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IN VITRO AND IN VIVO CHARACTERIZATION OF SODIUM ALGINATE BASED IN SITU GELLING SYSTEM OF MELOXICAM FOR STOMACH SPECIFIC DRUG DELIVERY

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ABSTRACT
Meloxicam is a non-steroidal anti-inflammatory agent, used in the treatment of rheumatoid arthritis, osteoarthritis, joint diseases and dental pain and in the management of acute post-operative pain. It is selected as model drug candidate because of its wide spectrum of anti-inflammatory activity together with less gastric and local tissue irritation. The present study deals with the development and evaluation of a novel, stomach specific floating in situ gelling system (IGS) of MLX as a means of sustaining the drug release and improving the compliance of dysphagic and geriatric patients who have difficulty in handling and swallowing solid oral dosage forms. The prepared gels were characterized for solution viscosity, floating lag time, physical appearance, water uptake study, *in vitro* drug release studies. It was observed that both the concentration of sodium alginate and the concentration of calcium carbonate have significant influence on the prepared in situ gelling system characteristics of viscosity, drug content, 50 % and 80 % drug release and similarity factor. *In vitro* drug release study indicated that the release of the drug from the gel matrix followed non- Fickian diffusion. Pharmacodynamic studies carried out in albino rats revealed significantly increased analgesic/anti-inflammatory response from IGS compared to conventional suspension. Rat pylorus ligation method was employed for *in vivo* study of the optimized formulation and the results show the formation of gel in gastric juice of the stomach. Studies of the short term stability indicated little or no significant changes. This investigation demonstrates the feasibility of preparing a liquid; stomach specific IGS of MLX for better patient compliance.
Keywords: Meloxicum, Sodium Alginate, In situ Gelling Systems (IGS), Pylorus Ligation.

INTRODUCTION

Many patient's especially dysphagic, pediatric and geriatric patient populations express difficulty in swallowing solid dosage forms such as tablets and hard gelatin capsules, tending to non-compliant with the prescribed medication resulting in ineffective therapy.[1] Recent advances in novel drug delivery systems (NDDS) and polymer sciences have given scope to enhance safety and efficacy of drug molecules by formulating a convenient dosage form for a better patient compliance.[2] IGS gels have received considerable attention over past few years because of their capability to release the drugs in a prolonged way to yield relatively constant plasma profiles. This interest has been sparked by advantages shown by IGSs including ease of administration and reduced frequency of administration, improved patient compliance and comfort.[3] Pre-formed hydrogels, however, still have some drawbacks in the form of dose accuracy and reproducibility. Being liquid formulations, the compliance to these types of therapeutic regimen is higher because of their liquid nature and ease of swallowing.[4] In effect, IGS combine the advantages of both solutions and preformed gels.[5] These IGSs can be easily prepared and offer homogeneity of drug dispersion when compared to other conventional suspensions. These IGSs, are liquid at room temperature but undergo gelation when in contact with body fluids because of a change in pH, temperature or ionic content.[6] Gelation involves formation of double helical junction zones followed by aggregation of the double helical segments to form three dimensional network complexes with cations and hydrogen bonding.[7] Gelation occurs via the cross linking of polymer chain involving covalent bond formation (chemical cross linking) or non covalent bond formation i.e. physical cross linking.[8] Gelation of the orally administered liquid formulations (Ion activated system) was ensured by the inclusion of calcium ions in the formulation as a soluble complex designed to break down to release free calcium ions on encountering the acidic environment of the stomach.[9] The gelation was delayed until the orally administered solution reached the stomach by complexing the calcium with sodium citrate.[10] The use of natural polymers such as, chitosan, pectin, sodium alginate, methyl cellulose, gellan gum as vehicles for sustained/controlled release of drugs has received favorable attention recently.[11] Alginic acid is a linear block polysaccharide copolymer made of β-D-mannuronic acid (M) and α-L-guluronic acid (G) residues joined by 1,4 glycosidic linkages. The aqueous alginate solutions could form firm gels in presence of di- and tri-valent metal ions by a cooperative process involving consecutive guluronic residues in the G blocks of the alginate chain.[12] Gastro-retentive in-situ gelling system helps to increase bioavailability of drugs compared to conventional liquid dosage form. The gels formed from IGS, being lighter than gastric fluids, floats over the stomach contents. The SR formulations of non-steroidal anti-inflammatory drug (NSAID) have been proved to minimize the side effects.[13] MLX a non-steroidal anti-inflammatory (NSAID) agent was selected as a model drug, which is used in the treatment of rheumatoid arthritis, osteoarthritis, joint diseases and dental pain and in the management of acute post-operative pain. It is selected as a drug candidate because of its wide spectrum of anti-inflammatory activity together with less gastric and local tissue irritation.[14] The present investigation was mainly undertaken to prepare liquid formulation of MLX with in situ gelling properties and assessed for its potential sustained oral delivery.

MATERIALS AND METHODS

Materials: Meloxicam was a gift sample from Gujarat, India. Sodium alginate calcium bicarbonate and sodium citrate were obtained from commercial sources (S.D. fine chemicals,

Mumbai, India). All other chemicals and reagents used were of analytical grade.

