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Research Article

CHRONOTHERAPEUTIC DELIVERY OF DICLOFENACSODIUM USING ALMOND GUM AS CARRIER FOR THE TREATMENT OF RHEUMATOID ARTHRITIS

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ABSTRACT

Objective: The objective of the present work was to develop and evaluate a matrix system for chronotherapeutic delivery of diclofenac sodium using almond gum as a carrier for the treatment rheumatoid arthritis.

Methods: Matrix tablets of diclofenac sodium were prepared using 30, 40, 50, 60, and 70% w/w of tablet using almond gum as a carrier by wet granulation technique. These tablets were compression coated with Eudragit S100 to prevent drug release in the stomach. All formulations were evaluated for hardness, friability, weight variation, drug content, *in vitro* and *in vivo* studies. The release kinetics were studied. The almond gum was characterized by viscosity measurements and Fourier transform infrared spectroscopy (FTIR) analysis. The coated (FC1 to FC5) and uncoated tablets (F1 to F5) were evaluated for *in vitro* release of diclofenac sodium after sequential exposure to pH 1.2, pH 7.4, and pH 6.8, respectively, for 2 hr, 3 hr, and 19 hr in the absence as well as presence of rat cecal content. The selected formulation was subjected to *in vivo* targeting efficacy studies by roentgenography technique.

Results: *In vitro* release studies indicated that the matrix tablets (F1 to F5) failed to control the drug release in the physiological environment of the stomach and small intestine. On the other hand, compression-coated formulations were able to protect the tablet cores from premature drug release. In the presence of rat cecal contents, FC5 formulation has shown highest release for longer period when compared to that of FC5 in the absence of cecal contents. The values of the correlation coefficient indicated that the drug release followed zero order drug release kinetics with Peppas drug release mechanism. FTIR studies confirmed that there was no interaction between the drug and the carrier. X-ray studies confirmed that the tablet successfully reached colon without getting disintegrated in upper gastrointestinal tract.

Conclusion: Based on the results, selective delivery of diclofenac sodium to the colon could be achieved using 70% w/w (FC5) of almond gum matrix tablets compression coated with Eudragit S100 as a carrier.

Keywords: Diclofenac sodium, Gum almond, Eudragit S100, Roentgenography, Rat cecal content.

INTRODUCTION

The site specificity of drugs to the colonic part is advantageous for the localized and systemic treatments of various diseases conditions. Colon targeting was attained a significant role in the treatment of local pathologies and chronotherapy of various disorders includes asthma, rheumatoid arthritis (RA), and hypertension [1].

RA is an autoimmune disease. The patient suffers from severe pain in early morning hours due to release of inflammatory cell mediators such as interleukin-6, cortisol, and melatonin. Diclofenac is drug of choice for treatment of RA [2]. Present work has been aimed for the development of site-specific drug delivery systems of diclofenac for colon region in the form of oral tablet dosage form. When the formulation was administered at night time, the symptoms that are experienced during early morning hours can be treated. The system is based on lag time in drug release. Conventional formulation fails to produce the desired drug release due to rapid absorption [3].

Various natural gums have employed as rate controlling polymers. In recent years, gums are found in the literature because they are cheap and easily available [2]. In this work, it explores the feasibility of natural almond gum for colon-specific drug delivery. Almond gum is a natural polysaccharide obtained from stems and branches of *Amygdalus communis* belonging to the family rosaceae [4]. The monosaccharide of almond gum contains glucose, xylose, galactose, arabinose, and little rhamnose and fructose and their molar ratios of monosaccharide were 24.35:9.25:33.75 :31.60:0.74:0.31. The main chain of polysaccharide of almond gum could contain 1, 6-linked galactose and 1, 4-linked arafinose [5].

The aim of this study was to explore the feasibility of the natural gum-dependent chronotherapeutic drug delivery system (CDDS), diclofenac sodium being selected as a model drug.

