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# Preparation and Evaluation of Oral Stomach Specific In Situ Gelling Emulsion of Piroxicam

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## ABSTRACT

The aim of the present study is to minimize the local gastrointestinal irritation which is one of the major side effects of Piroxicam (PR) by the formulation oral stomach specific in situ gelling emulsion ingestion by kinetic control of drug release. Material and method: In situ emulgel were prepared by using castor oil as oil phase ,tween 80 and span 80 as emulsifiers, sodium alginate was used as gelling agent, xanthan gum was used as release retardant ,calcium carbonate was used as cross linking agent, pH triggered ionic gelation is the mechanism involved in the present study. Various evaluation tests were done for all formulations Results: Formulation F9 containing 2.5% of sodium alginate, 2 % of CaCO3, 1 % of sodium bicarbonate and 0.8% of Xanthan gum was selected as optimized batch based on Q10 86.02±0.17 %, floating time 122.15±2.47 sec and drug content 91.86±1.02 %. The release pattern of drug was found to follow Korsemeyer and Highuchi model. The DSC study exposed that there was no incompatibility. Pharmacodynamic study on Wistar rats were showed significant anti inflammatory and anti arthritic activity of the optimized formulation. Further, in vivo toxicity studies carried out in wistar rats revealed no signs of gastric ulceration upon prolonged dosing. Conclusion: It was concluded that the oral stomach specific In situ gelling emulsion of piroxicam could be an effective dosage form which minimize the gastric irritation by coating drug with castor oil and remains buoyant and control the drug release for 24hrs.

**Keywords:** In situ gelling emulsion, Piroxicam, Castor oil, Gastric retention, In vitro release, Gastric irritations.

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# INTRODUCTION

Oral route is the most commonly adopted and most convenient route for the drug delivery. Oral route of administration has received more attention in pharmaceutical field because of the more flexibility in the designing of dosage form than drug delivery designs for other routes. [1]

Development of controlled -release liquid oral dosage forms manner gastric irritant non steroidal anti inflammatory drugs is beneficial for best therapy with respect to the safety, efficacy and patient compliance. Compare to tablets and Capsules dosage form, Oral liquid dosage forms are more easily acceptable and offer better patient compliance because tablet and capsule cause quick gastrointestinal transit. The drugs with absorption window in the stomach have this serious problem. The strategy of liquid in situ gelling systems use for the gastric retention of oral liquid formulations containing such drugs. These in situ gel formulations respond to chemical or physical signals, including pH, metabolite, ionic factor, or temperature. The polymers which used for in situ gel formulations are following include alginates, gellan, pectin, chitosan, xanthan gum and so forth. Even though in situ gelling systems possess a number of advantages in terms of biodegradability and biocompatibility, these systems are too fragile and do not have mechanical strength to hold the entrapped drug(s) in many cases. Combining lipid materials with hydrophilic polymers has been used in the past to resolve the problem of fast drug release from hydrophilic matrices. Upon the literature survey, it was observed that there is not have of studies reporting combination of lipids, oils with hydrophilic polymers to develop liquid in situ gelling systems. The lipid and oils systems formed in this way acts similar to in situ activated gel-forming polymer systems and can be used for the application for a wide variety of drugs.

Piroxicam is commonly used NSAID for long term treatment of chronic diseased likes rheumatoid arthritis, osteoarthritis and so forth to improve patient's health and ability to function. Piroxicam is also associated with elevated risk of gastrointestinal toxicity such as ulcers and bleeding. The gastrointestinal toxicity may be higher for the people who are older in age, drink large amount of alcohol, have poor health. Irritation can vary from minor gastric suffering to bleeding and ulceration of the mucosa and is not only caused by the inhibition of prostaglandin synthesis, but is probably also due to direct contact of the Piroxicam with the gastric mucosa and to enterohepatic recirculation. Oral delivery of stomach specific *in situ* gelling emulsion not only prevents the direct contact of the drug with gastric mucosa but also controlled the release of embedded drug leading to better treatment efficacy, safety, and patient compliance. Castor oil also have arthritic

activity and drug which coated with castor oil get partitioned from oil to gastric medium. After come in contact with gastric fluid drug directly get absorbed and show activity emulgel

Development of a appropriate drug delivery system may decrease the contact time of the drug with the gastric mucosa, while the application of an enteric coating may offer additional protection.[2]

## MATERIALS AND METHOD

**Materials**:

Piroxicam was purchased by Yarrow chem. products. (Mumbai, India). Sodium alginate was purchased from Thomas Berkers and Chemicals. Xanthan gum was purchased from Hi Media. Castor oil was purchased from Rajesh chemical company. Tween 80 was purchased from pallav chemicals and solvents private Ltd. Span 80 was purchased from Thomas Bekers and chemicals. Calcium carbonate was purchased from Thomas Bekers and Chemicals. Sodium bicarbonate was purchased from Thomas Bekers and Chemicals. Sodium saccharin was purchased from Chemy lab .Distilled water used in the formulations and all other chemicals used were of analytical grade.

**Methods**

**Measurement of melting point of Piroxicam**

Melting point was determined by taking small amount of Piroxicam in a capillary tube closed at one end. The capillary tube was placed in an electrically operated digital melting point apparatus and the temperature at which the drug melts was recorded. This was performed thrice and average value was noted.

**Preliminary study for all excipients**

**Polymer screening studies**

Polymer screening was done according to gelling properties and swelling index of various polymer using various concentrations.

