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FORMULATION AND EVALUATION OF METRONIDAZOLE EMULGELS USING VARIOUS POLYMERS

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ABSTRACT

The purpose of the present study was to develop and optimize the emulgel system for Metronidazole using different types of gelling agents: HPMCK4M, Carbopol 940 and Xantham Gum. The prepared emulgels were evaluated in terms of appearance, pH, spread ability, viscosity, drug content and in-vitro drug release. In-vitro release study demonstrated diffusion controlled release of metronidazole from formulation up to 12 hours. The drug release profile exhibited zero order kinetics. All the prepared emulgels showed acceptable physical properties concerning colour, homogeneity, consistency, spreadability, and with higher drug release than conventional gel as per USP. In case of all evaluation parameters carbopol based formulation showed better properties so, As a general conclusion, it was suggested that the Metronidazole emulgel formulation prepared with carbopol highest concentration was the formula of choice.

KEYWORDS: Metronidazole, Carbopol 940, Xanthan Gum, optimization, Anti-Protozoal activity.

INTRODUCTION

Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. These are apply a wide spectrum of preparations for both cosmetic and dermatological, to their healthy or diseased skin. These formulations range in physicochemical nature from solid through semisolid to liquid. Drug substances are seldom administered alone, but rather as part of a formulation, in combination with one or more non medicated agents that serve varied and specialized pharmaceutical

function. Drugs are administered topically for their action at the site of application or for systemic effects. Drug absorption through the skin is enhanced if the drug substance is in solution, if it has a favorable lipid/water partition coefficient and if it is a no electrolyte. For the most part, pharmaceutical preparations applied to the skin are intended to serve some local action and as such are formulated to provide prolonged local contact with minimal systemic drug absorption.. The main advantages of topical delivery system is to bypass first pass metabolism. Avoidance of the risks and inconveniences of intravenous therapy and of the varied conditions of absorption like pH changes, presence of enzymes, gastric emptying time are other advantages of topical preparations. The topical drug delivery system is generally used where the others system of drug administration fails or it is mainly used in fungal infection. Human skin is a uniquely engineered organ that permits terrestrial life by regulating heat and water loss from the body while preventing the ingress of noxious chemicals or microorganisms. Gels are a relatively newer class of dosage form created by entrapment of large amounts of aqueous or hydroalcoholic liquid in a network of colloidal solid particles, which may consist of inorganic substances, such as aluminum salts or organic polymers of natural or synthetic origin. They have a higher aqueous component that permits greater dissolution of drugs, and also permit easy migration of the drug through a vehicle that is essentially a liquid, compared with the ointment or cream base. These are superior in terms of use and patient acceptability. In spite of many advantages of gels a major limitation is in the delivery of hydrophobic drugs. So to overcome this limitation, emu gels are prepared and used so that even a hydrophobic therapeutic moiety can enjoy the unique properties of gels.[1-2]

There are three primary mechanisms of topical drug absorption: transcellular, intercellular, and follicular. Most drugs pass through the torturous path around corneocytes and through the lipidbilayer to viable layers of the skin.

They are convenient to apply on hairy skin due to absence of greasiness and lack of residues upon application.

Rationale of Emulgel

Many widely used topical agents like ointment, cream, lotion have many disadvantages. They have very sticky causing uneasiness to the patient when applied due to some reasons. Moreover they also have lesser spreading coefficient and need to apply with rubbing which may cause dermatitis. And they exhibit the problem of stability also.

Due to all these factors within the major group of semisolid preparations, the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparations. A gel is colloid that is typically 99% wt liquid, which is immobilized by surface tension between it rubbed into the skin have been used for years to deliver pain medication and infection fighting drugs to an affected site of the body.

Strategies to Enhance Drug Penetration and Absorption

Table –I: A suitable data is given below for this section.