Methods

Preliminary screening

The influences of various concentrations of calcium chloride and sodium citrate on the gelling properties of the in-situ gels were examined. The optimum quantities of calcium chloride and sodium citrate that maintained fluidity of the formulation before administration and resulted in gelation, when the formulation was added to simulated gastric fluid (SGF), were determined by preliminary tests.

Preparation of IGS

The different concentrations of sodium alginate were prepared in de-ionized water containing 0.25 % of sodium citrate at 70^{o}C in a beaker with stirring. Calcium carbonate was added to the above solution after cooling to below 40^{o}C, with continuous stirring using magnetic stirrer. Meloxicam (20 mg) was added and dispersed well. The formulations were sonicated using bath sonicator for 15 minutes and the IGS were stored in amber bottles until further use (Table 1).

Table 1: Formulation of In-situ Gel

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Meloxicam	20	20	20	20	20	20	20	20	20
Sodium alginate	1500	2000	2500	1500	2000	2500	1500	2000	2500
Calcium carbonate	-	500	500	500	1000	1000	1500	1500	1500
Sodium citrate	250	250	250	250	250	250	250	250	250
De-ionized water to make up 100 ml	100	100	100	100	100	100	100	100	100

Fourier Transform Infrared Spectroscopy (FTIR)

The presence of any possible drug-polymer interaction was studied by FTIR spectroscopy. IR spectra for drug and the drug-loaded IGSs were recorded in a Fourier transform infrared (FTIR) spectrophotometer (FTIR-8400 S, Brucker, Japan) with Potassium bromide (KBr pellets). The scanning range was 400– 4000 cm^{-1}.

Physical Appearance and PH Measurement

All the prepared batches of IGSs were checked for their clarity (visually) and P^{H} by a calibrated digital pH meter at 25^{0}C.[15] The measurements of pH were made in triplicate and depicted in Table 2.

Measurement of Rheological Properties of IGSS[16]

Viscosity of the prepared IGS sols were determined using a Brookfield digital viscometer (Brookfield viscometer, model DV-II proviscometer) and the temperature of the 2 ml samples was kept at 25 ± 1°C during each measurement. The experiments were performed in triplicate. Viscosities were determined at different shear rates from 00 to 100 rpm using suitable spindle number1.[16] The measurements on each sol were performed in triplicate.

***In-vitro* Gelling Capacity**

Gelling capacity of formulations was evaluated in order to identify the formulations suitable for in-situ gelling systems. Gelling capacity was determined by mixing the prepared sols with SGF 1.2 pH (0.1N HCl) and examined visually. The gelling capacity of solution was evaluated on the basis of stiffness of formed gel, time it takes to float and time period during which the formed gel remains in floating state.[17]

Measurement of Water Uptake by the IGS

The IGS formed in 40 mL of buffer (pH 1.2) was used for this study. The initial weight of the gel was weighed and to this gel 10 mL of distilled water was added and for every 30 minutes of the interval, water was decanted and the weight of the gel was recorded. The difference in the weight was calculated and reported.

***In-vitro* Floating Ability**

The *in-vitro* buoyancy study was performed using the USP dissolution apparatus II with 500 mL of simulated gastric fluid (pH = 1.2). 10 mL sample of the sol was drawn up with a disposable syringe and placed into a Petri dish. Petri dish was placed in the dissolution vessel containing the medium without much turbulence. The time for the gel to come to surface (floating lag time) and the time the gel remained floated on the medium surface (floating time) were recorded.[18]

***In-vitro* Release Studies**

The study of the MLX release from the in-situ gelling preparation was carried out similar to the method described by Zatz and Woodford.[19] with slight modification using USP 24 dissolution test apparatus with paddle stirrer at a rate of 50 rpm using 900 ml of pH 1.2 buffer as a dissolution medium (n = 6). IGS equivalent to 10 mg of MLX (10 ml) was used for the test. The slow speed prevented breaking of the gelled formulation and ensured a low level of agitation. 5 ml of aliquot was withdrawn at predetermined time intervals of 5, 10, 15, 20, 30, 60, 120, 180, 240, 300, 360, 420 and 480 minutes. The contents were filtered using 0.45 µ nylon filters and analyzed at 362 nm spectrophotmetrically. Same volume of dissolution fluid maintained at 37 ± 0.5°C was replaced immediately.[20] The absorbance of the sample was measured at 262 nm using a UV spectrophotometer (Shimadzu, UV-1601, Japan) for analysis of drug content. Each experiment was carried out in triplicate.

Selection of the Optimized Batch

The selection of best batch depends on percentage drug released, viscosity and drug content, Q50, Q80 and similarity factor. The viscosity of F; which is easy for swallowing and good ability for gellation immediately after oral administration, Drug content for the batch which is highest than the other batches. Dissolution data and graph are recorded in table no. and respectively in the batches F F the rate of drug release are very high and in the batches F the rate of drug release very slow while, in batch F controlled release of drug at an appropriate time period is found. The amount of drug released for the batch F5 at 10 h were 53 % which was similar to theoretical release profile and the 90 % drug release from the formulation with in 8 h means it is a prominent batch for the sustained release formulation. The similarity factor of the batch S5s was 72.75 which was nearer to the hundred instead of other batches so, the batch S5 is selected for further study.