**Table 1: Gelling and swelling Properties of Polymers**

| Sr.no. | Polymer | Gelling property | Swelling index |
|---|---|---|---|
| 1 | Sodium alginate | +++ | 98.4±0.2 |
| 2 | Gellan gum | ++ | 82.78±0.1 |
| 3 | HPMCK4M | ++ | 84.68±0.15 |
| 4 | Carbopol | + | 89.17±0.12 |
| 5 | Chitosan | + | 82.05±0.27 |
| 6 | Guar gum | + | 86.21±0.3 |
| 7 | Sodium CMC | + | 80.17±.10 |
| 8 | Methyl cellulose | + | 87.2±0.09 |
| 9 | Pectin | ++ | 97.59±0.18 |
| 10 | Xanthan gum | +++ | 99.25±0.21 |

Fair = +**;** Good = ++ ; Excellent = +++

**Selection of Oil phase and surfactants**[3]

Emulsion was prepared by RHLB method in which oil phase was selected according to HLB value and RHLB was calculated then emulsifier was choose .

Selection Of oil : castor oil was selected due to its anti-inflammatory activity.

Selection Of Emulsifier: Tween 80, Span 80

According to RHLB calculations 6% oil phase required 4% of combination of emulsifier Having RHLB From higher end to lower end.

**Table 2:Trial Batches For Combination Of Polymers**

| Sr. no. | Polymers | Highest Concentration(%) with 2.5% sodium alginate | In vitro drug release in 1 hr(%) |
|---|---|---|---|
| 1 | Gellan gum | 0.75 | 91.51% |
| 2 | Pectin | 3 | 60% |
| 3 | HPMC K4 | 1 | 83.76% |
| 5 | Xanthan gum | 1 | 30.75 |

Sodium alginate was used as gelling agent and other polymers were used as release retardants. Different batches of formulation where prepared using combination of sodium alginate and other polymers. Even at their highest concentrations they showed burst release of drug within an hour except xanthan gum which showed required release of drug.

**Table 3: Selection and Optimization of Calcium Carbonate**

| Ingredients | Calcium carbonate (%) | Appearance of Formulation |
|---|---|---|
| Drug + | 1.5 | ++ |
| Sodium alginate + xanthan gum | **2** | **+++** |
| | 2.5 | + |

Three concentrations of calcium carbonate were taken. Among these three concentrations, 2% calcium carbonate showed gelling property, total floating duration and appearance in acceptable limit. hence 2% was selected for all the formulations. Increasing the calcium carbonate content in the formulation simultaneously increased the viscosity at all polymer concentrations studied (Table 2).

**Table 4: Selection and optimization of sodium bicarbonate**

| Ingredients | Sodium bicarbonate (%) | Floating lag time (Sec) |
|---|---|---|
| Drug + Sodium alginate + xanthan gum +calcium carbonate | 0.25 | 280±1.0 |
| | 0.5 | 190±0.58 |
| | **1** | **100.2±1.20** |

Three concentrations of sodium bicarbonate were taken. Among these three concentrations,1% sodium bicarbonate shows floating lag time (100.2±1.20) which is in acceptable limit.So,1% was selected for all the formulations.

**Table 5: Selection and optimization of sodium saccharin sweetener**

| Ingredients | Sodium saccharin (mg) | Taste |
|---|---|---|
| Drug +sodium alginate+ xanthan | 100 | Not acceptable |
| gum+ Calcium carbonate + | 200 | Not acceptable |
| Sodium bicarbonate | 300 | Not acceptable |
| | **400** | **Acceptable** |

Four Concentrations of Sodium Sacchain Were taken among these Four Concentrations 400mg Saccharin Sodium Enhanced Flavor Systems And Masked Some Unpleasant Taste In The Acceptable Limit. Hence 400mg Was Selected For All The Formulations.

**UV Absorbance Maxima and Calibration Curve of Piroxicam in 0.1 N HCl (pH 1.2)**[7]

Stock solution of Piroxicam in acid medium with proper dilution was initially scanned in UV Visible spectrophotometer within wavelength of 200-400 nm. For calibration, 100 mg of Piroxicam was dissolved in100 ml of 0.1N HCl. The solution was then diluted with 0.1 N HCl To obtain 2, 4,6, 8and 10 µg/ml solution. It was then measured by UV visible Spectrophotometer.

**Drug-Excipient Interactions**.

While designing any drug delivery system, it is imperative to consider the compatibility of drug and polymers used within the system. Therefore, it is necessary to confirm that the drug is not interacting with polymers under experimental conditions and shelf life. For the present study, the drug-polymer interaction studies were performed using Fourier Transform Infrared Spectroscopy (FTIR). FTIR spectra were recorded for pure polymers, drug and, drug loaded dried in situ gelling formulations using a FT-IR facility (Shimadzu, model 8400S).The samples were prepared in KBr disks (2mg sample in 200mg KBr). For FTIR analysis, the scanning range was 400–4000 cm−1 and the resolution was 2 cm−1.

Differential Scanning Calorimeter (DSC) Studies Thermograms were recorded for Piroxicam and in situ gelling emulsion using Differential Scanning Calorimeter. Accurately weighed samples (3.00 mg) were placed on aluminum plates sealed with aluminum seals and heated at constant temperature of 5°C/min over a temperature range of 0-400 °C.

**Preparation of In Situ Emulgels**.

In situ emulgel containing 10mg of Piroxicam were prepared formula & formulated various batches.

**a)** Weigh accurately drug, polymers and other excipients. The active ingredient piroxicam, all polymers and other excipients were get sifted through sieve no. 40#.

**b)Aqueous phase**:

Sodium alginate at various concentrations (1.5% to 2.5% w/v) was dissolved in half quantity of distilled water with concentration of sodium bicarbonate(1%),sodium sacccharin(0.4%),methyl paraben under continuous stirring on magnetic stirrer at 700 c. then in remaining quantity of water soaked release retardant xanthan gum(0.6%to 0.8 %w/v) After dissolving all ingridents in aqueous phase , soaked release retardant polymer xanthan gum were add in aqueous phase under continous strring on magnetic strrier at 700 C

**c)Oil phase** :

Then required quantity of oil (castor oil) , surfactant (Tween 80) ,co surfactant (span 80) and propyl paraben was taken in another beaker and placed on magnetic stirrer then and weighed quantity of drug was added to it while continuous stirring at 700 c.