Chemical	Bio-Chemical	Physical
Water Solvents Surfactant	Peptides Metabolic- inhibitors	Stripping Iontophoresis Electroporation Ultrasound (thermal) Ultrasound (cavitational) Thermal ablation Mechanical abrasion Microneedles

MATERIALS AND METHODS

MATERIALS: All materials (AR Grade) used were obtained from different sources and all instruments used in work that are as given in Table respectively.

Table –II: Materials Used.

Instruments	Companies
UV-Visible Spectrophotometer	PG INSTRUMENTS,T60,
Weighing Balance (XB120A)	Essae-Teraoka ltd, DS-852j
Over Head Stirrer	Techno Scientific products, Bangalore
pH Meter (pH Tutor)	Techno Scientific products, Bangalore
Rheometer (DV-E)	Brooke Field Viscometer
Magnetic Stirrer	MB instruments, MB575, Delhi
Mechanical Stirrer	MB instruments, MB575, Delhi
Dissolution apparatus	DS 8000 Lab india

S.No.	Materials	Sources
1	Metronidazole	Sun pharmaceutical Ltd, Mumbai.
2	HPMCK4M	Color cone Asia Ltd., Verna, Goa.
3	Carbapol 940	MJ Biopharmaceuticals, Mumbai
4	Xanthan gum	MJ Biopharmaceuticals, Mumbai
5	Tween 20	MJ Biopharmaceuticals, Mumbai
6	Span 20	MJ Biopharmaceuticals, Mumbai
7	Propyleneglycol	SD FINE CHEMICALS
8.	Methyl paraben	SD FINE CHEMICALS
9.	Benzalkoniumchloride	SD FINE CHEMICALS
10	Methanol	SD FINE CHEMICALS
11	Water	Narmada chemicals

Method[3-12]

Solubility studies: Solubility of Metronidazole was carried out in different solvents like 0.1N HCL, Water and 6.8 and 7.4 pH buffer. Saturated solutions were prepared by adding excess drug to the vehicles and shaking on the shaker for 24hrs at 25°C under constant vibration. Filtered samples (1ml) were diluted appropriately with suitable buffer and solubility of Metronidazole was determined spectrophotometrically at 276nm.

Drug-excipient compatibility study

a) Physical mixtures of drug and excipients were prepared by grinding specific ratios of drug and excipients in a mortar. Sample of 3-4 g was loaded in a glass vial, covered with rubber stopper, sealed with aluminum cap and labeled properly. Samples were observed and color was recorded for initial evaluation and loaded into stability chambered at 40^0 c temperature and 75% relative humidity for 30 days to study the Compatibility study. Samples were removed after 15 days and 30 days and observed for any change in the color.

b) FTIR spectroscopy

The physical compatibility between the pure drug and polymers used in the research was tested by Infra Red (IR) spectroscopy. FTIR absorption spectra for pure drug and physical mixture were recorded in the range of 400-4000cm-^{1} by KBr disc method using FTIR spectrophotometer.

Determination of Absorption maxima by UV spectrophotometer

Solution of drug were prepared in 0.1N HCl and scanned in the range of 200 to 400 nm using PG INSTRUMENTS UV spectrophotometer of (model No.T60), in order to determine the absorption maxima for analysis of dissolution samples.

Preparation of calibration curve of Metronidazole

10mg of Metronidazole was dissolved in 10 ml of 0.1N HCl by slight shaking (1000 mcg/ml). 1 ml of this solution was taken and made up to 10 ml with 0.1N Hcl, which gives 100 mcg/ ml concentration (stock solution). From the stock solution, concentrations of 5, 10, 15, 20, 25 and 30 µg/ml in 0.1N Hcl were prepared. The absorbance of diluted solutions was measured at 278 nm and a standard plot was drawn using the data obtained. The correlation coefficient was calculated.

