Formulation and Evaluation of Floating Oral In-Situ Gel of Nitazoxanide

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Abstract:

Utilising gelling ingredients including HPMC, Sodium Alginate, and Sodium Carboxymethylcellulose, the Nitazoxanide oral In situ gel F1, F2, F3, F4, F5, and F6 was created. FT-IR spectroscopy was used to conduct a chemical compatibility analysis, and the results showed that there was no change in the principal peaks, indicating that there was no interaction between the medicine and excipients. Nitazoxanide's calibration curve was created in simulated stomach juice with a pH of 1.2. Six different nitazoxanide formulations In situ gel was prepared using varying concentrations of different polymers such as HPMC, Sodium Alginate and Sodium Carboxymethylcellulose as the release retardants. The prepared formulations (F1- F6) were evaluated for physical appearance, pourability, pH, viscosity, In vitro gelation study, In vitro buoyancy study, density, drug content and In vitro drug release. All of the formulations looked excellent on the outside. Except for F5, all of the formulations quickly formed and dispersed in a solution that contained only sodium alginate and HPMC as the primary polymers. All of the formulations demonstrated floating with a lag time of less than one minute and for longer than eight hours. All of the formulations had densities that were less than the 1.04gcm3 density of stomach fluid. The percentage of medicines in each formulation ranged from 88.34 to 96.78%, showing a consistent distribution of the pharmaceuticals. Only formulation F5 released 98.68% of the drug at the end of 8 hours, according to an in vitro drug release study; the other formulations released more than 97.62% of the drug even before 8 hours had passed. The optimised formulation F5 in vitro release kinetics investigation revealed that the formulation adhered to zero order kinetics. According to the stability analyses, the optimised formulation F5 was stable and did not exhibit any appreciable changes in its physical characteristics, pH, floating time, viscosity, drug content, or in vitro drug release after three months. The overall findings show that the controlled release of the medicine is achieved by the formulation of nitazoxanide as an oral floating in situ gel. Due to the simplicity of administration and decrease in dosage frequency, this may result in better patient compliance. In order to treat patients' diarrhoea (protozoals), the created formulation can be utilised instead of the usual dosage form.

Keywords: *Nitazoxanide, Floating time, Diarrhoea (protozoals), Gelation*

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Introduction:

Floating Drug Delivery System is one of the novel systems of drug delivery. Various dosage forms are formulated in the form gastro retentive floating systems such as microspheres, micro beads, tablets, capsules, films etc. In-situ gelling system is a new trend in floating DDS. In-situ gelling system have its application in different routes of administration like oral,

nasal, ophthalmic, peroral, rectal, vaginal and also parenteral route. In situ forming polymeric drug delivery systems has many advantages such as ease of administration, increased local bioavailability, reduced dose frequency, improved patient compliance and has less complex method of production and so is cost effective. Gastro retentive FDDS have bulk density lower than gastric fluid and hence remain buoyant in stomach without affecting the gastric emptying rate for a long period of time. When the gel so formed float on gastric fluid the drug get released slowly at desired rate from the floating gel. After drug is released from floating system, the residual part is emptied from stomach. This may increase GRT and also control the fluctuations in plasma drug concentration (PCD). Floating system are the controlled or sustained release dosage form and have properties similar to hydrophilic matrices and so called as hydro-dynamically balanced system (HBS) as they form a low density polymeric gel barrier at outer surface. Drug is slowly released from the matrices same as that in case of conventional hydrophilic matrices. This form may remain buoyant (8-10 hours) on gastric contents without affecting the rate of gastric emptying. Different polymer systems are used in floating drug delivering dosage forms. Among those some are polysaccharides, polymethacrylates, hydrocolloids etc. in this cellulose ether polymers are most popular, especially HPMC. The formulation of floating in situ gelling solution may sustain and prolong drug action, improve patient compliance and reduce frequency of administration of the drug in comparison to conventional drug delivery system [1-9].

In-Situ Gelling System:

This novel drug delivery system promotes importantly ease and convenience of administration, deliverance of accurate dose as well as to prolong residence time of drug in contact with mucosa that problems generally encountered in semisolid dosage forms. In situ gel formation occurs due to one or combination of different stimuli like pH change, temperature modulation and solvent exchange. Smart polymeric systems represent promising means of delivering the drugs; these polymers undergo sol-gel transition, once administered. From the early 1970's natural and synthetic polymers began to be investigated for controlled release formulations. The advantages of using biodegradable polymers in clinical applications are apparent. Various natural and synthetic polymers are used for formulation development of in situ forming drug delivery systems [10].