Animal Studies

Pharmacodynamic Studies

Analgesic activity by tail immersion method

The pre-screened animals (reaction time 7-8 sec) were divided into three groups with each group having three animals. The animals were housed in polypropylene cages, with free access to a standard laboratory diet and water. All surgical and experimental procedures were reviewed and approved by the Animal and Ethics Review Committee, Balaji institute of pharmaceutical sciences, Laknepally, Narsampet, Warangal. A.P. India. One group served as the control was treated with 1 ml/kg of saline orally. The second group that served as standard was given meloxicam suspension (1 mg/kg) by the same route. Third group served as experimental group were treated with the Optimized formulation (F4) at a dose of 1 mg/kg orally by intubation. The tail flick latency was assessed by the analgesiometer (Inco, India). The strength of the current passing through the naked nichrome wire was kept constant at 6 Amps. The distance between the heat source and the tail skin was 1.5 cm.[21] The site of application of the radiant heat in the tail was maintained at 2.5 cm, measured from the root of the tail. The cut-off reaction time was fixed at 10 sec to prevent tissue damage. The initial reading was taken immediately before administration of test and standard drugs and then by 30, 60, 90, and 120 minutes after the administration. The animals were kept under standard laboratory conditions, at 25 ± 10^0C and 50 ± 5 % relative humidity with a 12 h light/dark cycle.

***In vivo* Studies/ Assessment of in situ Gel-forming Property in Rat Stomach**

In vivo study was conducted as per pylorus legation method in rats to check whether the gel was formed or not in the pylorus portion of stomach.[22]

Male Wister rats, weighing 230-330 g were selected for the studies and were divided into 3 groups.

Group 1: Served as control.

Group 2: served as control and immediate treatment (solution)

Group 3**:** Served as treated. (In-situ gels.)

The rats were fasted for 24 h with free access to water. The selected formulation ( ) was given orally with help of Sandoc syringe. The animals were anaesthetized with ether and after 3 h the animals were sacrificed and the stomach was removed, and checked.

Stability Study

Optimized formulation was filled in a plastic container (well stoppered) bottle and kept at 25 ± 1 ºC temperature and normal humidity conditions for three months. Samples were taken out periodically (initial, 1, 2 and 3 months interval) samples were taken out and evaluated for pH, viscosity, drug content.[23]

RESULTS AND DISCUSSION

IGSs are liquids at room temperature, but undergo gelation when in contact with body fluids due to cation induced gelation and are expected to release the loaded drug, MLX, in a sustained manner. The formulations should have an optimum viscosity that will allow easy swallowing as a liquid, which then undergoes a rapid sol-gel transition as a result of ionic interaction.[24] These preparations can be easily formulated in bulk and give homogeneity of drug distribution when compared to other conventional suspensions. Meloxicam loaded IGSs are expected to float in the form of a matrix gel, gradually releasing the drug to the absorption site, thus, controlling both rate and extent of drug absorption, without causing significant gastric discomfort.

Drug-excipient Interaction

Drug release profile and its stability in the formulation depend on the drug -excipient interactions. The FTIR spectrum is useful in clarifying the drug-excipient interactions at the various functional groups between the drug and excipients. The FTIR spectra of pure Meloxicam represent (Figure 12) absorption band at due to tertiary amine 3291.07 cm^{-1}, 1620 cm^{-1} and amidic keto group at 1580 cm^{-1}. The FTIR spectra of sodium alginate show that (Figure 13) peaks at 1610.66 and 1402.85 cm^{-1} are due to asymmetric and symmetric stretching of carboxylate groups. The absorption band at 2925.52 cm is attributed to $–CH_2$ group. The FTIR spectra (Figure 14) of dried IGSs revealed that there was no significant shift of functional peaks. It can also be observed that there is no overlapping of characteristic peaks and no appearance of new peaks and absorption peaks of the drug still could be detected in the mixture. Hence it concluded that the drug is stable in the formulation.

Rheological Properties of the Sols

All the prepared IGSs sols have shown that the viscosity has increased as a function of increasing polymer concentration with shear thinning behavior. From the Table 2, it can be observed that gel must contain minimum 1.5 % w/v concentration of SA, for the formation of good in-situ gel. With lower concentration below this, the formulations either failed to undergo gel to sol transition or formed gels were with low viscosity. All the formulated gels exhibited pseudo plastic flow (Table 3). Flow curve of the formulation F5 is shown in Figure 1

Viscosity of in-situ Gelling Systems

The solutions showed a marked increase in viscosity with increasing concentration of calcium carbonate and sodium alginate. It was observed that calcium carbonate concentration had a significant effect on viscosity (Table 2). Increasing calcium carbonate concentration in formulations increased the viscosity at all polymer concentrations studied. Calcium carbonate being insoluble; is present as insoluble dispersion in the formulations. Hence, an increase in its concentration, probably, enhanced the number of particles dispersed, thus contributing to the increased viscosity.

