International Journal of Pharmacy and Pharmaceutical Sciences
ISSN- 0975-1491 Vol 2, Issue 3, 2010

Research Article

FORMULATION AND CHARACTERIZATION OF MATRIX AND TRIPLE-LAYER MATRIX TABLETS FOR ORAL CONTROLLED DRUG DELIVERY

SYED IZHAR AHMED[A], LAKSHMI NARSU MANGAMOORI[B], YAMSANI MADHUSUDAN RAO[C]

Jayamukhi College of Pharmacy, Warangal-506332, Centre for Biotechnology, IST, JNT University, Hyderabad-85,University College of Pharmaceutical Sciences, Kakatiya University, Warangal-506009, A.P. INDIA. Email: syed.izharahmed@gmail.com

Received: 20 Feb 2010, Revised and Accepted: 18 March 2010

ABSTRACT

This study explored the application of anionic Sodium Carboxyl Methyl Cellulose (SCMC) as release retardant layer on the hydrophilic matrix core with an aim to develop a constant rate delivery formulation of diclofenac sodium to release the drug in intestine. Matrix tablets and triple-layer matrix tablets were formulated by using locust bean gum (LG), Xanthan gum (XG) and a mixture LG: XG in 1:1 ratio as matrix forming agent, and anionic SCMC were compressed on both the surfaces of the matrix core. The granules were prepared by wet granulation technique. *In-vitro* dissolution studies revealed that the drug release from F1, F2 and F3 matrix tablets was more than 90%, where as triple-layer matrix tablets decreased the drug release depends on the quantity of SCMC layer on the matrix core. After 12hrs the amount of drug released from matrix tablets (F3) and triple-layer matrix tablets (F3L3), showed a significant difference statistically. The influence of layers on matrix core and release rate were described by the peppas, increasing the quantity of layers lead to increased values of *n* and decreased *k* values, in a linear relationship. Model independent approach mean dissolution time (MDT) and dissolution efficiency (D.E $_8$%). MDT for F3 and F3L3 was found to be 3.38h and 13.98h, D.E $_8$% was 80.28% and 66.00 % respectively, indicated that the release of drug is slower with a constant release rate from the triple-layer matrix tablets. FT-IR and DSC studies revealed there is no interaction between the excipeints and drug used in the study. Stability studies show that the formulation was stable at 45°±2°C and 75±5%RH. It could be concluded that hydrophilic polymer as matrix core and anionic SCMC as retardant layers in the form of triple-layer matrix tablets will provide a linear drug release.

Keywords: Triple-layer matrix tablets, Diclofenac sodium, Locust bean gum, Xanthan gum

INTRODUCTION

The design of oral modified release dosage form is intended to optimize a therapeutic regimen by providing controlled delivery of drug over entire dosing interval. Among the various route of administration oral intake has long been the most convenient and commonly employed route. There are many ways to intend modified release dosage forms for oral administration and one of them is multi layered matrix tablet. Multi layered matrix tablet is a drug delivery device, which consists of a matrix core containing the active solute and one, or more barriers (modulating layers) incorporated during tabletting process[1]. The modulating layers serve to control the rate of hydration of the matrix core, there by restricting the surface area available for diffusion of drug and at the same time controlling solvent penetration rate[2].

The rate and duration of drug release from this system is regulated by the exposed surface area and volume of the core dimension. During the subsequent dissolution process, the swollen barriers erode and the surface area available for drug release slowly increases[3]. There by the delivery rate is decreased due to the increase in diffusion path length (saturation effect) is counter balanced by the simultaneous increase of the volume of the core available for drug release[4-5]. Thus by combining a time-dependent control of the hydration rate of the device with the reduction of tablet surface exposed to the dissolution medium, it is feasible to achieve a linear release profile.

Hydrophilic naturally occurring biocompatible polymeric materials are widely used in the matrix systems because of their flexibility to provide a desirable drug release profile, cost effectiveness, and broad regulatory acceptance[6]. Locust Bean Gum (LG) is homo polysaccharide (neutral) galactomannan. LBG is composed of a 1-4-linked β – D mannan backbone with 1-6ά-linked D galactose side groups. The galactose substance in galactomannan is strongly influenced by the physico-chemical properties. Galactose with longer side chain produces a stronger synergistic interaction with other polymers and greater functionality[7]. While Xanthan gum (XG) is hetro polysaccharide (anionic), Xanthan gum secreted from Xanthomonas campestris (a Gram-negative, yellow pigmented bacterium). It is used for the fabrication of matrices with uniform drug release characteristics[8]. Xanthan gum is the bacterial polysaccharide produced industrially on a large scale. It is a natural carbohydrate commercially produced by fermenting glucose with the appropriate microorganisms. Xanthan gum contains glucose 37%, mannose 43.4%, glucuronic acid 19.5%, acetate 4.5%, and pyruvate 4.4%.[9] LG and XG found to be sensitive to pH and ionic strengths, synergistic gelation and independent of pH over the range of 5-10.[10-11]