Materials and Methods

Materials Used:

Table.1: List of Chemicals

S. No	Drug and Excipients	Brand
1	Nitazoxanide	Medivac International Rohini New Delhi
2	Sodium Alginate (Sa)	Agra Public Institute of Technology & Computer Education
3	HPMC	-
4	Ethyl Cellulose	-
5	Sodium Carboxy-methylcellulose	-
6	Sodium Bicarbonate	-
7	Calcium Carbonate	-

Equipments Used:

Table.2: List of Equipments Used

Instrument	Supplier
UV-Vis Spectrophotometer	Shimadzu 1800, Japan
Weighing Balance	MC Dalal, Chennai
Magnetic Stirrer	REMI Instruments, Mumbai
pH Meter	MC Dalal, Chennai
Brookfield Viscometer	DV-II+ Pro
Dissolution Apparatus	Thermonik, Campbell Electronics, Mumbai
Stability Chamber	Remi-chi 6 plus, Mumbai
FT-IR	8400S, Shimadzu, Japan

Preformulation Study:

Preformulation study is defined as "investigation of physical and chemical properties of the drug substance alone and combined with the excipients". Preformulation studies are the first step in the rational development of dosage form of drugs. It involves the application of biopharmaceutical principles to the physicochemical parameters of the drug with the goal of designing an optimum delivery system that is stable, bioavailable and can be mass produced [11].

Determination of Melting Point of Nitazoxanide:

The melting point of Nitazoxanide was determined by the capillary tube method according to the USP. A sufficient quantity of Nitazoxanide powder was filled into the capillary tube to give a compact column of 4-6 mm in height. The tube was introduced in an electrical melting point apparatus and the temperature was raised. The melting point was recorded, which is the temperature at which the last solid particle of Nitazoxanide in the tube passed into liquid phase [12].

Determination of λ_{max} of Nitazoxanide:

100mg of Nitazoxanide was accurately weighed and transferred to a 100ml volumetric flask. The drug was dissolved in solvent and the volume was made up to 100ml to obtain a stock solution of 1000µg/ml (Stock I). 10ml of this stock solution was again diluted with 0.1 HCl up to 100 ml to obtain a solution of 100µg/ml (Stock II). From the stock II, 10ml of the solution again diluted with 100ml of the 0.1 HCl. The resulting solution was scanned between 200nm and 400nm in a double beam UV-Visible spectrophotometer [13].

Solubility:

Solubility is an important parameter for pre-formulation studies. Because it affects the dissolution of the drug and the bioavailability of the drug is directly affected by dissolution and absorption of drug by oral administration [14].

Preparation of Calibration Curve for Nitazoxanide:

Standard solution was prepared by dissolving accurately 100mg of bulk Nitazoxanide in 5 ml of methanol and made up to the volume with 0.1N HCl. 10ml of the stock solution of was pipetted out in a separate 100ml standard flask and the volume was made up using 0.1N HCl. From the resulting solution 2, 4, 6, 8 and 10ml were pipetted out into separate

100ml standard flask and made up to volume using 0.1N HCl. The absorbance was measured at 346nm against the reagent blank. Then, the calibration curve was obtained by plotting concentration versus absorbance [15].

Chemical Compatibility Study:

Fourier transform infrared (FTIR) spectroscopy was performed using a Shimadzu FTIR 8400 spectrophotometer from 4000 to 400 cm^{-1} region. The procedure consists of dispersing the sample (drug alone, mixture of drug and excipients) in KBr and made into disc form by compressing it with a pressure of 3 tons in a hydraulic press. The pellet was placed in the light path and the spectrum was recorded [16].

Preparation of oral *In situ* Gel of Nitazoxanide:

- Various concentrations of Gelling polymer Sodium Alginate was dissolved in de-ionized water with a weighed amount of sodium Bicarbonate on a magnetic stirrer at 70ºC.
- Sodium Carboxy Methyl Cellulose solution was prepared separately by dissolving in de-ionized water containing sodium Bicarbonate and heating to 80ºC while stirring.
- In another beaker, the required quantity of release retardant polymer HPMC was soaked in de-ionized water until completely dissolved.
- Then, all the three solutions were mixed together with continuous stirring.
- After the above solution was cooled down to 40ºC, Calcium Carbonate, Sodium Bicarbonate and Nitazoxanide previously dissolved in water were added.
- Ethyl Cellulose and preservative were then mixed.

Table.3: Composition of the *In situ* Gel Formulation

INGREDIENTS	F1	F2	F3	F4	F5	F6
Nitazoxanide (mg)	100	100	100	100	100	100
HPMC % w/v	0.5	0.5	0.4	0.6	0.8	0.8
Sodium Alginate % w/v	0.6	0.6	0.6	0.6	0.6	0.6
Ethyl Cellulose % w/v	0.4	0.4	0.4	0.4	0.4	0.4
Sodium bicarbonate % w/v	0.20	0.20	0.20	0.20	0.20	0.20
Calcium Carbonate % w/v	0.4	0.4	0.4	0.4	0.4	0.4
Na- Carboxy Methly Cellulose % w/v	0.10	0.10	0.10	0.10	0.10	0.10
De-ionized Water to Produce (ml)	100	100	100	100	100	100

Evaluation of Floating Gel:

Appearance:

All the formulations were visually inspected for their appearance, clarity and consistency [17].

pH Measurement:

The pH of the formulations was measured using a calibrated pH meter. The readings were recorded three times for each of the formulations and the averages of the readings were considered [18].