***In- vitro* Gelation**

The IGSs gel should maintain its integrity without dissolving or eroding for an extended period of time to aid the sustained release of drugs locally. All the formulations F1 to F9 formulations are formed gel immediately upon contact with (simulated gastric fluid) SGF and remained for few hours as such (Figures 8 to 10). Formulations with low concentration of polymer started to erode early probably because of weak cross linking of three dimensional network. Formulations F5, F6 and F8 exhibited gel formation immediately and maintained good integrity for extended period.

***In-vivo* Gel Formation**

In case of group 1 which was kept as control there was formation of gel (Figure 11 A). Also, with the control and immediate treatment there was no sign of formation of the gel

(Figure 11 B), where as in case of the treated one the formation of gel was evident (Figure 11 C) indicating that the gel formation occurs in the stomach of the tested animals.

PH and Floating Ability of in-situ Gelling Solutions

Results of pH measurement of formulation F1 to F 9 were shown in Table 2. All the formulation has a pH around neutral or slightly alkali. Maximum pH 7.5 was observed in F2 and F3 formulation and minimum pH 7.0 was observed in F9 formulation. All the prepared batches were evaluated for their floating properties in simulated gastric fluid. The time for formulation to come to the medium surface (floating lag time) and the time the formulation maintained floated on the medium surface (duration of floating) were determined and the values were shown (Table 2). The lowest amount of calcium carbonate which produced a buoyant gel system for the duration of drug release study was found to be 0.5 % at all polymer levels. On increasing the calcium carbonate concentration, the floating lag time was reduced and the duration of floating was extended. The increasing amounts of Ca^{++} and CO_2 resulted from the increase in calcium carbonate concentration, are responsible for the observed reduction in floating lag time and increasing duration of floating. Similarly an increase in polymer concentration resulted in decreased floating lag time and increased floating duration of the prepared systems.[25]

Water Uptake by IGS

The results of the water uptake are depicted in Figure 3. It is evident from the data the IGS absorbed and swelled linearly with time up to seven hours during which there is 80 % uptake by the prepared formulation. These studies prove that the formulation will swell in the gastric fluids after coming in contact with gastric fluids.

***In-vitro* Duration of Floating of IGS**

The total floating time of the prepared formulations were performed in 0.1 N HC (pH 1.2). Results of *in vitro* total floating time of formulation F1 to F9 were presented in Table 7. FI has shown the less floating lag time of 55 which may be attributed to escape of carbon dioxide air bubbles from the gelling network because of low concentration of polymer. F6 and F9 formulations have a total floating time of more than 8 hours.

***In vitro* Drug Release**

The release profiles and the effect of the polymer amount on the formulations of MLX IGSs were shown in Figure 2. The drug release from the sols was characterized by an initial phase of rapid release (burst effect). However, as gelation continued, the remaining drug was released at a slower rate exhibiting bi-phasic pattern of release. This type drug release is a characteristic of the matrix diffusion kinetics.[26] As the percentage of calcium carbonate increased, it is noticed that the release rate is regarded as a result of formation stronger gel in presence of increasing concentrations of Ca^{++} ions. The change of the polymer concentration of these gels, appears to affect the diffusion pathway and subsequently the drug release[27]. Moreover, as the viscosity of the polymer sols increased with concentration, the solvent penetration into the core of the matrix is decreased, and the drug release is retarded[28]. It is found that the initial burst effect was significantly decreased with an increase in sodium alginate concentration. The release of MLX from the IGS followed higuchi model and the release mechanism was found to occur by an anomalous diffusion-controlled mechanism.

Pharmacodynamic activity

Human volunteers can serve as excellent models for *in- vivo* studies of newer formulations. However, because of the various constraints, it is desirable to use animal models in the initial stages of product testing. Table 6 shows the comparison of the analgesic effect at 1 mg/kg body weight from the control, conventional suspension, and the IGS. It is evident from the data the test formulation exhibited better analgesic effect for a prolonged period during the test period.

Drug Release Kinetics

The data of average values were processed as per zero order, first order, higuchi and kormeyer peppa's models.[29] is given in Table 3 and the release data of MLX from all formulations were depicted in Figure 4 to 7 respectively. Data of the *in-vitro* release were fit into different equations and kinetic models to explain the release kinetics of the MLX from IGSs. On the basis of R^2 value F1 to F3 followed first order drug release kinetics and all other formulations F4, F5, F6, F7, F8 and F9 followed zero order kinetics. Better fit (highest R^2 value) was observed in case of Higuchi's model. Hence it is assumed that the mechanism of drug release from the IGSs formulations F1 to F9 was of diffusion controlled. Koresmeyer Peppas model indicates that the release is not well known or more than one type of phenomenon could be involved. According to the Koresmeyer Peppas model a value of slope of less than 0.5 indicates fickian diffusion. Hence, it is assumed s that the formulation F5 followed fickian diffusion.