METHODS

Materials

Diclofenac sodium and potassium dihydrogen orthophosphate were purchased from Qualigens Fine Chemicals, Mumbai, India. Almond gum was obtained from the bark of the Prunus Communis tree. Magnesium Stearate is a gift sample from S.D Fine Chemicals Pvt., Ltd., Mumbai, India. All reagents and chemicals were of analytical grade and used as received.

Drug and excipient compatibility studies

Fourier transform infrared spectroscopy (FTIR)

IR spectra were recorded between 400 and 4000/cm by a Perkin Elmer 1600 Series FTIR (Norwalk, USA). Each sample was mixed with KBr (FTIR Grade, Aldrich, Steinhelm, Germany) and compressed at 70 kN with a Perkin-Elmer hydraulic press.

Determination of viscosity and swelling index of the polymer

Viscosity and swelling index of almond gum were measured in water, 0.1 N HCL, pH 7.4 phosphate buffer, and pH 6.8 phosphate buffer. Viscosity in these buffers was measured using Brookfield viscometer using spindle number SC 4-18. 1 g of gum was added to 10 ml of distilled water.

The measuring cylinder was shaken vigorously for 10 minutes and allowed to stand for 24 hrs. Swelling capacity was expressed as:

Swelling capacity (%v/v)= $(X_v/X_l)*100$

Where X_v is the final volume occupied by swollen material after 24 hrs and X_l denotes the initial volume of the powder in graduated measuring cylinder. The results were tabulated.

Physical properties of pure drug and carrier [6]

Various physical properties such as bulk density, compressibility index, Hausner's ratio, and angle of repose [7] were determined for pure drug and carrier. Angle of repose was determined by fixed funnel method by placing ten grams of powder blend in a plugged glass funnel and was then allowed to flow through the funnel orifice by removing the cotton plug from the funnel orifice. The height of the heap (h) formed as well as the radius of the heap (r) was noted. The angle of repose (α) was calculated as: Tan α = (h/r). Bd and Td of 10 g of powder blend were determined using 50 ml graduated cylinder. The volume occupied by the granules was read, and the (Bd) calculated in g/ml. The cylinder containing the granules was tapped until constant volume was obtained using Bd apparatus from a height of 2 cm, and the Td calculated in g/ml. The percentage compressibility (CI) was calculated from the difference between the Td and the Bd divided by the Td and the ratio expressed as a percentage. The HR is the ratio between the Td and Bd [7].

Preparation of core tablets

Accurately weighed quantities of the drug, polymer (almond gum) lactose and binder (PVP-K 30) were physically mixed with a mortar and pestle. Required quantity of solvent (Isopropyl alcohol) was added and was mixed thoroughly to form a damp mass suitable for the preparation of granules. The dough mass was passed through sieve # no 10 to form granules which were dried in an oven at 50°C. Finally, talc and magnesium stearate were added to granules before punching the tablet. These granules were subjected to evaluate various flow properties. Now, the granules were compressed to form tablets in a Rotary punch tablet machine using 9 mm round concave punches at an optimum pressure. Ten formulations were prepared by varying the amount of gum almond, 30, 40, 50, 60, and 70% w/w of the tablet and coded as F1, F2, F3, F4 and F5 and FC1, FC2, FC3, FC4 and FC5, respectively. The composition of different formulations was shown in the Table 1.

Compression coating of core tablets using Eudragit S 100

The prepared tablets were compression coated with Eudragit S 100 in order to retard the drug release in the stomach. Each core tablet is coated with 200 mg of Eudragit S 100 granules (made with IPA). Initially, half of the coating material (100 mg) was placed in the 11 mm die cavity upon which the core tablet is kept and the remaining half of the coating material (100 mg) was placed on it. Then the contents are compressed under optimum pressure to form coating on the core tablets.

In-process quality control (IPQC) parameters for tablets [8]

The formulated tablets were evaluated for different IPQC parameters such as drug content, weight variation, hardness, and friability. The results were tabulated.