Viscosity Measurement:

Viscosity of the prepared in situ gel formulations of Nitazoxanide was determined using a rotational viscometer (Finlab Nigeria Ltd). Viscosity was measured at different angular velocities (from 20 to 100 rpm) using spindle number 2 at room temperature [19].

Floating Behaviour:

The floating ability of the prepared formulations was evaluated in (0.1N HCl, pH 1.2) Solution. The floating time of the prepared formulation took to emerge on the medium surface (floating lag time) was found to be 60sec.The time the formulation constantly floated on the dissolution medium surface (duration of floating) was evaluated to be 12hrs resulting the formation of thick gel with good floating tendency [20].

Gelling capacity:

5ml of the simulated gastric fluid (0.1N HCl, pH 1.2) was taken in a 10 ml test tube, maintained at 37ºC, followed by the addition of 1 ml of the formulation using a pipette. The pipette was positioned facing the surface of the fluid in the test tube and slowly the formulation was released from the pipette. When the formulation came in contact with the gelation medium, it was quickly converted into a gel-like structure. Based on the stiffness of gel as well as the duration for which the gel remains as such the *in vitro* felling capacity was investigated [21].

The *in vitro* gelling capacity was mainly divided into three categories based on gelation time and the time period of the formed gel remains.

- (+): gelation in few seconds, disperse immediately.
- (++): gelation immediate, remains for few hours.
- (+++): gelation after few minutes, remains for extended period.

Determination of Drug Content:

5 ml of the formulation equivalent to 100mg of the drug was added to 100ml of 0.1N HCl (pH 1.2) in a 100ml standard flask and stirred well. After 1 hr, the solution was filtered. The drug concentration was then determined by UV-Vis spectrophotometer at 346nm against a suitable blank solution [22].

In-Vitro Floating Study:

The studies were conducted in a USP Type II dissolution apparatus using simulated gastric fluid (pH 1.2) as the medium at 37±0.5ºC. About 10 ml of the *In situ* gel formulation was placed in the medium. The time taken by the *In situ* gel formulation to float on the surface of the medium (floating lag time) and time period for which the formulation remained buoyant (duration of floating) was noted [23-24].

In-Vitro Drug Release Study:

The dissolution studies were performed using a USP was 500ml of 0.1N HCl (pH 1.2), maintained at 37ºC. The stirring rate was adjusted to 50 rpm. This speed believed to

stimulatethe *In vivo* existing mild agitation and was slow enough to avoid the breaking of the gelled formulation. At the predetermined time intervals, 10ml samples were withdrawn and replaced by fresh dissolution medium, filtered through whatmann filter paper, diluted and assayed at maximum absorbance at 346nm using UV-Vis spectrophotometer [25-26].

Release Kinetic Study:

To study the in vitro release kinetics of the optimized formulations of Nitazoxanide oral *In situ* gel, data obtained from dissolution study were plotted in various kinetic models [27].

Zero Order Kinetics:

The zero-order release can be obtained by plotting cumulative % drug release vs. time in hours. It is ideal for the formulation to have a release profile of zero order to achieve pharmacological prolonged action.

$$C = K_0 t$$

Where,

K_0 = zero order constant.

t = time in hours.

First Order Kinetics:

The graph was plotted as log cumulative % drug remaining vs. time in hours.

$$\text{Log } C = \log C_0 - Kt/2.303$$

Where,

C_0 = initial concentration of drug.

K = first order.

t = time in hours.

Higuchi Kinetics:

The graph was plotted with cumulative % drug released vs. square root of time.

$$Q = Kt^{1/2}$$

Where,

K = constant reflecting design variable system (differential rate constant).

t = time in hours.

The drug release rate is inversely proportional to the square root of time.

Korsmeyer – Peppas Kinetics:

To evaluate the mechanism of drug release, it was further plotted in Korsmeyer – Peppas equation as Log cumulative % of drug released Vs Log time.

$$Mt/M\alpha = Kt^n$$

Where,

Mt/Mα = Fraction of drug released at time t.

T = Release kinetics**.**

K= Kinetics constant.

N = Diffusional exponent indicative of the mechanism of drug release.

Stability Studies:

The optimized formulation of the *In situ* gel was placed in an amber colour bottle. It was tightly sealed. The stability study was carried out as per the ICH guidelines, i.e., Accelerated temperature 40 ± 2 °C / 75 ± 5 % RH for 1 month. Samples were withdrawn periodically (0 and 30 days) and evaluated for visual appearance, pH, floating behavior, gelling capacity, drug content as well as *In vitro* drug release [28-30].

Results and Discussion

Preformulation Study:

Melting point of Nitazoxanide:

Melting point was measured using capillary tube method. It was found to be 199ºC. The melting point of Nitazoxanide is within the limits (198-202º C).

Determination of λ_{max} of Nitazoxanide:

The maximum absorbance of the Nitazoxanide was studied and found to be 346nm. Hence, the wavelength of 346nm was selected for estimation of drug content and analysis of drug in dissolution media.