Stability Study

Samples were withdrawn at the interval of one month for three months and evaluated for *in-vitro* drug release profile, pH viscosity and drug content. From the data, it is evident that the viscosity of formulation decreased from 279 to 261 which may be attributable to the loss of water during storage. However, it did not alter the rheological properties to a significant extent. Results of rheological studies during stability studies are depicted in (Table 5). The P^H of the formulations did not differ much before and after storage. *In vitro* drug release profile before and after storage was shown in (Table 7).

Table 2: Evaluation of IGS formulations

Formulation Code	Floating lag time (Sec)	pH	Gelling time (sec)	Floating time (h)	Viscosity cps	% Drug Content (± SD)
F-1	55	7.4	25	< 1	468	97.14 ± 0.34
F-2	65	7.5	27	< 4	479	95.33 ± 0.53
F-3	58	7.5	35	< 8	485	100.17 ± 0.6
F-4	76	7.4	28	< 4	469	96.4 ± 0.37
F-5	63	7.2	31	< 8	482	94.11 ± 0.31
F-6	60	7.3	26	< 8	488	97.34 ± 0.49
F-7	78	7.1	31	< 8	470	92.24 ± 0.40
F-8	67	7.4	31	< 6	484	98.54 ± 0.45
F-9	80	7.0	33	< 6	491	95.74 ± 0.49

Table 3: Flow behavior F4

Shear rate (s^{-1})	Shear stress (dyne cm^{-2}) Increase in rpm	Shear stress (dyne cm^{-2}) Decrease in rpm
0.31	0.78	0.95
0.61	1.5	1.75
0.92	2.22	2.45
1.22	2.99	3.01
1.53	3.71	3.98
1.83	4.45	4.54
2.14	5.16	5.45
2.45	5.88	5.98
3.06	7.31	7.4