Diclofenac sodium is a potent non steroidal anti inflammatory drug (NSAIDs) of aryl acetic acid class used for the treatment of degenerative joint disease such as osteoarthritis, anklylosing spondylitis, rheumatoid arthritis and also has both analgesic and antipyretic properties[12]. The most commonly adverse effects of its are peptic ulceration gastritis and depression of renal function. Diclofenac sodium has a pKa value of 4 and its half life 1-2h. Due to its adverse effect and short biological half life, it is considered as an ideal model drug for controlled drug delivery. Diclofenac sodium is practically insoluble in acidic solution, but dissolves in intestinal fluids. To diminish its associated adverse effects, effective enteric coating or sustained release dosage forms have been developed[13-14]. The purpose of this study was to develop a constant rate delivery formulation of a model NASID Diclofenac sodium in intestine, layering with anionic SCMC as retardant on the hydrophilic matrix core.

EXPERIMENTAL

Materials

Diclofenac Sodium was obtained as a gift sample from Amoli Organic Ltd., Mumbai, India. locust bean gum (LG), Xanthan Gum (XG) and Sodium Carboxy Methyl Cellulose (SCMC) (high viscosity grade), were gift samples from Lucid gums, Mumbai, India. Raj Enterprises, Mumbai, India and Reliance Cellulose Product, Hyderabad. India, respectively. Lactose was procured from M/s Loba Chem Pvt. Ltd. Mumbai, India. All other chemicals and reagents used were of analytical grade.

Methods

Preparation of Diclofenac sodium matrix core granules

The matrix formulations were prepared with 30% of locust bean gum, Xanthan gum and a mixture of LG: XG in 1:1 ratio and were

coded as F1, F2 and F3 respectively. For the formation of the granules lactose was used as diluent, starch paste (10%w/v) was used as binding agent. The wet mass was screened through sieve No 14 and the granules were dried at 50°C for 1hr in a tray dryer. The dried granules were passed through sieve No 18 and lubricated with a mixture of talc and magnesium stearate. The composition of formulations is shown in table I.

Preparation of SCMC as release retardant layer granules

The wet granulation method was used, SCMC and 10% starch paste were mixed well and the resulting mass was passed through sieve No 14, and dried at 35° C for an hour. The dried granules were passed through sieve no 18 and lubricated with talc and magnesium stearate.

Preparation of triple-layer matrix tablets

The formulation of triple-layer matrix tablets were made using different combination of drug loaded matrix core granule and release layer granules as shown in table 1. Initially the volume of die cavity was adjusted equivalent to total weight of triple-layer matrix tablets (350mg, 400mg and 450 mg). Then pre-weighed amount of polymer granules of SCMC equivalent to bottom layer (25mg, 50mg, and 75mg) were taken and placed in the die cavity and uniformally spreaded. The upper punch was lifted up and 300mg of matrix core granules were placed over the bottom layer of polymer granules in the die cavity and slightly compressed. The remaining volume of die cavity was filled with pre weighed amount of polymer granules equivalent to top layers (25mg, 50mg and 75mg) are coded as L1, L2 and L3 respectively. Finally compressed on a rotary compression machine (Riddhi, Ahmedabad, India). The hardness of matrix tablet and triple-layer matrix tablets was adjusted to 5-6kg/cm^2.

Physicochemical characterization of matrix and triple-layer matrix tablets

The tablets hardness was determined using a hardness tester (Pfizer hardness tester). The tablet thickness was measured using a (Vernier caliper). The friability was determined as the percent weight loss from 20 tablets. Twenty tablets were weighed and rotated for 100 revolutions in 4 min in a friabilator (Roche friabilator. Pharma lab, Ahmedabad, India). The drug content of the prepared tablets of each batch was determined in triplicate.