Method of Preparation of Metronidazole emulgels

Take 100ml beaker, in that beaker take HPMC K4M and then mix with 400ml distilled water, now heat the mixture at 60°C till solution occurs using a heating magnetic stirrer (Gelling phase). Take another beaker, in this add Span 20 along with liquid paraffin and kept aside. Then take another beaker and add Tween 20 and water, benzalkonium chloride and propylene glycol and kept aside. Now take another beaker, add 5 ml of methanol with drug, then add all the three mixtures are mixed at 60°C. Then add this final mixture to the gelling phase, and stirred for 30 mins and kept aside for cooling for the formation of emulgels.

Metronidazole emulgels were prepared using compositions given in Table.

Table III: Formulation table.

Ingredients	F1	F2	F3	F4	F5	F6
Metronidazole(mg)	200	200	200	200	200	200
HPMCK4M(gm)	0.5	-	-	1	-	-
Xanthan gum	-	0.5	-	-	1	-
Carbapol 940	-	-	0.5	-	-	1
Tween 20	0.3	0.3	0.3	0.3	0.3	0.3
Span 20	0.5	0.5	0.5	0.5	0.5	0.5
Propyleneglycol(ml)	5	5	5	5	5	5
Methyl paraben	0.01	0.01	0.01	0.01	0.01	0.01
Benzalkonium chloride	0.01	0.01	0.01	0.01	0.01	0.01
Light liquid paraffin(ml)	5	5	5	5	5	5
Methanol(ml)	5	5	5	5	5	5
Water	50	50	50	50	50	50

EVALUATION PARAMETERS OF EMULGELS

Visual Appearance and Clarity: Visual appearance and Clarity was done under fluorescent light against a white and black back ground for presence of any particulate matter.

PH Measurement: The pH of the prepared in-situ gelling system after addition of all the ingredients was measured using pH meter.

Determination of drug content: Accurately 10 ml of formulation from different batches was measured and transferred to 100 ml volumetric flask. To this 50-70mL of 0.1 N HCL was added and sonicated for 30 min. Volume was adjusted to 100mL. Complete dispersion of contents was ensured visually and the dispersion was filtered using Whattman Filter Paper. From this solution, 10 ml of sample was withdrawn and diluted to 100ml with 0.1 N

HCL. Contents of Metronidazole was measured at maximum absorbance at 276 nm using UV-Visible Spectrophotometer (PG INSTRUMENTS, T60,].

Spreadability: Spreadability is determined by apparatus suggested by Mutimer et al (1956) which is suitably modified in the laboratory and used for the study. It consists of a wooden block, which is provided by a pulley at one end. By this method, spreadability is measured on the basis of 'Slip' and 'Drag' characteristics of emulgels. A ground glass slide is fixed on this block. An excess of emulgel (about 2 gm) under study is placed on this ground slide. The emulgel is then sandwiched between this slide and another glass slide having the dimension of fixed ground slide and provided with the hook. A 1 Kg weight is placed on the top of the two slides for 5 minutes to expel air and to provide a uniform film of the emulgel between the slides. Excess of the emulgel is scrapped off from the edges. The top plate is then subjected to pull of 80gms. With the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 7.5 cm be noted. A shorter interval indicate better spreadability. Spreadability was calculated by using the formula,

$$S = M.L/T.$$

Measurement of viscosity of Emulgels: Viscosity of the dispersion was determined using a Brookfield digital viscometer (NDJ-5S Viscometer). The samples (200 mL) were sheared at a rate of 100 rpm/min using spindle number 2 at room temperature. Viscosity measurement for each sample was done in triplicate, with each measurement taking approximately 30 seconds.