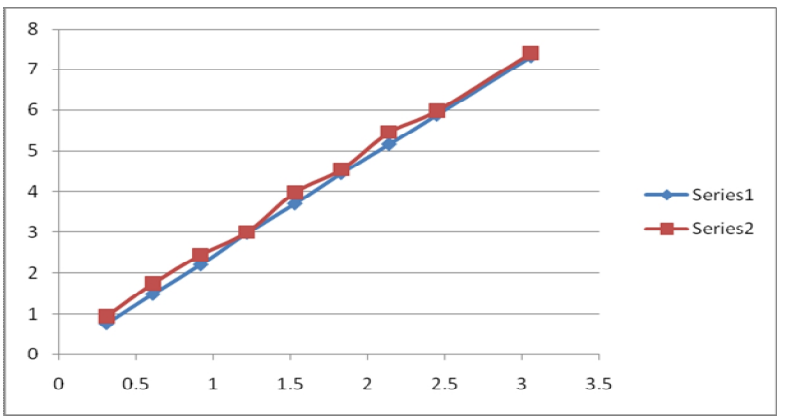

Figure 1: Flow curve of F5

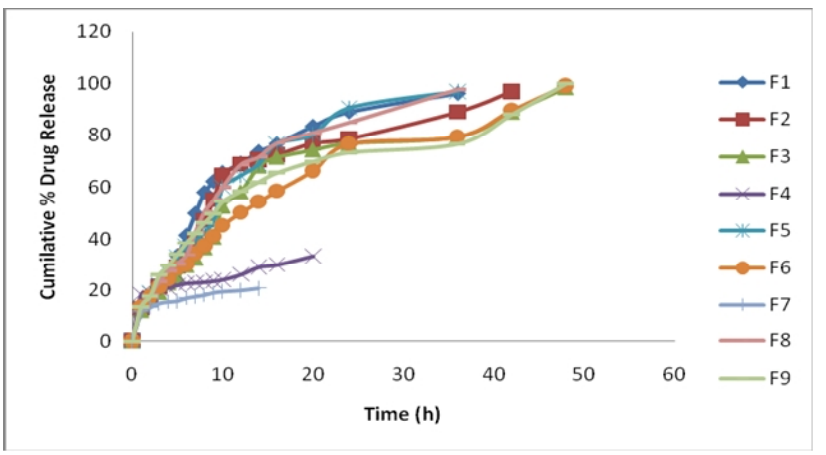

Figure 2: *In-vitro* Release Study of Insitu Gel Formulations

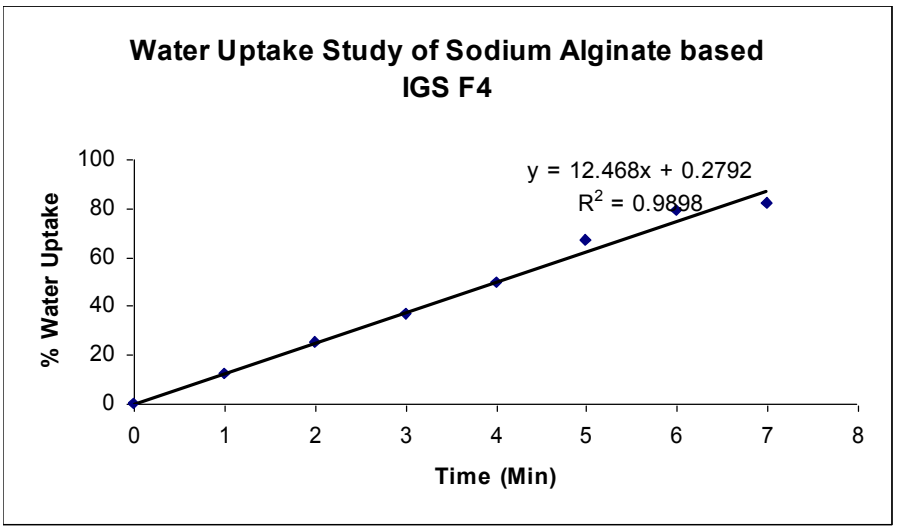

Fig 3: % Water Uptake Study

Table 4: kinetics of drug release

Batch No	Regression			
	Zero order	First Order	Higuchi	Korsmeyer-Peppas
F1	0.716	0.4100	0.8277	0.9103
F2	0.7477	0.5000	0.8624	0.9301
F3	0.8112	0.5001	0.891	0.9296
F4	0.8882	0.9170	0.9515	0.9254
F5	0.9932	0.8824	0.9786	0.9174
F6	0.9898	0.9678	0.9793	0.9973
F7	0.9899	0.9605	0.9820	0.9925
F8	0.9950	0.9644	0.9758	0.9953
F9	0.9961	0.9653	0.9618	0.9916