**d)** Aqueous phase was added to the beaker containing oil phase to make emulsion under continuous stirring on magnetic stirrer at 700 c. After cooling to below 400C,calcium carbonate(2%) was added under continuous stirring. Finally volume was made up to 100% with distilled water. Resultant solution was stirred well.

**Table 6: Formulation batches**

| Ingredient | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Piroxicam(mg) | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Castor oil (%) | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Tween 80(%) | 3.6 | 3.6 | 3.6 | 3.6 | 3.6 | 3.6 | 3.6 | 3.6 | 3.6 |
| Span80(%) | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 |
| Sodium alginate (%) | 1.5 | 2 | 2.5 | 1.5 | 2 | 2.5 | 1.5 | 2 | 2.5 |
| Xanthan gum (%) | 0.6 | 0.6 | 0.6 | 0.7 | 0.7 | 0.7 | 0.8 | 0.8 | 0.8 |
| Calcium carbonate (%) | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Sodium bicarbonate (%) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Me. paraben & pro. paraben | 9:1 | 9:1 | 9:1 | 9:1 | 9:1 | 9:1 | 9:1 | 9:1 | 9:1 |
| Sodium saccharin(mg) | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Distilled Water(upto 100ml) | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |

**Figure 1: Different Formulation Batches (F1-F9)**

## Characterization of floating oral in situ gel

**Appearance [4]:**

All formulations were evaluated for clearness by visual observation against black and white surroundings.

**pH [5]:**

The PH of formulations was measured using a calibrated digital PH meter at RT. The measurement is carried out in triplicate and average values are taken.

**Floating lag time [6,11]:**

Floating lag time was carried out using 0.1 N HCL (pH1.2). The medium temperature was kept at 37 º C. 10 ml formulation was introduced into the dissolution vessel containing medium with no much disturbance. The time the formulation took to come out on the medium surface (Floating lag time) and the time the formulation continuously floated on surface of the medium (Floating duration) were noted.

**Sol to gel time[7]**

In vitro gelation time was determined by using USP (Type II) dissolution apparatus containing 500 mL of 0.1N HCl (pH 1.2) at 37±0.5 0C was observed that within fraction of seconds the solution converted into gel later it floated in medium. As the formulation was coming in contact with 0.1N HCl, (pH 1.2) it converted from sol to gel and time was measured.

**Viscosity [8]:**

The viscosities of the solutions were determined by Brook field viscometer (Model RVDV-II+P). The samples (100 ml) were sheared at a rate of 100 rpm using spindle no 64 at room temperature. Viscosity measurement for each sample was done in triplicate, and average was taken.

**Density [6,7]:**

For stomach specific system density is an important parameter and which less than the stomach fluid density (< 1.004). The Densities of all formulations were measured by forming gel of 10ml solutions were placed in measuring cylinder and weight of this gel was noted by using calibrated balance. Finally, the densities of different formulations were noted in triplicate.

**Swelling index [9,10]:**

A gel of 100mg was weighed accurately (W1). It was kept in a petridish and 50ml of 0.1 N HCl was added. The petridish was kept aside for 24 hrs. The weight of swollen matrix gel (W2) was measured and swelling index was calculated using following formulae: Swelling Index = (W2-W1/W1)*100 Where, W1 = initial weight of gel (100mg), W2 = weight of swollen matrix after 24 hrs.

**Drug content[12]:**

10 ml of In situ gel (equivalent to 10 mg of drug) was measured and transferred to 100 ml of volumetric flask containing 0.1N HCL and stirred for 1hour on magnetic stirrer. The solution was filtered and suitably diluted with (0.1N HCl, pH 1.2 medium) and the drug concentration was determined by using a UV-visible spectrophotometer at 334.3 nm against a pH 1.2 medium as blank solution.1 The drug content was calculated as:

$$\% \text{ Drug Content} = ( \text{Analysed value} / \text{Theorotical Value} ) \times 100$$

**In vitro dissolution studies [13]:**

The release of drug from the formulations was determined using a USP/24 dissolution test apparatus with a paddle stirrer at 50 rpm. The dissolution medium used was 900 mL of 0.1 N HCL pH 1.2and temperature was maintained at 37 ± 0.2 °C. Ten mL of the formulation was added into the dissolution vessel containing dissolution media avoiding any disturbance using test tube. At each time interval, a precisely measured sample of the dissolution medium was pipetted out and replenished with fresh medium. Drug concentration in the aliquot was determined spectrophotometrically. Each study was conducted in triplicate.

**Kinetic analysis of release data[14,16,17,18]**

The dissolution data obtained was fitted to Zeroorder, First order, Higuchi,Hixon -Crowell and Korsmeyer- Peppas equations to understand the rate and mechanism of drug release from the prepared formulations. The correlation coefficients values were calculated and used to find the fitness of the data.

Zero order equation Q t = Qo + Kot 14, describe the systems where the drug release rate is independent of concentration of the dissolved substance, where, Qo = initial amount of drug, Qt =cumulative amount of drug release at time t, Ko=zero order release constant, t = time in h

First order release equation Log Qt = Log Qo +Kt/2.303 15, the drug release rate depends on its concentration, where, Qo = initial amount of drug, Qt = cumulative amount of drug release at time t, K = first order release constant, t = time in h

Hixon-crowell equation Mo1/3 - Mt1/3=K 16, describes the drug release by dissolution and with the changes in surface area and diameter of the particles or tablets. Mo = Initial amount of drug, Mt = Cumulative amount of drug release at time t, K = Hixson-crowell release constant, t = time in h. Higuchi release equation Q=KH t½ or Mt/Mo =Kt½17 , the Higuchi equation suggests that the drug releases by diffusion mechanism. Q = cumulative amount of drug release at timet, KH = Higuchi constant ,t = time in h

Korsmeyer-Peppas: F = (Mt /M∞) = Km t n 17, which described drug release from a polymeric system, Where F=Fraction of drug released at time t, Mt=Amount of drug released at time t, M∞=Total amount of drug in dosage form, Km= Kinetic constant, ent, t = time in h.