***In-vitro* dissolution studies**

Drug release was studied using a dissolution apparatus type 2 (Lab India, DISSO 2000, Mumbai, India) with a shaft at a speed of 50 rpm. To study the effect of dissolution medium, drug release was studied in 900-mL HCl of pH 1.2 for 2 hours and then the pH of medium was raised to 6.8 by adding 4.6g Sodium hydroxide, 4.005g dibasic sodium phosphate and 3.06g mono basic potassium phosphate at 37±1°C for 12h. Samples were collected at specific time intervals and assayed by a UV spectrophotometer (Elico, Model SL-150, Mumbai, India.) at a wavelength of 276 nm. During the drug release studies, the tablets were observed for physical integrity. The experiments were repeated thrice and the results were taken as average of three test readings with standard deviations.

Characterization of release data

The description of dissolution profiles has been attempted using different release models. The data were evaluated according to the following equations.

Zero order: $M_t = M_o + K_o t$

First order: $\ln M_t = \ln M_o + K_1 t$

Higuchi model: $M_t = K_H \sqrt{t}$

Korsmeyer –Peppas model: $M_t/M_o = K_k t^n$

Where M_t is the amount of drug dissolved in time t, M_o the initial amount of drug, $K_1$is the first order release constant, K_0 the zero order release constant, K_H the Higuchi rate constant, K_k the release constant and *n* is the diffusional release exponent indicative of the operating release mechanism. The correlation coefficient (r^2) was used as an indicator of the best fitting, for each of the models considered.

The other dissolution parameter used for comparing the formulations was mean dissolution time (MDT) and D.E_8%. MDT is a measure of the rate of the dissolution process. It is calculated from the amount of drug released to the total cumulative drug; the higher the MDT, the slower the release rate. The following equation was used to calculate the MDT from the mean dissolution data: [15]

$$MDT = \frac{\sum_{i=1}^{i=n} t_{mid} \times \Delta M}{\sum_{i=1}^{i=n} \Delta M} \qquad \text{eq.[1]}$$

Where i is the dissolution sample number, n is the number of dissolution sample time, t mid is the time at the midpoint between i and i-1 and ΔM is the additional amount of drug dissolved between i and i-1.

Dissolution efficiency (D.E) (Banakar, 1992) after 8hr of release test was used.[16]

$$DE_8\% = \frac{\int_0^t y\ dt}{y_{100}\ t} \times 100 \qquad \text{eq [2]}$$

FT-IR study

Infrared spectrum was taken (FT-IR, Spectrum RX1, Perkin Elmer Ltd, Switzerland) by scanning the sample in Potassium bromide discs. The samples of pure drug and formulated tablets were scanned individually.

DSC studies

DSC scan was performed by accurately weighing the sample of pure drug Diclofenac sodium and the triple-layer matrix tablets F3L3 (DSC- 827e, Mettler, Toledo- Inc.,1900,U.S.A) aluminum pans were used in the experiment and the empty pan were also sealed which are used as references. The temperature was calibrated with indium as standard. The scanning rate of samples was from 40-300°C at 10°C/min, nitrogen gas was allowed at 20ml/min.

Stability studies

[17]Triple-layer matrix tablets (F3L3) was kept in the humidity chamber (Lab top, Mumbai, India) subjected to stability at 40 ± 2°C and 75 ± 5 % RH for a period of six months. After six months tablets F3L3 was analyzed for physicochemical characteristics and drug release studies.

Statistical analysis

In-vitro release data of diclofenac sodium from the matrix tablets (F3) and optimized formulations of triple-layer matrix tablets (F3L3) were subjected to the one-way analysis of variance (ANOVA) at different time intervals of drug release upto 12h. By applying Newman-Keuls multiple comparison test using Graph pad prism version 4. (Graph pad prism Software, Inc)

RESULTS AND DISCUSSION

Matrix and triple-layer matrix tablets of Diclofenac sodium were prepared using hydrophilic polymers such as locust bean gum (F1), Xanthan gum (F2) and LG:XG in 1:1 (F3) ratio as matrix forming agent. The ratio 1:1 of non ionic (LG) and anionic (XG) produces a synergistic increase in viscosity. The triple-layer matrix tablets of Diclofenac sodium were developed to retarded the drug release from the surfaces of matrix core by compressing anionic SCMC on both the surfaces.

Physicochemical characterization of matrix and triple-layer matrix tablets

The physical parameters such as hardness, thickness, friability weight variation and drug content of the matrix and triple-layer matrix tablets are shown in table 2. All the values were found to be with in the limits indicating that the tablets were of sufficient

standards. The hardness and thickness of the tablets were increased as the amount of layers of SCMC was increased. The hardness of triple-layer matrix tablets tended to increase, the friability decreased and the compression force was increased. Drug content uniformity was with in the range of 103.2 ± 2.65% to 98.3± 2.06 %.