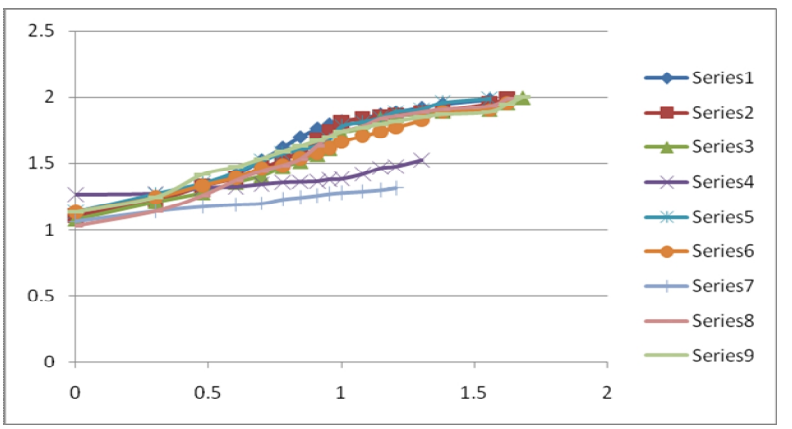

Figure 4: zero order plot

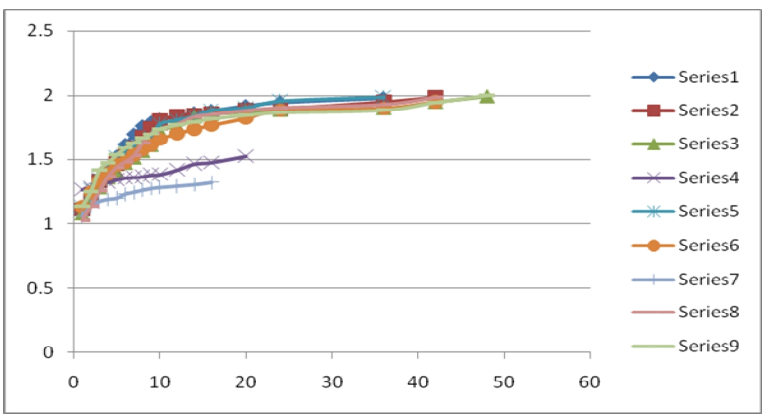

Figure 5: **First order plot**

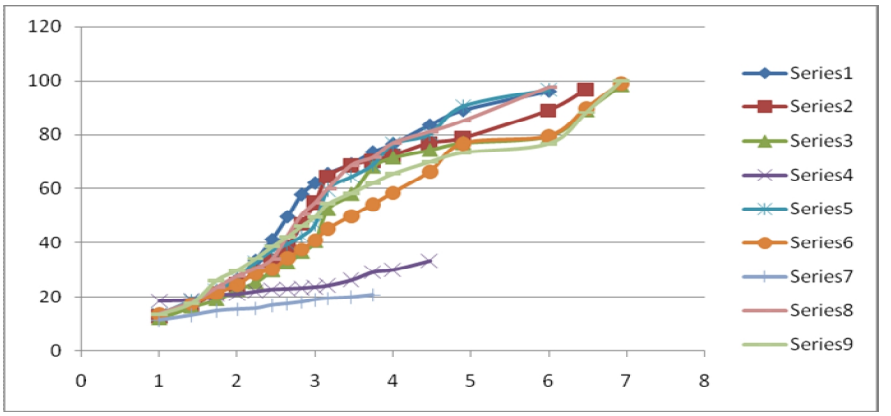

Figure 6: Higuchi plot

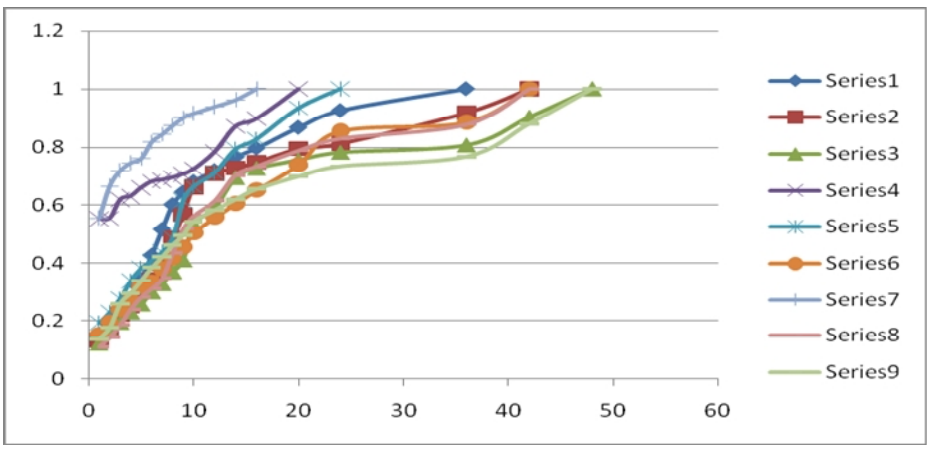

Figure 7: Koresmeyer Peppas plot

Table 5: Stability study for sodium alginate based IGS Formulation (Batch-F4)

Time Period for Sampling	pH	Viscosity (cp)	Drug Content (%)
Initial	7.4	479	96.4 ± 0.37
After 1 Month	7.42	472	96.12 ± 0.42
After 2 Month	7.48	470	95.89 ± 0.72
After 3 Month	7.59	461	95.57 ± 0.27

Table 6: Pharmacodynamic activity (analgesic activity)

Treatment	Dose	Analgesic response (mean time in seconds ± SEM)			
		30 Minutes	60 Minutes	90 Minutes	120 Minutes
Control (Normal Saline)	1 ml/kg	7.12 ± 0.38	7.28 ± 0.56	7.58 ± 0.24	7.39 ± 0.27
Standard (Meloxicam Susspension)	1 mg/kg	14.72 ± 0.39	15.48 ± 0.47	18.16 ± 0.82	17.31 ± 0.79
Test (F4)	1 mg/kg	17.25 ± 1.08	21.51 ± 1.71	24.93 ± 0.79	22.25 ± 1.33

Table 7: *In-vitro* drug release profile of meloxicam from FG5 formulation during stability study

Time	Initial	After 1 month	After 2 months
0.00	0.00	0.00	0.00
4	22.26	21.29	21.21
8	42.60	40.12	41.10
12	64.49	62.23	61.17
16	76.81	75.44	74.39
20	80.28	78.43	77.76
24	90.55	88.16	88.10

All the values are in mean ± SD (n = 3)

Figure 8: Gel Formation from sodium alginate based In situ solution F4 of MLX in pH 1.2 buffer

Figure 9: Gel Formation from sodium alginate based In situ solution F6 of Meloxicam in pH 1.2 buffer

Figure 10: Gel Formation from sodium alginate based IGSs F4 in dissolution apparatus

Figure 11 A: *In vivo* study for the sodium alginate based In- situ solution of MLX from batch F4 in rat Group 1 served as control

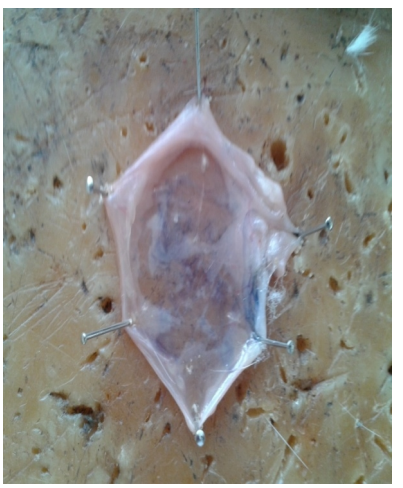

Figure 11 B: Group 2 Served as control plus immediate treatment by sodium alginate based in situ solution of batch F4

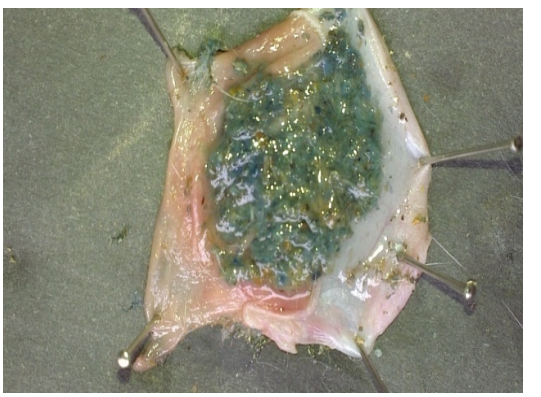

Figure 11 C: Groupe 3 served as treated plus sodium alginate based in situ solution of MLX batch batch F4