**Stability study [15,19]:**

Prepared in situ gel formulation of ramipril was stored in an amber colored glass Containers (well stoppered) for three months and the stability of the in situ gel Suspension formulation of Ramipril was monitored up to 3 months at Controlled Temperature (40 µ $20^0$C) and controlled humidity (75 µ 2 % RH) conditions. Periodically (Initial, 1,2and 3 months) samples were removed and evaluated for pH, viscosity, and Drug Content and in vitro release.

## RESULTS AND DICUSSION

**Melting Point of Piroxicam**

Melting point of Piroxicam was determined by capillary tube method and it was found to be 198 $^0$c. This value is similar as that of the literature citation 200 $^0$c -198 $^0$c .

**Absorbance Maxima and Calibration Curve of Piroxicam in 0.1 N HCl(pH 1.2)**

Absorption spectrum of Piroxicam indicated λmax at 334.3 nm which is very close to its reported λmax value that is 334nm.

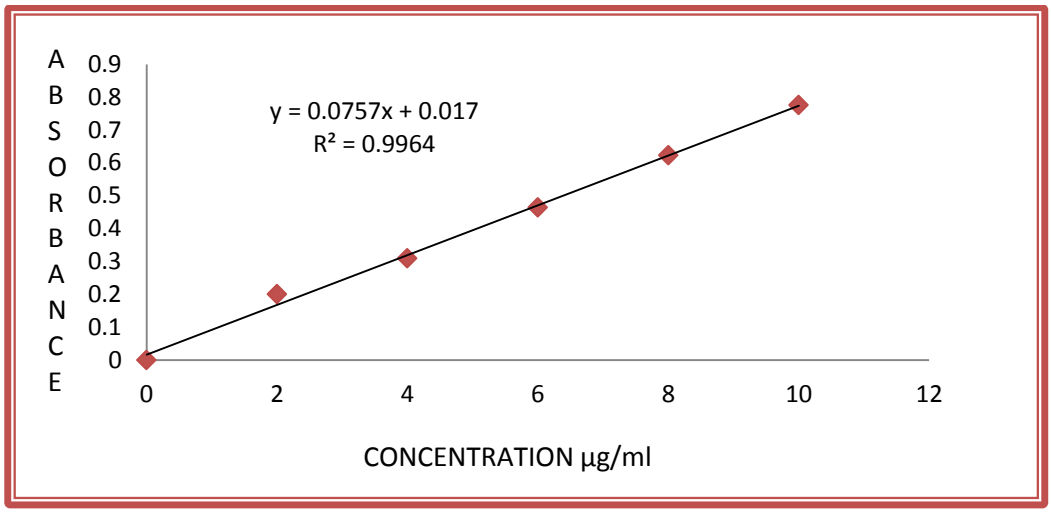



**Figure 2: Calibration curve of Piroxicam in 0.1N HCl**

**Drug-Excipient Interactions**.

Drug-excipients interactions are one of the most important characteristics that regulate the drug release and pattern from the formulations and its stability in the formulation. Drug-excipient interactions were studied at the very outset before the beginning of the development of formulations. Various methods such as DSC and FTIR spectra. are frequently used to study drug excipient interaction. The FTIR spectrum can accurately clarify drug-excipient interactions at the various functional groups between the drug and excipient molecules.

The FTIR spectra of pure Piroxicam represent (Figure 1) absorption band at 3338.07 cm−1 which indicate that the drug is in the cubic polymorphic form. Absorption band at 771.172, 1147.44, 1351.66, 1444.42, and 1634.02 cm−1 corresponds to stretching of ortho-di-substituted phenyl, stretching of – SO2-N-group, stretching of symmetric methyl group, stretching of asymmetric methyl group, and stretching of amide carbonyl, respectively. The FTIR spectra of sodium alginate show that (Figure 1) 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 –CH2 group. The FTIR spectra (Figure 1) of dried emulgels showed that there was no major shifting of functional peaks and no overlapping of characteristic peaks and also there was no appearance of new peaks. This indicates that the dried emulgel spectra were only the summation of spectra of Piroxicam and individual excipient.[1]