***In vitro* drug release studies**

Dissolution studies were carried out using USPXXII, Paddle method (apparatus II). The stirring speed was maintained at 100 rpm. The tablets were placed in simulated gastric fluid (SGF - pH 1.2) for 2 hrs, simulated intestinal fluid (SIF pH 7.4) for 3 hrs the average small intestine transit time is about 3 hrs. Then the dissolution medium was replaced with simulated colonic fluid (SCF pH 6.8) and the study was continued for a period of 19 hr. Sampling was done at predetermined time intervals, and the samples of 5 ml were collected and estimated for drug content after suitable dilution by UV method.

***In vitro* drug release testing in the presence of rat cecal content medium [9]**

The experimental protocol was subjected to the scrutiny of the Institutional Animal Ethical Committee (IAEC/VIII/8/BCOP/2014) and was approved before commencement of the experimentation on animals.

In vitro drug release, studies were investigated in the presence of rat cecal content after 5 hrs of dissolution (first 2 hrs in 0.1 N HCl and another 3 hrs in pH 7.4 phosphate buffer). The albino rats weighing between 150 and 200 g were kept on normal diet and administered the 2.5 ml of 1% w/v solution of almond gum in water with the help of Teflon tubing directly into the esophagus region via oral cavity. The treatment was continued for 7 days to induce enzyme responsible for gum degradation, animals were sacrificed before 30 min of commencing drug release studies and the cecum was exteriorized for content collection. The cecal content (anaerobic) were immediately transferred into buffer saline solution pH 6.8 to obtain the appropriate 4% w/v concentration solution which was bubbled with carbon dioxide gas to maintain an anaerobic environment. Using USP dissolution rate testing apparatus Paddle type (100 rpm, 37±0.5°C) in anaerobic conditions with modifications the procedure was done. A beaker containing 250 ml of 4% w/v rat cecal content medium was immersed in dissolution bowl and the bowl volume was adjusted to 900 ml with phosphate buffer pH 6.8, which was kept in the water bath of the apparatus. The best formulation was placed in the Paddle of the apparatus and immersed in the rat cecal content medium. As the cecum is naturally anaerobic, the experiment was carried out with continuous CO_2 supply into the beakers. At different time intervals, 5 ml of the samples was withdrawn without a pre-filter and replaced with 5 ml of fresh phosphate buffered saline bubbled with CO_2 and the experiment was continued for 19 hr as the usual colonic transit time is 20-30 hr.

Drug release mechanism and kinetics [10]

The dissolution data were fitted to popular release models such as zero-order, first-order, Higuchi and Peppa's-Korsemeyer equation models. The order of drug release from matrix systems was described by using zero order kinetics or first orders kinetics. The mechanism of drug release from the matrix systems was studied using Higuchi equation and Peppa's-Korsemeyer equation.

Drug dissolution from dosage forms that do not disaggregate and release the drug slowly can be represented by the zero order release kinetics equation: $Q_t = Q0 + K0_t$; Where Q_t is the amount of drug dissolved in time t, Q0 is the initial amount of drug in the solution (most times, Q0 = 0) and K0 is the zero order release constant expressed

Table 1: Composition of diclofenac sodium matrix tablets

Serial number	Ingredients	F1	F2	F3	F4	F5	FC1	FC2	FC3	FC4	FC5
1	Diclofenac sodium (mg)	100	100	100	100	100	100	100	100	100	100
2	Almond gum (mg)	150	200	250	300	350	150	200	250	300	350
3	PVP K30 (mg)	25	25	25	25	25	25	25	25	25	25
4	Lactose (mg)	215	165	115	65	15	215	165	115	65	15
5	Mg. stearate (mg)	5	5	5	5	5	5	5	5	5	5
6	Talc (mg)	5	5	5	5	5	5	5	5	5	5
7	Eudragit S100 (mg)	-	-	-	-	-	200	200	200	200	200
8	Total (mg)	500	500	500	500	500	700	700	700	700	700