***In-vitro* dissolution studies**

Drug release studies were carried out in pH 1.2 (0.1NHCl) for 2hrs and the pH of the media was raised to pH 6.8 for remaining 10hrs. The amount of Diclofenac sodium released from the matrix and triple-layer matrix tablets are shown in fig1. The percentage drug release from the formulations F1, F2 and F3 ranged from 99.3±0.12%, 95.13±0.11% and 92.21±0.12%. Similarly in case of formulations F1L3, F2L3 and F3L3, the drug release was upto 68.36±0.17%, 64.96±0.12% and 62.68±0.21%. The results described (fig 1a, b and c) indicated that the rate and extent of drug release were decreased for the triple-layer matrix tablets, which may be ascribed to increase in the thickness of retardant layers.

Table 1: Different formulations of Diclofenac Sodium matrix and triple- layer matrix tablets based on hydrophilic polymers and Cellulose derivatives

Formulation code	Ingredients(mg)								
	Diclofenac sodium	Locust bean gum	Xanthan gum	SCMC	Lactose	Starch	Talc	Mg stearate	Total weight
F1(L.G)	100	100	-		70	18	8	4	300
F1L1	100	100		50	70	18	8	4	350
F1L2	100	100	-	100	70	18	8	4	400
F1L3	100	100	-	150	70	18	8	4	450
F2 (X.G)	100	-	100	-	70	18	8	4	300
F2L1	100		100	50	70	18	8	4	350
F2L2	100	-	100	100	70	18	8	4	400
F2L3	100	-	100	150	70	18	8	4	450
F3(L.G:X.G)	100	50	50	-	70	18	8	4	300
F3L1	100	50	50	50	70	18	8	4	350
F3L2	100	50	50	100	70	18	8	4	400
F3L3	100	50	50	150	70	18	8	4	450

Table 2: Physico- chemical characterization of Diclofenac sodium matrix and triple-layer matrix tablets (Mean ± SD)

Formulation code	Average wt of tablets (mg)n=3	Hardness kg/cm² n=3	Thickness (mm) n=3	Friability (%)n=3	Drug content (%) n=3
F1(L.G)	300.1 ± 0.01	5.02± 0.10	3.02± 0.01	0.840± 0.015	102.3 ± 3.6
F1L1	351.2 ± 0.16	5.07± 0.02	4.01± 0.02	0.781± 0.036	103.2± 2.65
F1L2	401.2 ± 1.02	5.94± 0.05	5.80± 0.01	0.561± 0.025	98.15 ±2.25
F1L3	450.1± 0.13	6.05± 0.03	6.02± 0.02	0.369± 0.015	101.0± 0.32
F2 (X.G)	301.1 ± 0.01	5.14± 0.03	3.01± 0.01	0.751± 0.025	98.6± 2.06
F2L1	351.2 ± 0.15	6.11± 0.06	4.01± 0.02	0.365± 0.042	100.3± 0.91
F2L2	403.2 ± 1.02	6.04± 0.03	5.81± 0.02	0.302±0.001	101.0± 0.52
F2L3	451.1± 0.13	6.05± 0.02	6.01± 0.01	0.268± 0.012	103.0± 2.5
F3(L.G:X.G)	302.1 ± 0.02	5.06± 0.01	3.04± 0.01	0.820± 0.028	99.82 ±0.76
F3L1	352.2 ± 0.14	5.01± 0.03	4.01± 0.02	0.407± 0.013	98.3± 2.06
F3L2	403.2 ± 1.04	6.02± 0.03	5.82± 0.01	0.534± 0.001	98.5± 2.05
F3L3	452.1± 0.14	6.10± 0.02	6.02± 0.02	0.262± 0.026	100± 1.97

Table 3: *In-vitro* dissolution kinetics, MDT and DE_8% of Diclofenac sodium released from matrix and triple-layer matrix tablets (n=3)