Swelling Index: To determine the swelling index of prepared topical emulgel, 1 gm of gel is taken on porous aluminum foil and then placed separately in a 50 ml beaker containing 10 ml 0.1 N NaOH. Then samples were removed from beakers at different time intervals and put it on dry place for some time after it reweighed. Swelling index is calculated as follows:

$$\text{Swelling Index (SW)} \% = [(Wt - Wo) / Wo] \times 100.$$

In-Vitro Release Studies: *In vitro* drug release studies were carried out by putting the formulation on Millipore membrane filter (0.15 mm) between the donor and receptor compartments of an all-glass modified Franz diffusion cell. To simulate the corneal epithelial barrier, the Millipore membrane filter was used, as isolated cornea will not remain viable beyond 4 hr. The receptor compartment of an all-glass modified Franz diffusion cell was filled with 10 mL freshly prepared 7.4 pH, and all air bubbles were expelled from the

compartment. An aliquot (1 mL) of test solution was placed on the Millipore membrane filter, and the opening of the donor cell was sealed with a glass cover slip. The receptor fluid was kept at 37 ± 0.5°C with constant stirring using a Teflon-coated magnetic stir bead. Permeation study was continued for 12 hr, and samples were withdrawn from receptor and analyzed for Metronidazole content by measuring absorbance at 276 nm in a spectrophotometer.

Kinetic Studies: Mathematical models[16-26]

Different release kinetic equations (zero-order, first-order, Higuchi's equation and Korsmeyer-peppas equation) were applied to interpret the release rate of the drug from matrix systems for the optimized formulation. The best fit with higher correlation (r_2) was calculated.

Zero-order model: Drug dissolution from dosage forms that do not disaggregate and release the drug slowly can be represented by the equation

$$Qt = Q0 + K0t$$

To study the release kinetics, data obtained from *in vitro* drug release studies were plotted as cumulative amount of drug released versustime.

First Order Model: The first order equation describes the release from systems where the dissolution rate is dependent upon the concentration of the dissolving species.

Release behavior generally follows the following first order equation:

$$\text{Log } C = \text{Log } C_o - kt/2.303$$

A graph of log cumulative of % drug remaining vs time yields a straight line

The pharmaceutical dosage forms following this dissolution profile, such as those containing water-soluble drugs in porous matrices, release the drugs in a way that is proportional to the amount of drug remaining in its interior, in such way, that the amount of drug released by unit of time diminishes.

Higuchi model: The first example of a mathematical model aimed to describe drug release from a system was proposed by Higuchi in 1961. Initially conceived for planar systems, it was then sustained to different geometrics and porous systems. This model is based on the hypothesis that

- Initial drug concentration In this is much higher than drug solubility;
- Drug diffusion takes place only in one dimension (edge effect must be negligible);

- Drug particles are much smaller than system thickness;
- Swelling and dissolution are negligible;
- Drug diffusivity is constant; and,
- Perfect sink conditions are always attained in the release environment.

In a general way the Higuchi model is simply expressed by following equation

$$Q = K_H - t^{1/2}$$

Where, K_H is the Higuchi dissolution constant.

The data obtained were plotted as cumulative percentage drug release versus square root of time.

Korsmeyer-Peppas model: Korsmeyer *et al.* (1983) derived a simple relationship which described drug release from a polymeric system equation. To find out the mechanism of drug release, first60% drug release data were fitted in Korsmeyer-Peppas model,

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

In this model, the value of *n* characterizes the release mechanism of drug as described in the following table.

Table –IV: Drug transport mechanisms suggested based on 'n' value.

S. No	Release exponent	Drug transport mechanism	Rate as a function of time
1	0.5	Fickian diffusion	$t^{-0.5}$
2	0.45 < n = 0.89	Non -Fickian transport	t^{n-1}
3	0.89	Case II transport	Zero order release
4	Higher than 0.89	Super case II transport	t^{n-1}

To find out the exponent of *n* the portion of the release curve, where Mt / M∞ < 0.6 should only be used. To study the release kinetics, data obtained from *in vitro* drug release studies were plotted as log cumulative percentage drug release *versus* log time.

6. RESULTS AND DISCUSSION

6.1 Saturation Solubility of Metronidazole

Solubility of Metronidazolewas determined in water, 0.1 N HCL, & 6.8 and 7.4 pH phosphate buffer and values obtained were noted in the table given below.

Table- V: Solubility studies.