in units of concentration/time. The release of the drug, which followed first order kinetics, can be expressed by the first order release kinetic equation: Log C = log C0−Kt/2.303; where C0 is the initial concentration of drug, K is the first-order rate constant and t is the time. Higuchi equation defines a linear dependence of the active fraction released per unit of surface (Q) on the square root of time and can be expressed as $Q = K_H t^{1/2}$; Where, K_H is the release rate constant. This equation describes drug release as a diffusion process based on the Fick's law, square root time dependent. In order to define a model, this would represent a better fit for the formulation, dissolution data was further analyzed by Peppas and Korsmeyer equation. $Mt/M\infty = K t^n$; Where $Mt/M\infty$ is a fraction of drug released at time t, K is the release rate constant and n is the release exponent. In this model, the value of n characterizes the release mechanism of drug. For the case of cylindrical tablets, n=0.45 corresponds to a Fickian diffusion mechanism, 0.45<n<0.89 to non-Fickian transport, n=0.89 to Case II (relaxation) transport, and n>0.89 to super Case II transport.

In vivo targeting efficacy [11,12]

In vivo targeting efficiency study was carried out to check the efficiency of the formulation to target to colon after obtaining ethical clearance (IAEC/VIII/8/BCOP/2014). The evaluation of dosage form in animal model renders support to the *in vitro* studies. To closely simulate the human physiological environment of the colon, rabbits were selected as an animal model for evaluating the colon-specific delivery. Roentgenography study [12] a comparatively safer technique was carried out in healthy male albino rabbits to access the *in vivo* performance of the selected batch. The behavior of diclofenac sodium tablets in rabbit was observed using a radiographic imaging technique. It involves the use of radio-opaque marker like barium sulfate, incorporated in the formulation to determine the position of the tablet. Healthy rabbit of 1.58 kg was fasted overnight and on the next day morning tablet was administered followed by giving 25 ml of water. At different time intervals of 2 hrs, 5 hrs, 8 hrs, 17 hrs, and 20 hrs, X-ray images were taken under the supervision of a radiologist, to follow the nature, movement, location, and the integrity of the tablets in different parts of gastrointestinal tract (GIT).

RESULTS AND DISCUSSION

The present study was aimed at developing oral colon targeted formulations for diclofenac sodium using natural polymer, almond gum in various concentrations. Among the various approaches of colon targeting, bacterial degradation of the polymer in the region of the colon is an easy approach. For this purpose, matrix tablets of the diclofenac were prepared with almond gum employing various concentrations.

Table 2: Flow properties of drug and polymers

Serial number	Parameter	Diclofenac	Almond gum
1	Bulk density (g/ml)	0.685	0.598
2	Tapped density (m/ml)	0.921	0.923
3	Carr's index	33.13	35.21
4	Hausner's ratio	1.27	1.54
5	Angle of repose	38°	41°

FTIR analysis

The characteristic IR absorption peaks of diclofenac sodium were:

The FTIR spectra of the pure drug and formulations of almond gum indicated that no chemical interaction occurred between the drug, diclofenac sodium, and the carriers.

Physical properties of carrier and drug

Flow properties of the pure drug alone were poor when compared with the formulated granules. This may be due to the attractive forces between the molecules of the pure drug which are not allowing the particles to flow easily. Hence, in order to improve the flow properties, wet granulation technique is employed.

Evaluation parameters

Physicochemical characteristics of tablets

The hardness of the tablets was found to be 7 kg/cm^2. Weight variation, Friability, and drug content were within the pharmacopoeia limits.

Viscosity and swelling indexes

Viscosity and swelling index were observed for almond gum in water, 0.1 N HCl, pH 7.4 phosphate buffer and pH 6.8 phosphate buffer. Viscosities of almond gum were found to be high. The highest viscosity was found in 7.4 phosphate buffer which was about 122.1 Cp. Swelling index of almond gum was measured using the same buffers. Swelling index of Gum almond was found to be low, and the lowest swelling index was observed in pH 7.4 phosphate buffer which was about 8.3% v/v.