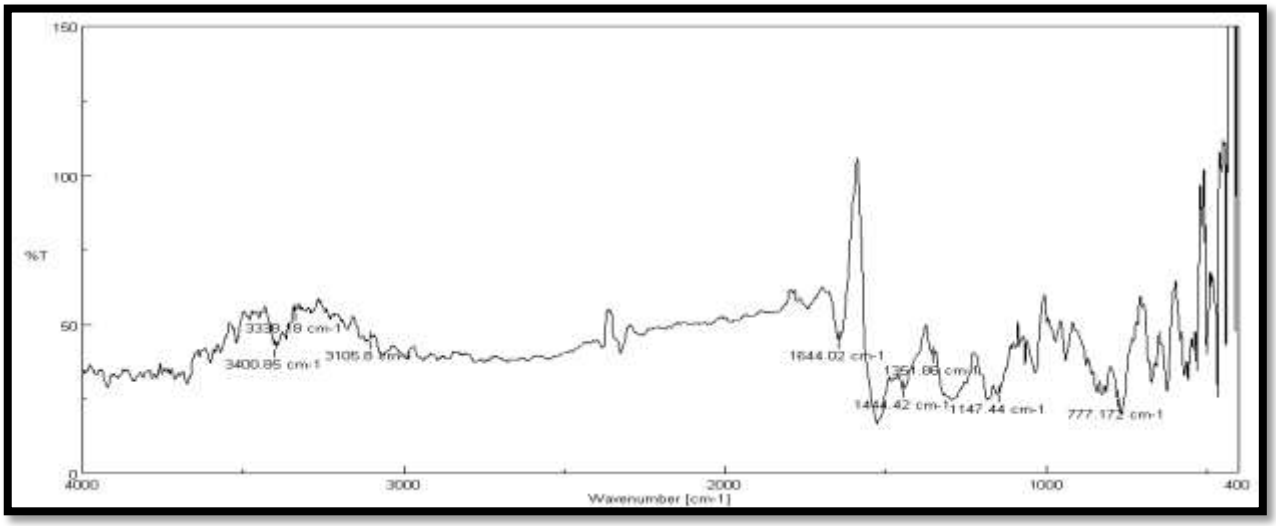



**Figure 3: IR Spectrum of Piroxicam**

**Table 7: IR values of Piroxicam**

| Functional Group | Wavenumber ($cm^{-1}$) |
|---|---|
| Cubic polymorphic form | 3338.18 |
| Aromatic C-H | 3105.8 |
| N-H group | 3400.85 |
| Streching of ortho –di-substituted phenyl | 771.172 |
| Stretching of SO2 –N-group | 1147.44 |
| Stretching of symmetric CH3 group | 1351.66 |
| Streching of asymmetric CH3 group | 1444.42 |
| Streching of amide carbonyl group | 1644.02 |

**Differential Scanning Calorimetry (DSC) Study**

The DSC analysis was carried out over 50–250∘C at 10∘C/min, using duplicate samples of 5mg in crimped aluminum pans. Indium samples were used to calibrate the DSC instruments.

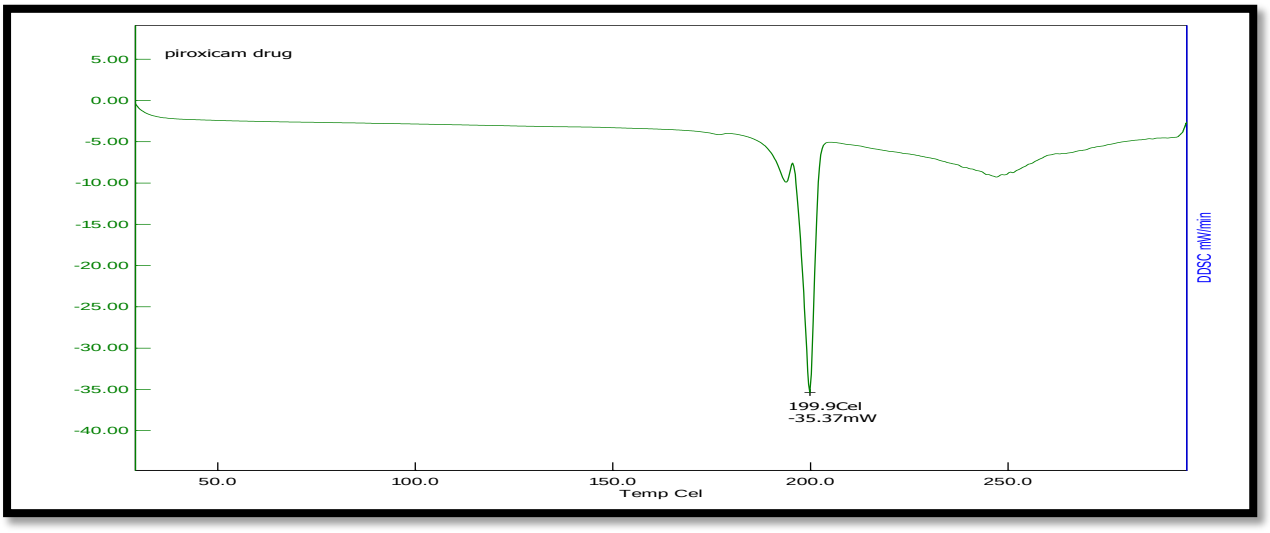



**Figure 4: DSC of Piroxicam**

**Table 8: Evaluation Test Results**

| Batch No. | Appearance | Density | pH | Viscosity (cps) | Floating buoyancy time(hr) |
|---|---|---|---|---|---|
| F1 | ++ | 0.998±0.04 | 7.2±0.55 | 57.76±0.78 | >24 |
| F2 | +++ | 0.891±0.09 | 7.4±0.23 | 73.23±0.34 | >24 |
| F3 | +++ | 0.978±0.08 | 7.5±0.12 | 129.29±0.19 | >24 |
| F4 | +++ | 0.884±0.2 | 7.4±0.37 | 74.66±0.08 | >24 |
| F5 | +++ | 0.992±0.06 | 7.1±0.69 | 87.61±0.07 | >24 |
| F6 | +++ | 0.792±0.3 | 7.7±0.54 | 150.05±0.29 | >24 |
| F7 | +++ | 0.964±0.05 | 7.4±0.26 | 96.23±0.96 | >24 |
| F8 | +++ | 0.992±0.06 | 7.3±0.78 | 105.56±0.24 | >24 |
| F9 | +++ | 0.985±0.09 | 7.5±0.11 | 171.06±0.03 | >24 |