S.No	Buffer	Solubility
01	WATER	0.097
02	0.1 N HCL	0.244
03	6.8 PH Buffer	0.147
04	7.4pH Buffer	0.321

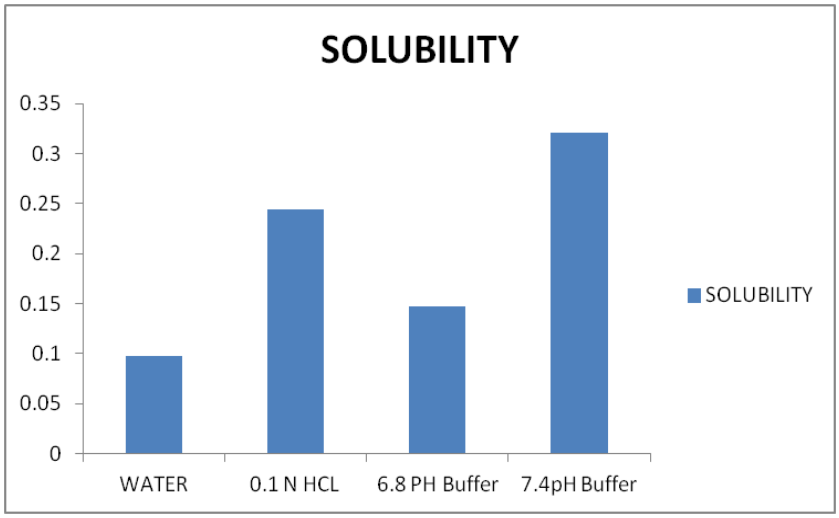

FIG I: Solubity graph.

DISCUSSION

From the above solubility data we can say that Metronidazole has more solubility in 7.4pH buffer.

6.2 Compatibility study of Metronidazole: Compatibility between the drug and polymers was studied by FT-IR method. Pure Metronidazole and optimized formulation were subjected for FT-IR spectroscopic analysis, to ascertain any interaction between the drug and polymers used. The position of characteristic peaks of pure Metronidazole was compared with those peaks obtained for optimized formulation. These characteristic bands for Metronidazole were identifiable and there was no major shift or disappearance in the peak positions. This indicated that the drug was intact and has not reacted with the excipients used in the formulation and hence they are compatible. Hence, it can be concluded that the drug is in free-state and can release easily from the polymeric network in the free form.

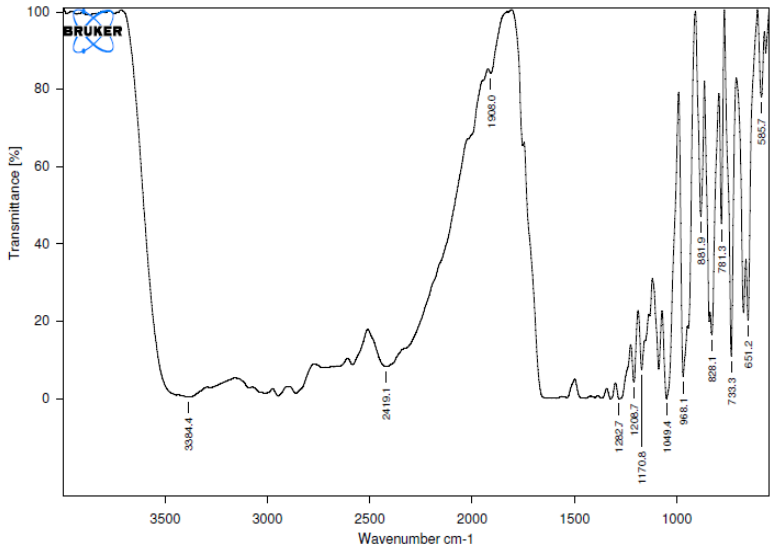

Fig –II: FTIR graph of pure Metronidazole.