In vitro drug release studies

In order to investigate the extent to which gum almond succeed in targeting the drug to the colon, ten formulations have been formulated and *in vitro* drug release studies have been conducted in the pH range, which normally accounted in the GIT. Further to mimic the colon environment, the colonic microflora was also taken into consideration for the *in vitro* release study, as polysaccharide polymers release the drug faster in the presence of colonic microflora as they release glycosidase. At the end of 2 hrs, the formulations without compression coat released 32.41%, 29.65 %, 22.93%, 19.03%, and 17.11%of the drug from F1, F2, F3, F4, and F5 gum almond formulations, respectively. Whereas, all the compression coated formulations (FC1, FC2, FC3, FC4, and FC5) released 0% drug during the same period. This indicates that compression coating with Eudragit S 100 succeeds in preventing the drug release in the stomach. This indicates that, almond Gum by increasing the concentration of polymer the drug release can be retarded. It was also observed that throughout release study; almond gum compression coated tablets containing a high concentration of polymer released the drug at slower pace.

Table 3: Physical characterization of diclofenac sodium granules formulated with almond gum by wet granulation method

Formulation	Angle of repose ($\bar{X}$±SD)	Bulk density (g/ml) ($\bar{X}$±SD)	Tapped bulk density (g/ml) ($\bar{X}$±SD)	Hausner's ratio ($\bar{X}$±SD)	Compressibility index (%) ($\bar{X}$±SD)
F1	21.5±0.33	0.275±0.012	0.321±0.016	1.143±0.052	11.89±0.25
F2	22.4±0.15	0.279±0.074	0.345±0.021	1.149±0.024	12.73±0.28
F3	21.3±0.18	0.283±0.015	0.322±0.021	1.175±0.031	12.75±0.27
F4	22.5±0.41	0.278±0.014	0.338±0.021	1.175±0.091	14.24±0.25
F5	22.3±0.11	0.255±0.016	0.311±0.012	1.144±0.004	15.19±0.28
FC1	23.3±0.43	0.216±0.019	0.346±0.013	1.243±0.006	16.87±0.54
FC2	21.2±0.12	0.277±0.014	0.313±0.011	1.223±0.026	16.0±0.09
FC3	21.6±0.18	0.285±0.014	0.326±0.022	1.245±0.023	17.15±0.67
FC4	23.2±0.23	0.267±0.014	0.321±0.014	1.167±0.031	18.92±0.09
FC5	23.6±0.28	0.279±0.019	0.353±0.012	1.158±0.038	19.58±0.09

SD: Standard deviation

The present investigation has revealed that in spite of using the natural polymer alone, the hydrophilic nature of the polymer makes vulnerable to release the drug to some extent in the upper digestive tract. As a result, the use of the polymer alone may not successfully target the drug to the colon. Hence, there is a need of further coating of the tablet with pH-dependent enteric polymer.

Among all the formulations belonging to almond gum, FC5 containing 70% of almond gum has shown the desired drug release profile. Hence, this formulation (70%) was selected to carry out the dissolution in the presence of rat cecal content.

When the drug release studies were carried out in the presence of rat cecal content, there was a significant increase in the drug release as compared to that of the release studies performed in the absence of rat cecal content. The rat cecal content in the release study was considered to mimic the human colonic environment as it contains microflora which releases many glycosidases and degrade the polysaccharide polymers.

Table 4: Physical properties of the diclofenac sodium matrix tablets formulated with almond gum by wet granulation method

Formulation	Weight variation (mg)	% Drug content	Hardness kg/cm²	% Friability
F1	501±0.7	99.23±0.18	7.2±0.02	0.39
F2	502±0.4	99.85±0.1	7.8±0.25	0.31
F3	499±0.6	101.39±0.21	7.9±0.34	0.35
F4	501±0.2	99.93±0.23	8.2±0.12	0.41
F5	498±0.5	101.88±0.39	8.8±0.06	0.39
FC1	702±0.8	100.16±0.51	8.2±0.58	0.32
FC2	701±0.3	99.64±0.63	8.5±0.40	0.38
FC3	699±0.1	101.24±0.17	8.6±0.24	0.35
FC4	698±0.6	101.16±0.39	8.8±0.45	0.28
FC5	702+0.9	100.18+0.69	8.9+0.67	0.19