Calibration Curve of Nitazoxanide:

The UV- Visible Spectrophotometry method was used to analyze Nitazoxanide. The absorbance of the drug in 0.1N HCL (pH 1.2), was measured at 346nm. The results are given in Table 6.1. The calibration curve is shown in Fig.4.

Table.4: Calibration Data of Nitazoxanide

Conc. (µg/ml)	Abs. (nm)
2	0.308
4	0.486
6	0.646
8	0.791
10	0.966

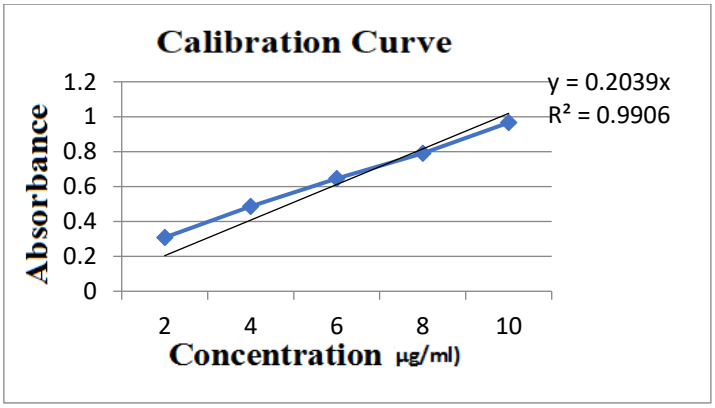

Fig.1: Calibration curve of Nitazoxanide

Solubility:

Solubility of Nitazoxanide was checked in various solvents.

Table.5: Determination of Drug Solubility in Various Solvents

S.No.	Solvents	Descriptive Term
1	Acetone	Soluble
2	Ethanol	Soluble
3	Water	Soluble

6.1.5 Chemical Compatibility Study:

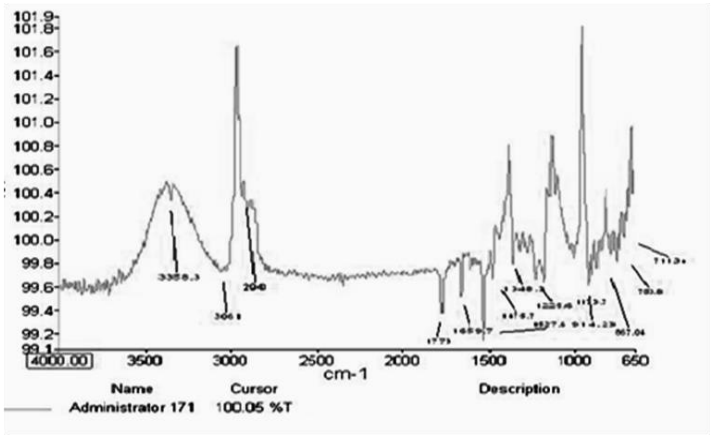

Fig.2: FTIR Study of Nitazoxanide

Table.6: Interpretation of IR spectra of pure drug

S.No.	Functional Group	Range (cm-1)	Observed Frequency (cm-1)
1	Carbonyl group ester linkage	1690-1760	1784
2	Amide linkage	1700-1680	1652.7
3	Nitro group	1500-1378	1532.56
	=CH Stretch	2960-2850	3092.28

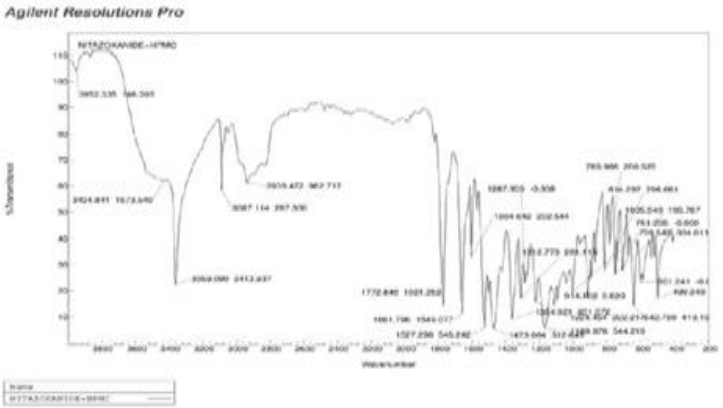

Fig.3: FTIR Study of Nitazoxanide & HPMC

Table.7: Interpretation of IR spectra of pure drug + HPMC Polymer

S.No.	Functional Group	Range (cm-1)	Observed Frequency (cm-1)

1	Carbonyl group ester linkage	1690-1760	1780
2	Amide linkage	1700-1680	1656.8
3	Nitro group	1500-1378	1532.56
	=CH Stretch	2960-2850	3090.32