**Note: All the values are expressed as mean ± SD, n=3**

**Table 9: Evaluation Test Results**

| Batch No. | Drug content (%) | Floating lag time(sec) | Sol to gel time (sec) | Swelling index |
|---|---|---|---|---|
| F1 | 96.02±0.45 | 140.69±3.70 | 7±0.38 | 90.63±0.3 |
| F2 | 89.67±1.51 | 126.54±3.70 | 5±0.25 | 95.56±0.15 |
| F3 | 107.13±2.87 | 131.25±1.45 | 4±0.67 | 91.12±0.27 |
| F4 | 98.60±5.96 | 175.18±1.57 | 3±0.28 | 97.15±0.10 |
| F5 | 82.02±0.57 | 136.87±2.67 | 8±0.7 | 93.25±0.2 |
| F6 | 97.54±1.36 | 119.46±2.38 | 3±0.45 | 94.02±0.1 |
| F7 | 95.63±0.86 | 127.12±2.76 | 6±0.57 | 91.55±0.3 |
| F8 | 99.08±3.98 | 139.66±4.10 | 5±0.21 | 92.33±0.4 |
| F9 | 91.86±1.02 | 122.15±2.47 | 7±0.69 | 96.02±0.3 |

**Note: All the values are expressed as mean ± SD, n=3**

**Appearance:**

The formulations were free running solutions and did not show any gelation at room temperature. All the formulations were milky yellow in appearance of all formulations.

**pH:**

They had pH in the range of 7-7.7 as shown in table 3, which was found to be satisfactory for orally administered formulation. Therefore there is no need for adjusting pH.

**Floating lag time:**

Results from table 3 depicts that all the formulations F1 to F9 showed in vitro floating lag time of less than 200 secs.

**Sol to gel time**:

All the formulations showed immediate gelation. Sol to gel time showed less than 10 secs.

**Viscosity:**

Results of viscosity formulation F1 to F9 were described in Table 7. The solutions showed a marked increase in viscosity with increasing concentration of gellan and sodium alginate.

**Density:**

The main condition of any floating system is that it should have density lesser than that of gastric contents (~1.004).The density of all floating in situ gel formulations were less than that of gastric contents.gm/cm3 This can obviously be a indicator to the floating ability of the formulations. The densities of F1-F9 formulations were found to be 0.792 to 0.998 gm/cm3 (Table 7).

**Swelling index:**

All the formulations exhibited the swelling index in the range of 90-99% shown I table no. 9.Because of xanthan gum showed highest swelling compare to other polymers in polymer screening.

**Drug content:**

The percent drug content of all formulations was present in the range of 82-107%,which shows loss of drug during the formulation .

**In Vitro Drug Release Studies**.

Drug release studies were carried out in USP type II dissolution rate test apparatus using 0.1 N HCL (pH 1.2) as dissolution medium at 37 ± 0.5∘C (Figure 6).In situ gelling emulgels are basically emulsions before coming into contact with acidic dissolution medium. When the in situ emulgel formulations come in contact with acidic dissolution medium, contained CaCO3 effervesces to release CO2 and Ca++. Free Ca++ ions then induce the gelation due to dimeric association of G block regions of sodium alginate. The release of drug from these gels was characterized by an initial phase of high release (burst effect). However, as gelation proceeds, the remaining drug was released at a slower rate followed by second phase as moderate phase. Initial burst release was reduced with increased concentration of polymers.

**Table 9: Dissolution studies of all above batches shows % cumulative drug release.**

| Time (hrs.) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 78.56± 0.2 | 71.81± 0.04 | 66.23± 0.2 | 61.75± 0.09 | 55.48± 0.1 | 51.48± 0.24 | 46.93± 0.3 | 40.54± 0.01 | 35.98± 0.12 |
| 2 | 85.63± 0.05 | 80.37± 0.4 | 74.39± 0.1 | 73.27± 0.05 | 63.81± 0.2 | 62.47± 0.36 | 60.17± 0.25 | 57.22± 0.15 | 46.93± 0.25 |
| 3 | 89.93± 0.25 | 85.86± 0.17 | 86.08± 0.14 | 80.68± 0.2 | 73.34± 0.14 | 69.76± 0.3 | 74.03± 0.14 | 66.01± 0.19 | 51.16± 0.34 |
| 4 | 95.49± 0.54 | 87.23± 0.21 | 89.98± 0.13 | 85.08± 0.24 | 80.37± 0.15 | 74.66± 0.37 | 76.16± 0.18 | 73.33± 0.05 | 59.99± 0.1 |
| 5 | 100.2± 0.56 | 92.57± 0.15 | 91.54± 0.18 | 87.41± 0.06 | 85.86± 0.24 | 77.57± 0.25 | 80.67± 0.2 | 80.12± 0.01 | 64.83± 0.05 |
| 6 | | 99.89± 0.06 | 93.78± 0.09 | 90.67± 0.08 | 87.81± 0.11 | 83.80± 0.18 | 81.67± 0.31 | 84.93± 0.02 | 70.32± 0.09 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 7 | 95.90± 0.1 | 92.48± 0.1 | 90.89± 0.15 | 88.05± 0.2 | 84.21± 0.27 | 85.95± 0.1 | 77.42± 0.26 |
| 8 | 98.23± 0.12 | 93.69± 0.19 | 92.55± 0.17 | 91.27± 0.4 | 86.41± 0.13 | 86.98± 0.06 | 84.23± 0.18 |
| 9 | | 94.24± 0.07 | 93.78± 0.04 | 92.82± 0.28 | 88.39± 0.26 | 88.96± 0.012 | 85.91± 0.07 |
| 10 | | 96.24± 0.07 | 95.26± 0.28 | 93.56± 0.3 | 91.82± 0.33 | 89.52± 0.09 | 86.02± 0.17 |