Table 5: Comparative dissolution profile of diclofenac sodium matrix tablets formulated using almond gum

Dissolution medium	Time (hr)	FC1 (30%)	FC2 (40%)	FC3 (50%)	FC4 (60%)	FC5 (70%)
SGF (0.1 n HCl)	1	0	0	0	0	0
	2	0	0	0	0	0
Simulated intestinal fluid (pH 7.4)	3	1.56	1.42	1.38	1.36	1.28
	4	5.65	5.12	4.69	4.25	3.96
	5	10.56	9.55	8.19	6.55	5.76
SCF (pH 6.8)	6	18.36	17.90	15.6	7.89	7.79
	7	27.52	26.39	24.69	15.40	14.19
	8	35.25	33.98	31.37	23.48	18.66
	9	41.45	40.23	38.64	30.86	22.87
	10	49.36	48.52	43.55	37.92	31.84
	11	55.81	53.32	48.58	43.84	39.82
	12	58.64	54.26	51.54	47.78	46.76
	13	61.65	58.84	55.12	50.64	50.11
	14	65.29	63.09	59.02	55.31	53.18
	15	69.23	67.61	63.33	58.10	57.07
	16	74.54	72.54	68.07	61.71	60.07
	17	80.52	77.52	72.03	65.24	62.89
	18	86.65	82.17	77.01	69.18	66.02
	19	92.28	90.04	83.12	72.55	71.08
	20	95.68	94.32	88.26	77.53	73.54
	21	98.23	96.64	93.67	82.34	76.44
	22				87.15	80.23
	23					86.67

SGF: Simulated gastric fluid, SCF: Simulated colonic fluid

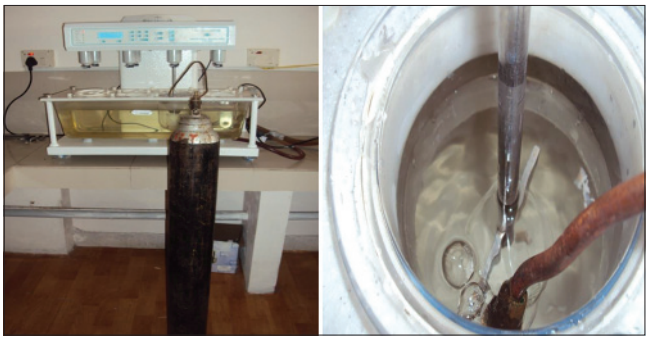

Fig. 1: *In vitro* drug release testing using rat cecal contents under anaerobic conditions (with continuous CO_2 supply, front view and top view)