Formulation code	Zero order		First order		Higuchi		Korsemeyer- peppas			MDT hrs	$D.E_8$%
	R^2	K_o (mg/h^{-1})	R^2	K_1(h^{-1})	R^2	K (mg.h^{-1})	R^2	*n*	K_0		
F1(LG)	0.882	19.81	0.923	0.40	0.965	32.96	0.973	0.58	1.14	3.58	95.91
F1L1	0.974	11.09	0.968	0.26	0.981	29.77	0.996	0.62	1.28	5.36	69.61
F1L2	0.993	2.19	0.988	0.12	0.985	27.97	0.991	0.93	0.90	7.18	69.33
F1L3	0.998	0.51	0.994	0.09	0.963	24.79	0.998	1.04	0.73	8.85	63.17
F2 (XG)	0.905	7.71	0.996	0.01	0.968	28.76	0.954	0.655	1.14	4.60	86.85
F2L1	0.966	7.33	0.988	0.15	0.957	26.32	0.973	1.006	0.93	5.73	76.26
F2L2	0.998	5.82	0.971	0.09	0.916	20.12	0.987	1.031	0.74	8.24	66.01
F2L3	0.995	4.94	0.959	0.07	0.878	16.73	0.988	1.309	0.38	10.47	62.35
F3(LG:XG)	0.936	9.30	0.995	0.28	0.987	35.21	0.958	0.930	1.09	5.80	80.28
F3L1	0.958	6.90	0.997	0.15	0.992	30.67	0.983	0.845	1.07	7.89	81.09
F3L2	0.998	1.14	0.958	0.12	0.964	27.77	0.985	0.871	0.93	8.94	67.51
F3L3	0.997	1.33	0.973	0.88	0.959	23.61	0.995	1.071	0.66	13.98	66.00

Characterization of release data

The dissolution mechanism was characterized by using different release models. The correlation co-efficient (r^2) was used as an indicator of the best fitting for each of the models considered. The correlation co-efficient (r^2) for zero order kinetics, first order kinetics and Higuchi model was shown in table 3. The results indicated that matrix tablets F1, F2 and F3 pre-dominantly followed first order release, indicated by their higher correlation co-efficient (r^2), where as triple-layer matrix tablets (F1L3, F2L3 and F3L3) with SCMC on both the surface of matrix core, provided better fit to zero

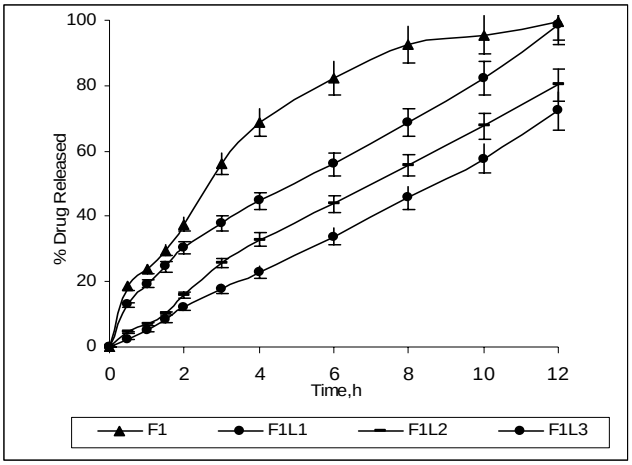
order kinetics than first order and Higuchi equation due to higher (r^2) values.

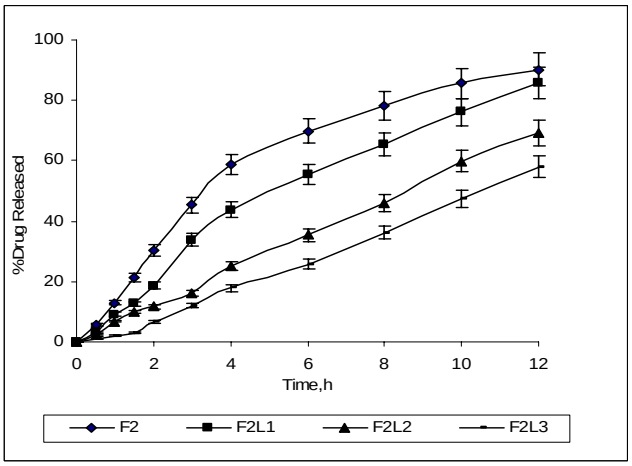
LG and XG were used alone with diclofenac sodium in the ratio of 1:1 as the matrix core in the formulation F1 and F2. Both the formulation released the drug completely with in 12h as shown in fig 1a and 1b. It might be due to degradation of LG and solubility of XG at high pH.

The release of diclofenac sodium was slower from the formulations (F3) with matrices LG: XG in 1:1 ratio as shown in fig 1c. When compared to LG and XG matrices alone (F1 and F2). The LG: XG matrix core formulations retarded the release of diclofenac sodium, than LG and XG matrices. This effect may be due to synergistic interaction between two hydrophilic polymers to produce a strong and elastic gel around the core of the matrices. Lactose was used as diluent, as it is water soluble and hydrophilic in nature. It facilitate gel formation and reduces the time to be taken by the dissolution medium to permeate the drug release from the matrix core, owing to formation of channeling agent by increasing in matrix porosity and decrease in tortuosity.[18] Ionic interaction between LG and XG resulted in decrease in the rate of polymer dissolution and the rate of solvent penetration, consequently the drug diffusion into the dissolution medium was diminished.