**Figure 5: Immediate gelation when placed in 0.1 N HCL**

**Figure 6:Optimized Batch F9**

**MECHANISM OF DRUG RELEASE**

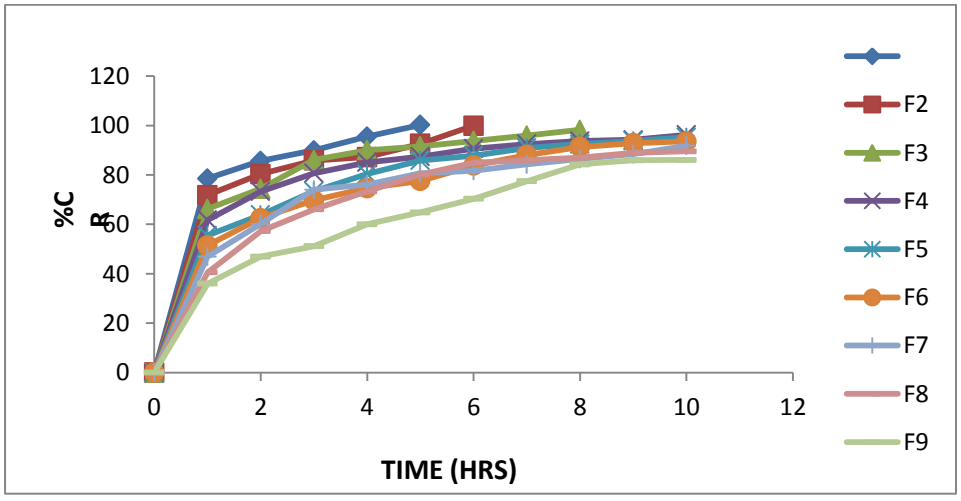
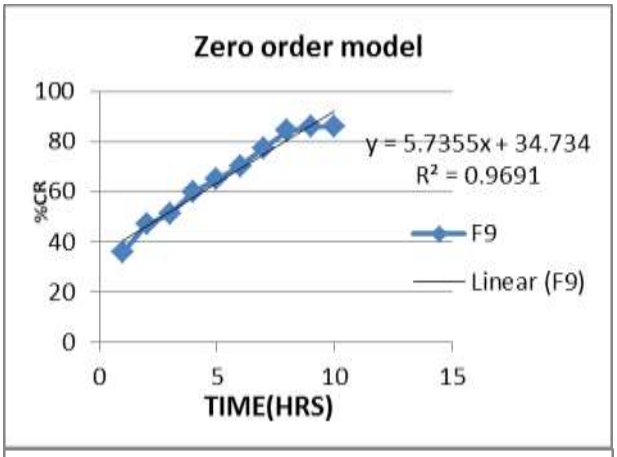


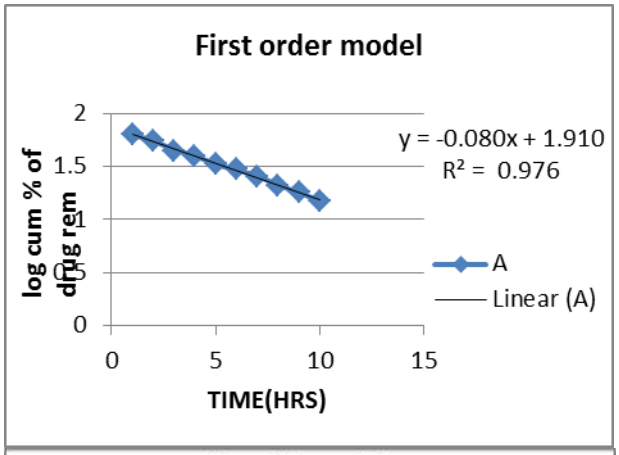

**Figure7 : In vitro drug release profile of batches (F1-F9)**

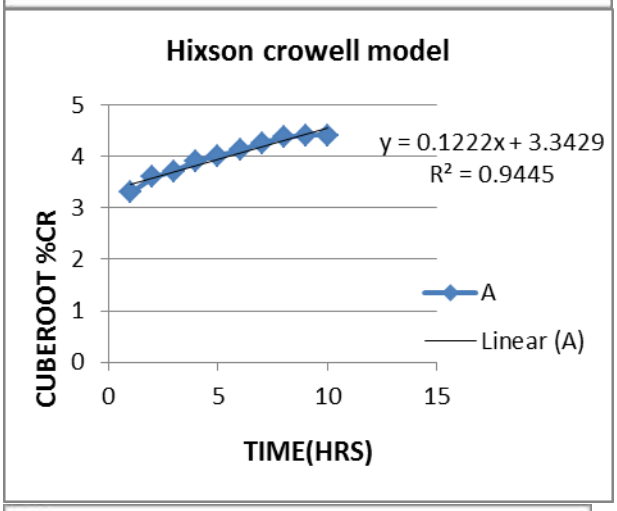
The in vitro release pattern of various formulations was analyzed by fitting the dissolution data into various kinetic models. Piroxicam release from in situ gelling emulgel showed linearity towards Higuchi square root model and krosmeyer release model (0.988, 0.988) for formulations Batch F9, indicating the release mechanism to be diffusion based. Higuchi model describes the release from systems where the solid drug is dispersed in an insoluble matrix and the rate of drug

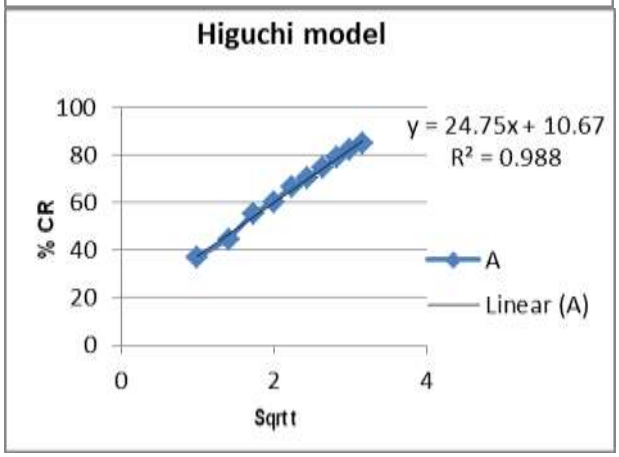
release is related to the rate of drug diffusion. krosmeyer release model indicating release mechanism for polymeric system formulation.