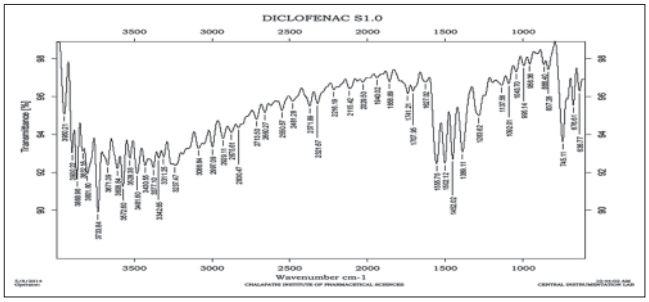

Fig 2: Fourier transform infrared spectra of the pure drug

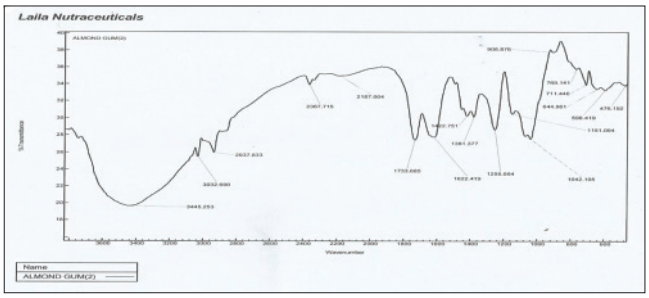

Fig. 3: Fourier transform infrared spectra of the pure almond gum

Table 6: Release kinetics for diclofenac sodium matrix tablets

Formulation	Zero order (R^2)	First order (R^2)	T50 (hr)	T90 (hr)	Higuchi (R^2)	Peppas (R^2)	K (µg/hr)	n
F1	0.980	0.968	8.98	15.17	0.893	0.905	5.56	0.598
F2	0.988	0.954	9.46	20.64	0.946	0.992	5.28	0.625
F3	0.990	0.977	11.36	22.86	0.943	0.978	3.48	1.175
F4	0.993	0.935	14.62	28.97	0.862	0.996	4.29	0.756
F5	0.996	0.980	16.77	30.20	0.965	0.997	4.98	0.254
FC1	0.996	0.912	11.46	17.69	0.938	0.987	4.36	1.026
FC2	0.991	0.973	15.43	21.77	0.842	0.993	3.24	1.236
FC3	0.996	0.921	18.91	29.61	0.872	0.994	3.87	1.021
FC4	0.997	0.978	19.16	31.08	0.924	0.978	2.48	1.642
FC5	0.995	0.959	21.06	34.11	0.933	0.917	3.68	1.365

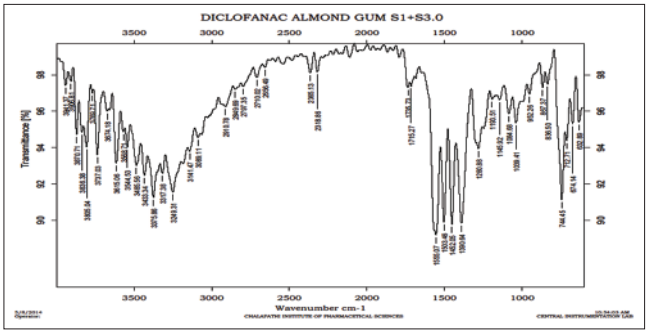

Fig 4: Fourier transform infrared spectra of combination of diclofenac and almond gum

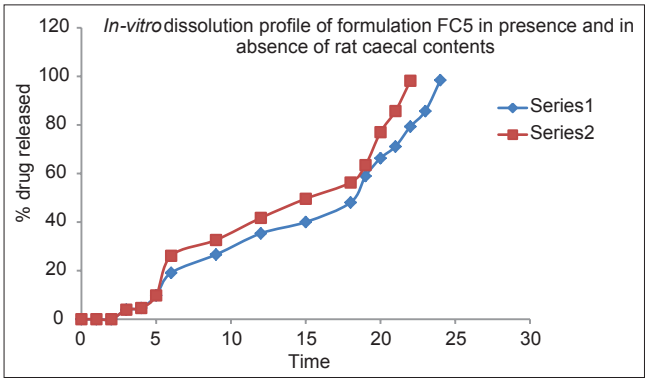

Fig. 5: Comparative dissolution profile of diclofenac sodium matrix tablets using almond gum (FC5) without cecal content and with cecal content