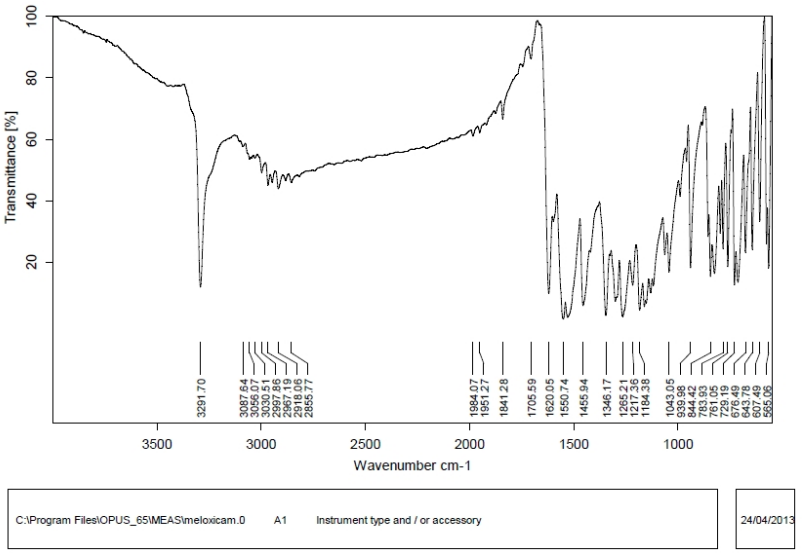

Figure 12: FT-IR Spectra of MLX

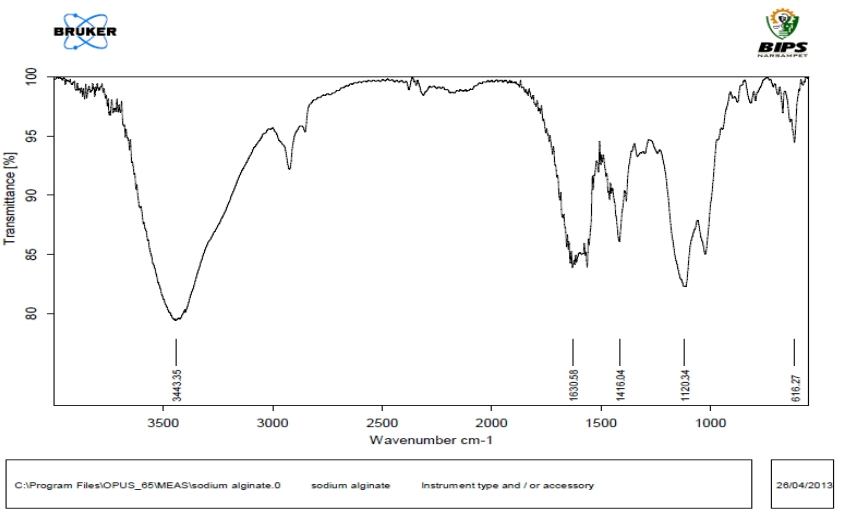

Figure 13: FT-IR Spectra of sodium alginate

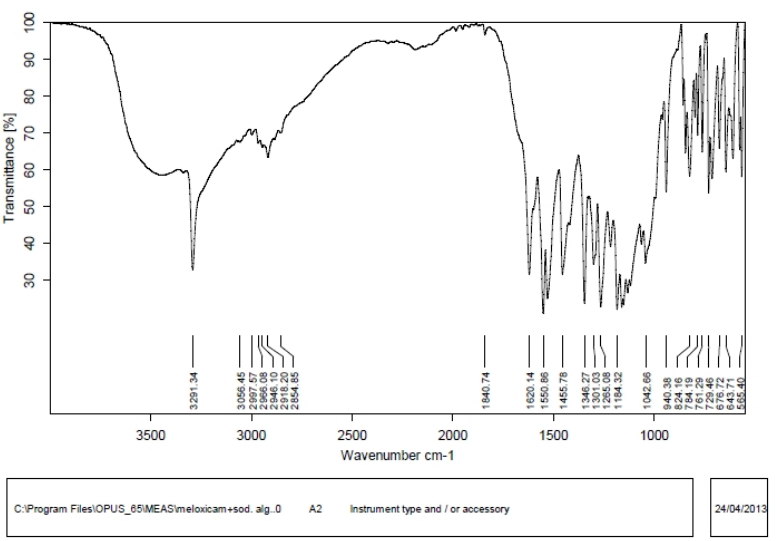

Figure 14: FT-IR Spectra of sodium alginate + MLX in IGS

CONCLUSION

The study demonstrated the feasibility of formulating novel in-situ gelling system in the form of a solution with the required viscosity with a pH value ranging from 7.0 to 7.5, drug content and having the gastro-retentive and drug releasing in a sustained manner. Stability data recorded over a period of three months under accelerated conditions indicated the formulation to be stable without any significant changes in its characteristics. Hence, it is concluded that by virtues of its liquid nature and *in vivo* gelling capability and gastric retention, the developed formulation could offer a viable alternative to conventional dosage forms especially for geriatric patients.

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