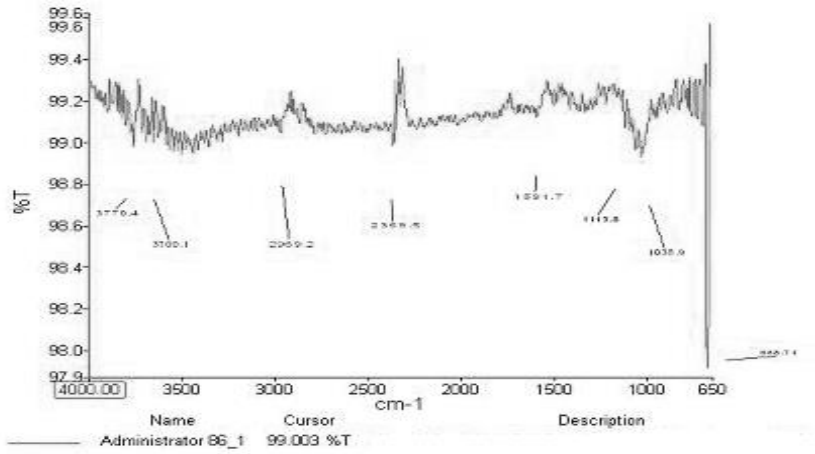

Fig.4: FTIR Study of Nitazoxanide & Sodium Alginate

Table.8: Interpretation of Nitazoxanide & Sodium Alginate

S.No.	Functional Group	Range (cm-1)	Observed Frequency (cm-1)
1	Carbonyl group ester linkage	1690-1760	1734
2	Amide linkage	1700-1680	1692.4
3	Nitro group	1500-1378	1432.43
	=CH Stretch	2960-2850	2942.18

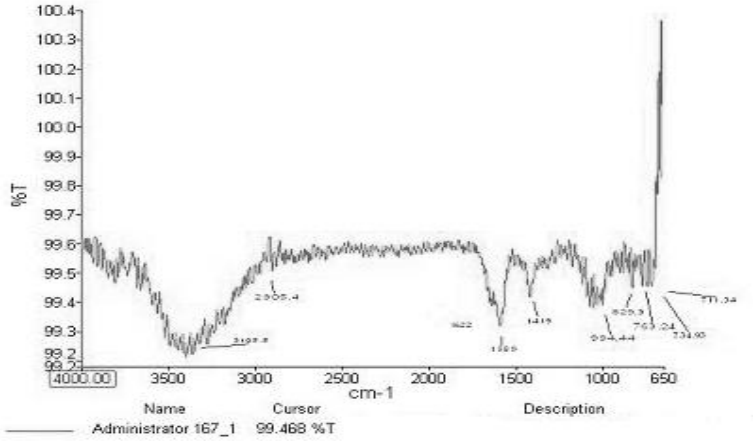

Fig.5: FTIR Study of Nitazoxanide & Sodium-CMC

Table.9: Interpretation of IR spectra of pure drug & Sodium-CMC

S.No.	Functional Group	Range (cm-1)	Observed Frequency (cm-1)
1	Carbonyl group ester linkage	1690-1760	1764
2	Amide linkage	1700-1680	1612.2

3	Nitro group	1500-1378	1512.23
	=CH Stretch	2960-2850	2998.24

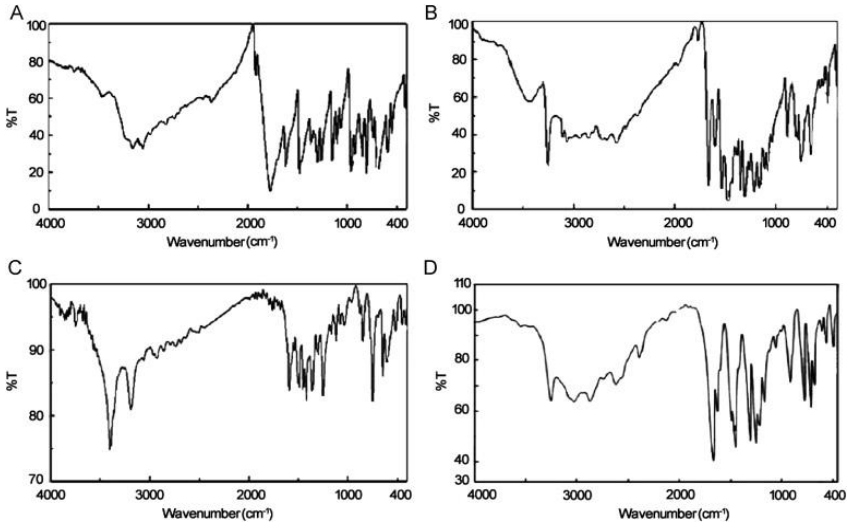

Fig.6: FTIR Study of Nitazoxanide, Ethyl Cellulose, Sodium Bicarbonate & Calcium Carbonate

Table.10: Interpretation of IR spectra of pure drug & Ethyl Cellulose, Sodium Bicarbonate & Calcium Carbonate

S.No.	Functional Group	Range (cm-1)	Observed Frequency (cm-1)
1	Carbonyl group ester linkage	1690-1760	1493
2	Amide linkage	1700-1680	1512.6
3	Nitro group	1500-1378	1452.43
	=CH Stretch	2960-2850	2898.74

Evaluation of Floating Gel:

Physical Appearance of Nitazoxanide oral *In situ* gel:

The visual appearance of the formulation is an important parameter as it has an impact on the patient compliance. All the formulations are visually inspected for their appearance, clarity and consistency. The results are given in Table.11.