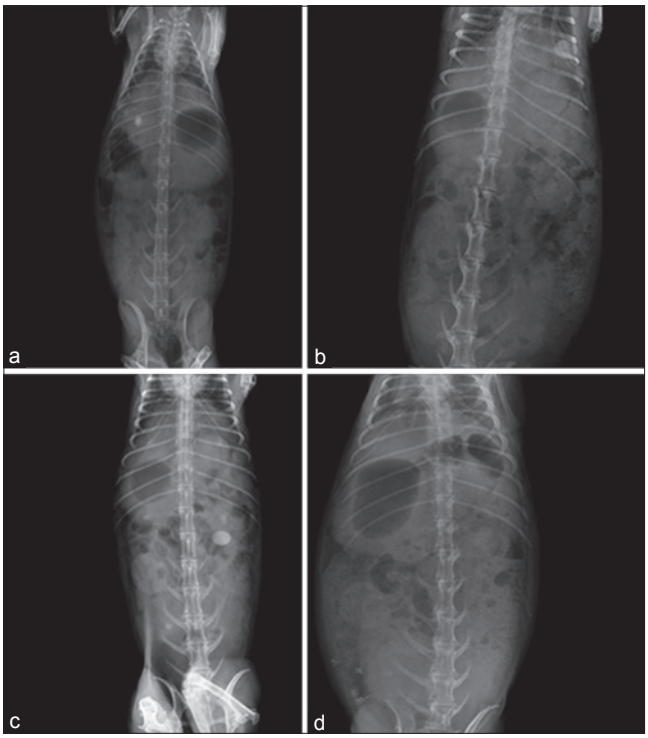

Fig. 6: (a) The X-ray studies that the tablet remained in the stomach for the first 2 hrs. (b) The X-ray studies that the tablet reached the small intestine at 5 hrs. (c) That tablet reached the large intestine and colon at 17 hrs. (d) That tablet disintegrated at 20 hrs

The drug release from Formulation FC5 was 0% in the first 2 hr. The drug release was negligible, i.e., it was only 9.83% at the end of 5hr. However, the release may be complete once the drug reaches the colon. Hence, a delayed action was observed. It was seen that Formulation FC5 released 98.5% at the end of 23 hrs in the presence of rat cecal contents, whereas, formulation FC5 released 86.67% at the end of 22 hrs in the absence of rat cecal contents. This indicates that the drug release from the formulation is mainly due to the presence of enzymes released by micro-organisms of rat cecal contents (degradation). From this data, it can be concluded that almond gum can be used for targeting the drug to the colon. Further, if, they are coated with enteric polymer, efficiently can be targeted to the colon by avoiding the release in the upper intestinal part and the release of the drug are basically dependent upon the colon microflora degradation rather than any other factors.

***In vivo* targeting efficacy**

To strengthen the *in vitro* release study finding, *in vivo* targeting efficiency study was carried out using formulation FC5. It is shown from the X-ray studies that the tablet remained in the stomach for the first 2 hrs (Fig. 6a) then it has reached the small intestine and remained intact for next 3 hrs (Fig. 6b). Then it has reached a large intestine and then reached colon and remained intact for 17 hrs (Fig. 6c) and finally tablet disintegrated in the 20 hr (Fig. 6d). It can be concluded from the X-ray images that the enteric coated tablets have remained intact in the upper part of the intestinal tract and swollen tablet picture in the colon indicates that the formulation releases the drug in the colon and hence, the colon specificity and the tablet remained intact without disintegration proving that the formulation is ideal for colon targeting.

From these results, almond gum can be successfully used for targeting the drug to the colon. The drug release from the polymer is dependent on the concentration of the polymer used, the more the concentration of the polymer the lesser is the drug release.

In all the formulations developed, the results were subjected to study the release kinetics. The values of the correlation coefficient indicated that the drug release followed zero order drug release kinetics with Peppas drug release mechanism. The values of T50% and T90% were found to be increased with increasing the proportion of polymers. The drug release mechanism was super case II transport as n>1.0.

CONCLUSION

The present work was aimed at developing colon targeted drug delivery of diclofenac sodium. A comparison study was done using various concentrations of almond gum in the preparation of matrix tablets of diclofenac sodium and matrix tablets are compression coated with Eudragit S100. Diclofenac sodium matrix tablets prepared with 70% (FC5) almond gum had slow drug release when compared with other formulations. The study shows that almond is able to target the drug to the colon. But it is dependent on the concentration of the polymer used. The release of the drug was more in the presence of cecal content than without the cecal content. The X-ray studies revealed that the formulated tablets are able to target the colon without getting disintegrated in the upper part of GIT. It was concluded that the compression coated matrix tablets of diclofenac sodium prepared by employing almond gum could be used for chronotherapy.

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