234-238.
4. British Pharmacopoeia 2005:75.
5. United States Pharmacopoeia. 2007, USP -30 NF -25.