Fig.7: Appearance of Nitazoxanide oral *In situ* gel

Table.11: Physical Appearance of *In situ* gel

S. No	Formulation Code	Appearance	Pourability
1	F1	Dull White	Pourable
2	F2	Dull White	Pourable
3	F3	Dull White	Easily Pourable
4	F4	Dull White	Pourable
5	F5	Dull White	Pourable
6	F6	Dull White	Pourable

Table.12: Evaluation Parameters of *In situ* gel

Formulation Code	pH Measurement	Viscosity Measurement	Floating Behaviour	Floating Lag Time (min)	Gelling Capacity	% Drug Content
F1	6.54	188	>8	<1	++	88.34
F2	7.38	156.76	>8	<1	++	92.96
F3	7.26	106.24	>8	<1	+	94.89
F4	6.64	162	>8	<1	+	90.45
F5	7.49	198.90	>8	<1	+++	96.78
F6	7.16	204.36	>8	<1	++	92.38

Inference:

The pH of all the formulations was within the orally acceptable range (i.e., salivary pH range 6.6-7.6). Therefore, it will not cause any irritation on administration of the formulations. The Gelling capacity (+) – Gelation in few seconds disperses rapidly. (++) – Gelation immediate remains for few hours. (+++)- Gelation after few minutes remains for extended period. All the *In situ* gel formulations had a floating lag time of <1 min and all the formulations floated for more than 8 hours except, formulation F5. Therefore, the extended duration of floating may be responsible for the controlledrelease of drug. The percentage drug content of all the formulations was in the range of 88.34–96.78% indicating equal distribution of drugs in all the formulations.

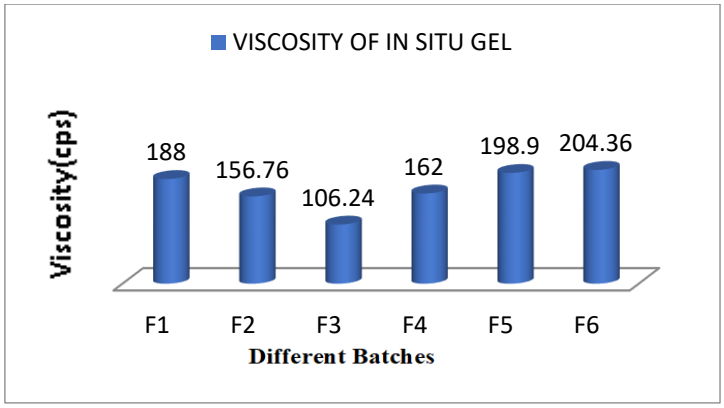

Fig.8: Viscosity of *In situ* Gel formulation

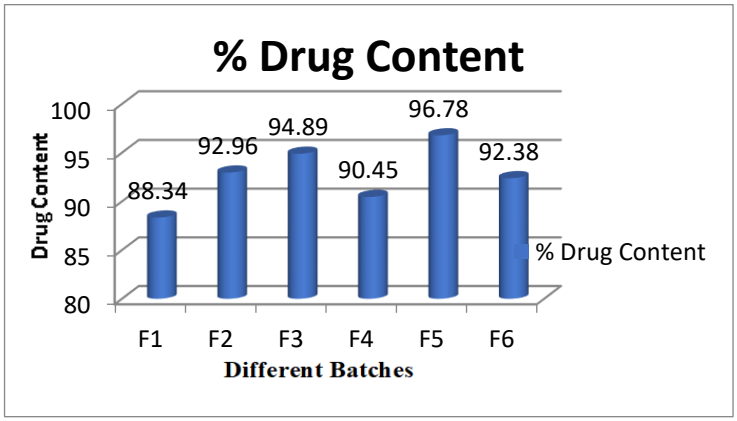

Fig.9: Percentage drug content of *In situ* Gel

In-Vitro Drug Release Study:

Table.13: In-Vitro Drug release of Nitazoxanide in situ gel Formulations (F1- F6)

Time (Hrs)	**% cumulative drug release from various batches**					
Formulation Code	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
0	0	0	0	0	0	0
1	18.10	21.06	16.65	26.76	22.50	23.70
2	30.09	30.76	20.86	38.40	34.61	32.84
3	46.34	46.52	28.56	49.32	48.30	40.12
4	62.54	62.08	38.18	58.32	56.59	49.16
5	74.86	77.24	48.80	66.92	69.45	56.97
6	84.12	82.12	68.73	76.41	78.82	68.42
7	90.66	89.15	78.35	88.16	88.42	78.90
8	94.86	95.94	90.87	97.62	98.68	89.10