At the end of 12h of dissolution testing, triple-layer matrix tablets (F3L3) were found to be swollen and retained their physical integrity, except that the edges of the swollen tablets were rounded off due to slight erosion of swollen SCMC layers.

On the basis of drug release data, it is evident that as thickness of the polymer (SCMC) layers increased the rate of drug release was found to be decreased. The release rate patterns of all the formulations are given in table 3. The results suggested that the developed triple-layer matrix tablets showed zero- order or case II release. The values of kinetic constant (k) were in accordance with the values of n, the diffusional exponents, with k having lower values when the mechanism was Case II and higher values for the formulations that released the drug by non-Fickian diffusion. The diffusional exponents (n) values for all formulations ranged from 0.58 to 1.30. It can be inferred that the release was dependent on both drug diffusion and polymer relaxation. The poor correlation coefficient (r^2) values (F1, F2 and F3) in kinetic parameter based on zero-order model equation were mainly due to the drug release mechanism. It was observed that the triple-layer matrix tablets swelled indicating that absorption of dissolution media and swelling process were taking place simultaneously. This indicates that polymer relaxation had a role in drug release mechanism; as a result the release of drug was extended for over a period of more than 12h. At the end of 12h of dissolution testing, the triple-layer matrix tablets (F3L3) released 66.68% in simulated gastro intestinal fluid. It is clear that about 33.32% of the drug is still left over in the formulation after reaching the physiological environment of colon that may be available for systemic delivery through colon at a controlled rate because of low absorption area [19].





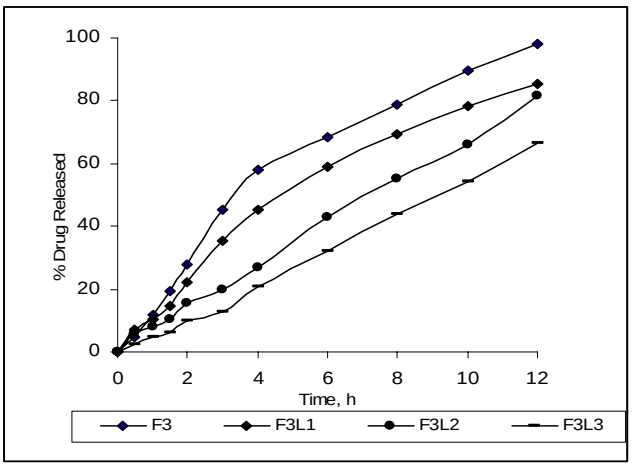


Fig. 1: Dissolution profiles of Diclofenac sodium from matrix and triple-layer matrix tablets conducted in pH 1.2 for 2 hrs and in pH 6.8 phosphate buffers remaining 10 hrs. a) F1, F1L1, F1L2 and F1L3 b) F2, F2L1, F2L2 and F2L3 c) F3, F3L1, F3L2 and F3L3

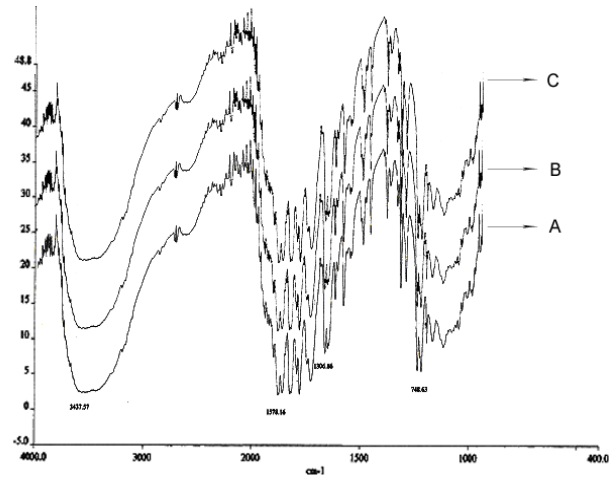


Fig. 2: FT –IR spectra of pure Diclofenac sodium (A), powdered sample of matrix tablets F3 (B) and powdered sample of triple-layer matrix tablets F3L3 (C)