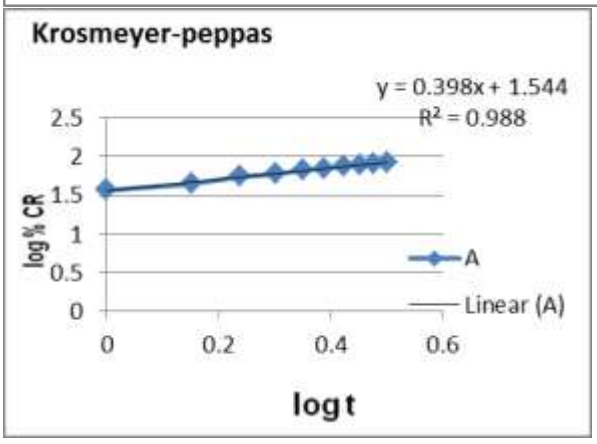
**Release kinetics of optimized batch(F9)**




| Release kinetic model | Regression coefficient ($R^2$) |
|---|---|
| Zero order | 0.969 |
| First order | 0.976 |
| Higuchi model | 0.988 |
| Hixson-Crowell model | 0.944 |
| Korsmeyer-Peppas model | 0.988 |

**Table 10: Stability Study at 25°C and 60% RH**

| Evaluation parameter | Initial | After 1 month | After 2 month | After 3 month |
|---|---|---|---|---|
| Appearance | +++ | +++ | +++ | ++ |
| PH | 7.5±0.11 | 7.6 | 7.7 | 7.9 |
| Floating lag time | 122.15±2.47 | 130.45 | 116.21 | 145.12 |
| Floating buoyancy time | >24 | >24 | >24 | >24 |
| Viscosity(cps) | 171.06±0.03 | 175.21 | 180.21 | 175.21 |
| Density | 0.985±0.09 | 0.971 | 0.948 | 0.915 |
| Swelling index | 96.02±0.3 | 91.47 | 94.23 | 92.71 |
| Drug content | 91.86±1.02 | 90.45 | 89.57 | 90.45 |
| In vitro drug release | 86.02±0.17 | 87.23 | 85.82 | 80.42 |

**Table 11: Stability studies at 30°C and 65%RH**

| Evaluation parameter | Initial | After 1 month | After 2 month | After 3 month |
|---|---|---|---|---|
| Appearance | +++ | +++ | ++ | ++ |
| PH | 7.5±0.11 | 7.6 | 8 | 7.8 |
| Floating lag time | 122.15±2.47 | 139.12 | 129.54 | 130.24 |
| Floating buoyancy time | >24 | >24 | >24 | >24 |
| Viscosity(cps) | 171.06±0.03 | 171.74 | 176.52 | 171.74 |
| Density | 0.985±0.09 | 0.854 | 0.944 | 0.839 |
| Swelling index | 96.02±0.3 | 95.62 | 96.41 | 94.24 |
| Drug content | 91.86±1.02 | 92.12 | 90.64 | 92.12 |
| In vitro drug release | 86.02±0.17 | 86.89 | 86.23 | 85.67 |

**Table 12: Stability studies at 40°C and 75%RH**

| Evaluation parameter | Initial | after 1 month | after 2 month | after 3 month |
|---|---|---|---|---|
| Appearance | +++ | +++ | +++ | +++ |
| PH | 7.5±0.11 | 7.7 | *7.9* | 8 |
| Floating lag time | 122.15±2.47 | 128.02 | 130.20 | 137.30 |
| Floating buoyancy time | >24 | >24 | >24 | >24 |
| Viscosity(cps) | 171.06±0.03 | 173.58 | 169.58 | 173.58 |
| Density | 0.985±0.09 | 0.963 | 0.890 | 0.805 |
| Swelling index | 96.02±0.3 | 93.15 | 95.66 | 91.63 |
| Drug content | 91.86±1.02 | 89.51 | 91.25 | 89.51 |
| In vitro drug release | 86.02±0.17 | 86.11 | 85.51 | 83.55 |

## CONCLUSION

In situ gelling emulsion was prepared by using oil phase Castor oil, Tween 80 as surfactant, Span 80 as co surfactant, Sodium alginate as gelling agent, Xanthan gum as release retardant, Other Excipients used were calcium carbonate as cross linking agent and sodium bicarbonate as effervescent agent. A floating in-situ gelling emulsion drug delivery system containing natural polymers was developed for stomach specific delivery of Piroxicam. It was concluded that Sodium alginate is important for in-situ emulgel behavior along with calcium carbonate and Xanthan Gum is vital for controlling and retardanting the release from formulations. It was observed from the in

vitro dissolution studies of nine batches ,batch 9 showed less burst release compared to other batches.F9 batch was selected as an optimized batch as all evaluation parameters results were satisfactory. Optimized batch F9 follows higuchi model and Korsmeyer -Peppas model release kinetics. Three month Stability study of optimized batch F9 indicated no significant change in physical parameters.

In the presented research, in situ gelling emulsion capable of floating on 0.1N HCL have been proposed as potential carrier for the controlled stomach specific delivery of gastric irritant drugs like NSAIDs. This study showed that in situ gelling emulsion have the possibility of forming gel both in vitro and in vivo and are capable of controlling the release of model drug, Piroxicam, over a period of 8 to 10 hours.

In conclusion, it is suggested that in situ gelling emulsion of Piroxicam may constitute a better option for controlled stomach specific delivery of gastric irritants drugs having absorption window in upper GIT, in terms of efficacy, patient compliance, and possibly improved safety profile especially for geriatric population.

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