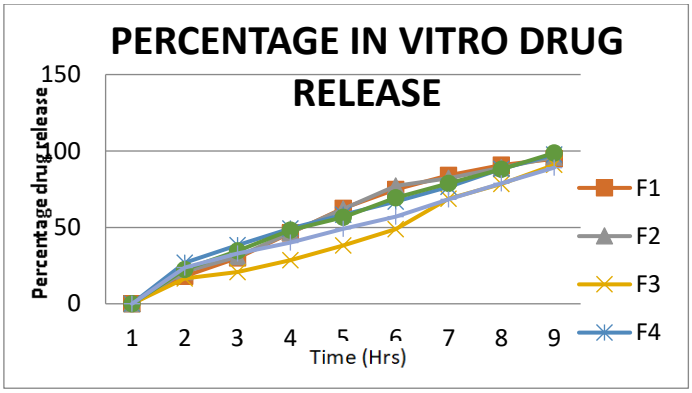

Fig.10: *In vitro* drug release study of *In situ* gel formulations (F1-F6) of Nitazoxanide

Inference

From the *In vitro* drug release studies of *the In situ* gel formulations, it was observed that only the formulation F5 containing the combination of both the polymers in higher concentration (HPMC and Sodium-CMC) provided prolonged release of the drug up to 8 hours. Other formulations released the drug even before the period of 8 hours. Formulation F5 containing both HPMC & CMC (ratio of 9:1) showed 98.68 % of drug release at the end of 8 hours.

Release Kinetics of In-vitro Drug Release:

Different kinetic models, including zero order, first order, Higuchi, and Korsmeyer-Peppas, were used to analyze in-vitro drug release data in order to derive the drug's release kinetics.

Table.14: Release Kinetics of In-vitro Drug Release

Formulation Code	Zero Order r^2	1st Order r^2	Higuchi r^2	Peppas r^2	Best Model
F1	0.971	0.970	0.985	0.691	Zero Order
F2	0.969	0.974	0.981	0.664	Higuchi
F3	0.981	0.948	0.988	0.718	Higuchi
F4	0.972	0.974	0.964	0.597	1st Order
F5	0.985	0.972	0.981	0.640	Zero Order
F6	0.980	0.978	0.955	0.613	Zero Order

The *In vitro* release of optimized formulation F5 data was fit into various kinetic models to find out the mechanism of drug release from Nitazoxanide oral *In situ* gel. Good linearity was observed with the zero order (R^2 = 0.985). The zero-order kinetics explains the controlled release of drug in the prepared *In situ* gel over the period of 8 hours. The slope of the regression line from the Higuchi plot (R^2 = 0.981) indicates that the rate of drug release follows both diffusion and dissolution mechanism. The slope of the Korsmeyer- Peppas plot (r = 0.640) Thus, the release kinetics of the optimized formulation showed zero order drug release with non fickian diffusion mechanism.

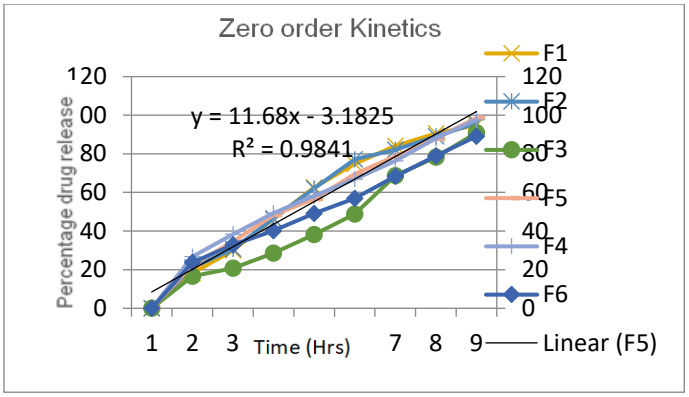

Fig.11: Plot of Zero order kinetics of optimized formulation (F1-F6)

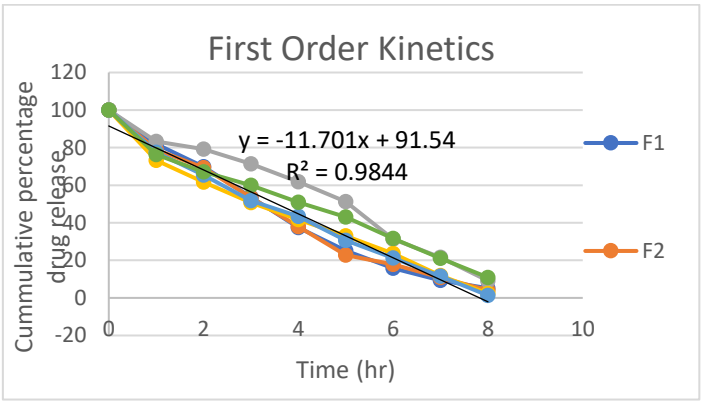

Fig.12: Plot of first order kinetics of optimized formulation (F1-F6)