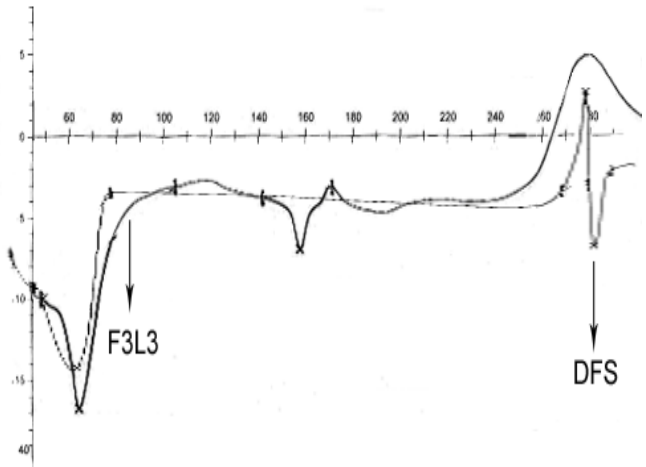


Fig .3: DSC thermogram of diclofenac sodium and formulation F3L3

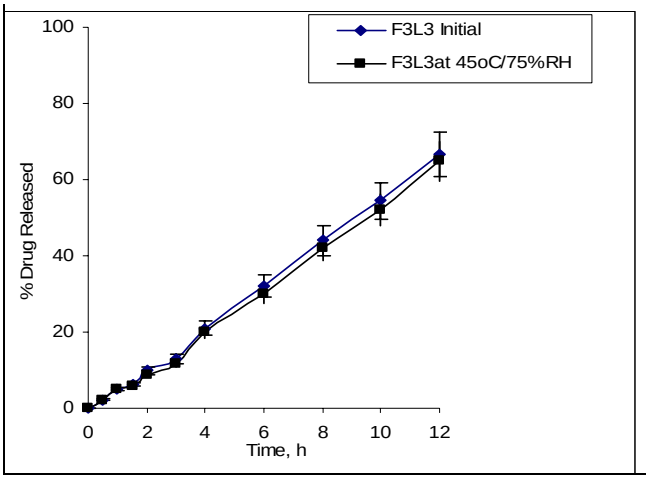


Fig. 4: Dissolution profiles of diclofenac sodium from matrix and triple-layer matrix tablets conducted in pH 1.2 for 2 hrs and in pH 6.8 phosphate buffers remaining 10 hrs. After storage at 40±2°C /75±5% RH for 6 months.

Model independent approaches were attempted to compare the dissolution profiles such as MDT and DE_8%. MDT of triple-layer matrix tablets is higher than matrix tablets shown in table 3. It also indicated that MDT is increased, while DE_8% is decreased, with increasing the polymer layers on the matrix core. MDT and DE_8% values of F1, F2, F3 F1L3, F2L3 and F3L3 formulations were found to be 3.58h, 4.60h, 5.80h and 8.85h, 10.47h, 13.98h and 95.91%, 86.85% 80.28% and 63.17%,62.35%,66.00% respectively. It indicated that the release of diclofenac sodium is slower from triple-layer matrix tablets.

FT-IR study

FT-IR spectrum reveals that the principal absorption peaks at 745.35 cm $^{-1}$ due to C-Cl stretching, 1578.16cm^{-1}(-C=O stretching of carboxyl ion) and at 3437.57 cm^{-1} (-NH stretching of the secondary amine) of pure diclofenac sodium. The matrix tablets (F3) and triple-layer matrix tablets (F3L3), showed similar spectra as shown in fig 2. Indicating that no chemical interaction occurred between the diclofenac sodium and the excipeints used in the study.

DSC studies

The thermogram obtained by these studies for the pure drug diclofenac sodium showed sharp endotherm at 284.26°C which correspond to its melting, and thermogram of the formulation (F3L3) showed the endotherm at 273.6°C as shown in fig 3. As melting point of diclofenac sodium and that of the formulation F3L3 are nearer it reveals that there is no much interaction between the drug and the excipeints used in the study.

Stability studies

The triple-layer matrix tablets (F3L3), after storing at 40±2°C /75±5% RH for 6 months showed no changes either in physical appearance, drug content and the dissolution profile as shown in fig 4.

Statistical analysis

Analysis of variance (single factor ANOVA) showed a significant difference ($P<0.05$) for the amount of drug released from matrix tablets (F3), and triple-layer matrix tablets (F3L3).

CONCLUSION

Many of the GI tract adverse effects associated with local irritation are due to the rapid localized dissolution and high concentration of diclofenac sodium, which may be prevented by controlled release of the dosage form. Diclofenac sodium drug particles are unlikely to go into solution in stomach, where pH is less than 4 and will empty from the stomach along with the liquids into duodenum and their release usually follow first order kinetics. However once drug reaches intestinal fluid pH>5, it dissolves with in a relatively large segment of intestine and is absorbed. However triple-layer matrix tablets formulation confirmed lower drug released compared to matrix tablets. It could be concluded that hydrophilic polymer as matrix core and anionic SCMC as retardant layers in the form of triple-layer matrix tablets will provide a linear release.

ACKNOWLEDGEMENT

The authors are thankful to Amoli Organic Ltd, Mumbai, India, Raj Enterprises, Mumbai, India, Lucid gums Mumbai, India and Reliance cellulose products, Hyderabad, India for generously giving the samples of Diclofenac Sodium, Xanthan gum, Locust bean gum and Sodium Carboxy Methyl Cellulose respectively.

REFERENCES

1. Colombo P, Conte U, Gazzaniga A, Maggi L, Sangalli M. E and Peppas N. A, et al. Drug release modulation by physical restrictions of matrix swelling. Int. J. Pharm. 1990; 63: 43-48.
2. Conte U and Maggi L. Modulation of dissolution profiles from Geomatrix® multi-layer matrix tablets containing drugs of different solubility. Biomaterials 1996; 17(9): 889-896.
3. Conte U, Maggi L, Colombo P, and La A Manna. Multi-layered hydrophilic matrices as constant release devices. J. Control. Rel. 1993; 26: 39-47.
4. Yihong Qui and Koplette F. Design of sustained release matrix system for a highly water soluble compound, ABT-089. Int J Pharm 1997; 157: 46-52.
5. Conte U, Colombo P, Maggi L, and Manna La A. Compressed barrier layers for constant drug release in swell able matrix tablets. STP Pharma Sci. 1994; 4:107-113.
6. Yeole PG, Galgatte UC, Babla IB and Nakhat PD.Design and evaluation of Xanthan gum-based sustained release Matrix tablets of Diclofenac sodium. Indian J Pharm Sci 2006; 68:185–189.
7. Sujja-areevath J, Munday D L, Cox P J. Khan K A. Relationship between swelling, erosion and drug release in hydrophilic natural gum mini matrix formulation. Eur. J. Pharm; 1998; 6: 207–217.
8. Talukdar MM and Vercammen JP. Evaluation of xanthan gum as a hydrophilic matrix for controlled release dosage forms. Drug Dev Ind Pharm 1993; 19:1037–1046.
9. Billa N and Yuen KH. Formulation variables affecting drug release from xanthan gum matrices at laboratory scale and pilot scale. AAPS Pharm Sci Tech 2000; 1:35–42.
10. Munday DL and Cox PJ. Compressed Xanthan and Karaya gum matrices: hydration, erosion and drug release mechanisms. Int J Pharm 2000; 203:179–92.

11. Dea I.C.M and Morrison A. Chemistry and interaction of seed galactomannans. Adv Carbohydrates chemistry and biochemistry. 1975; 31: 242-312.
12. Robinson M.H.E, Wheatley T and Leach I. Non steroidal anti inflammatory drug-induced colonic stricture. Digest. Dis. Sci. 1995; 40: 315-319.
13. Gonazalez –Rodriguez ML. *In vitro* release of sodium Diclofenac from central core matrix tablet aimed for colonic drug delivery. Eur. J. Pharm. Sci. 2003; 20(1):125-31.
14. Swabricks J and Boylan JC. Controlled and modulated–release drug delivery system. Ed Chein Y. W, Encyclopedia of Pharmaceutical technology, Vol- 3, Marcel Decker Inc, New York 1991. p. 286-289.
15. Gohel MC and Panchal M.K. Novel use of similarity factors f_2 and S_d for the development of diltiazem HCl modified-release tablets using a 3(2) factorial design. Drug Dev. Ind. Pharm 2002; 28(1): 77-87.
16. Banakar UV, Pharmaceutical Dissolution Testing, 1st ed. Marcel Decker Inc, New York 1992. p. 191-194.
17. Mathews BR., Regulatory aspects of stability testing in Europe, Drug Dev Ind. Pharm 1999; 25: 831–856.
18. Williams RO, Reynolds TD, Cabelka TD, Sykora MA, and Mahaguna. V. Investigation of excipeints type and level on drug release from controlled release tablets Containing HPMC. Pharm. Dev .Tech 2002; 7, 2 181-19.
19. Krishnaiah YSR, Karthikeyan RS and Satyanarayana V. A three-layer guar gum matrix tablet for oral controlled delivery of highly soluble metoprolol tartrate. Int J. Pharm 2002; 241: 353-366.