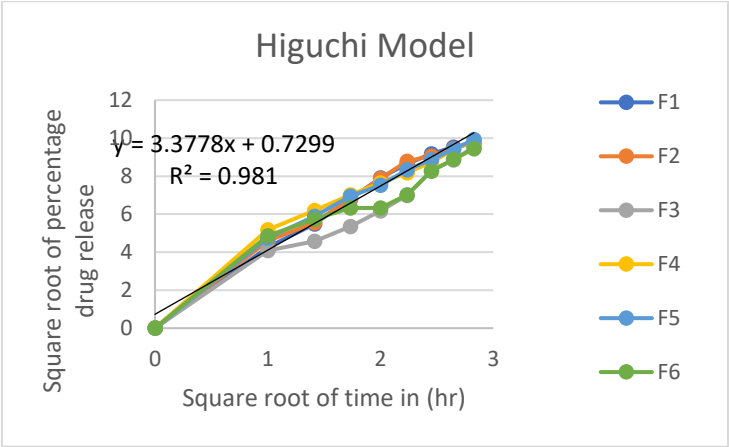

Fig.6.13: Plot of Higuchi Model of optimized formulation (F1-F6)

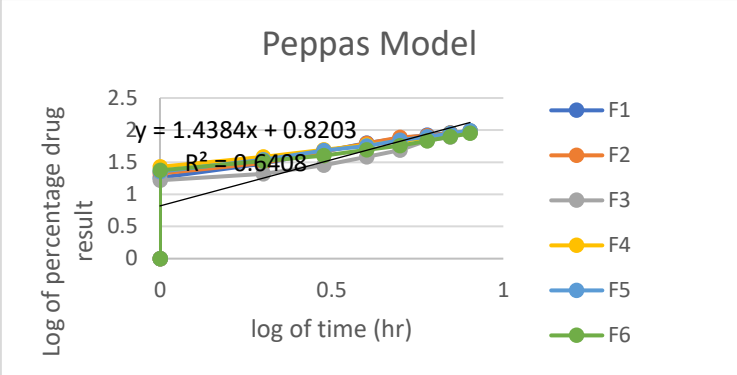

Fig.14: Plot of Peppas Model of optimized formulation (F1-F6)

Stability Studies:

The optimized formulation (F5) was subjected to stability studies as per ICH guidelines and shown in Table.15.

Table.15: Stability Studies of the best formulation F5

Parameter	**Condition: 40 ± 2º C / 75 ±5% RH**				
	Day 0	**Day 15**	**Day 30**	**Day 60**	**Day 90**
Visual appearance	Dull white	Dull white	Dull white	Dull white	Dull white
Ph	7.49	7.40	7.09	7.00	6.90
Gelling capacity	+++	+++	+++	+++	+++
Floating lag time (min)	<1	<1	<1	<1	<1
Floating duration(hrs)	>8	>8	>8	>8	>7
Viscosity (cps)	198.90	298.70	290.54	285.33	278.79
Drug content (% w/v)	96.78	96.54	96.35	96.24	96.14
In-Vitro Drug release study	98.68	98.68	98.60	98.10	97.68

Discussion:

The duration of stability studies of the Formulation F5, there is no major variation, the minor variation found in pH, Floating Duration (hrs), Viscosity (cps), Drug Content Uniformity & In-Vitro Drug release study that is adjustable, All data evaluated according to ICH guidelines at 40±2°C/75±5% RH for 90 days.

Summary and Conclusion:

The Nitazoxanide oral *In situ* gel F1, F2, F3, F4, F5 and F6 was developed using gelling agents such as HPMC, Sodium Alginate and Sodium Carboxymethylcellulose. Chemical compatibility study was performed using FT-IR spectroscopy and its studies revealed that there was no change in major peaks, thus confirming no interaction between the drug and

Excipients. Calibration curve of Nitazoxanide was constructed in simulated gastric fluid of pH 1.2. 6-formulations of Nitazoxanide *In situ* gel was prepared using varying concentrations of different polymers such as HPMC, Sodium Alginate and Sodium Carboxymethylcellulose as the release retardants. The prepared formulations (F1- F6) were evaluated for physical appearance, pourability, pH, viscosity, *In vitro* gelation study, *In vitro* buoyancy study, density, drug content and *In vitro* drug release. All the formulations had good physical appearance. All the formulations except F5 was formed dispersed rapidly in the containing only HPMC & Sodium Alginate as the main polymer. All the formulations showed floating lag time of less than 1 minute and duration of floating are greater than 8 hours. All the formulation exhibited lower density than the density of gastric fluid (~1.04gcm^{-3}). The percentage drug content of all the formulations was in the range of 88.34-96.78% indicating uniform distribution of drugs. *In vitro* drug release study showed that only the formulations F5 released 98.68% of drug respectively at the end of 8 hours, while the other formulations showed more than 97.62% of drug release even before the period of 8hours. *The In vitro* release kinetics study of the optimized formulation F5 showed that the formulation followed Zero order kinetics. The stability studies indicated that the optimized formulation F5 was stable and did not show any significant changes in the physical appearance, pH, floating time, viscosity, drug content and *In vitro* drug release at the end of 3 months. The overall results indicate that the formulation of Nitazoxanide as oral floating *In situ* gel provides controlled release of the drug. This may improve the patient compliance due to ease of administration and reduction in dosing frequency. Hence, the developed formulation can be used as an alternative to the conventional dosage form for the treatment of Diarrhea (Protozoals) in patients.

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