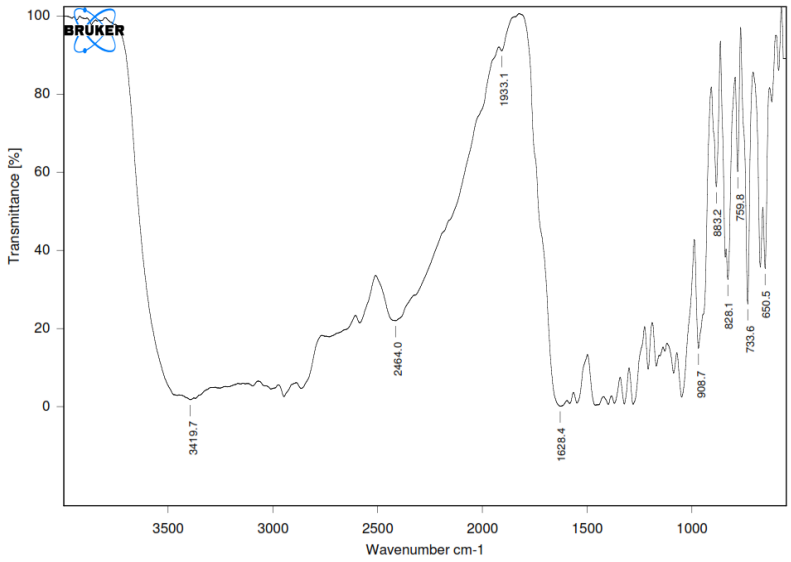

Fig –III FTIR graph of optimized formulation.

Spectral data: The major functional groups are primary amine, nitro, and carbonyl group obtained peak in IR spectra are as follows.

IR (KBr) cm-1: 3440-3305 (NH- stretching), 1724 (C=O stretching), 1265-1257 (C-N stretch in aromatic compound), 900-700 (C-H "oop" in aromatic compound) 813-750 (benzene ring bending).The spectral data confirm the structure of the compound.

6.3 Determination of absorption maximum (λmax) of Metronidazole

Determination of Metronidazoleλ-max was done for accurate quantitative assessment of drug dissolution rate.

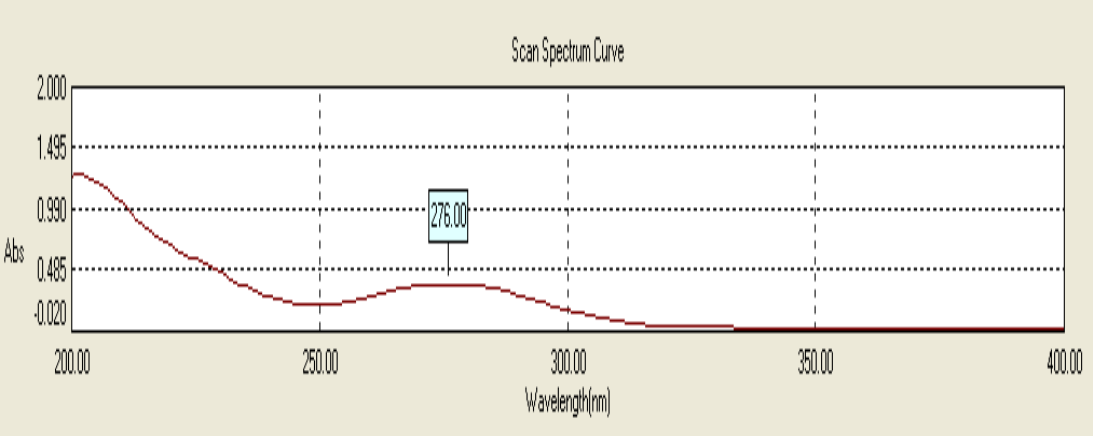

Fig IV Absorption maximum (λmax) of Metronidazole.

6.4 Standard calibration curve of Metronidazole

Table-VI: Calibration curve data.

Concentration	Absorbance
0	0
5	0.164
10	0.309
15	0.463
20	0.632
25	0.773
30	0.959

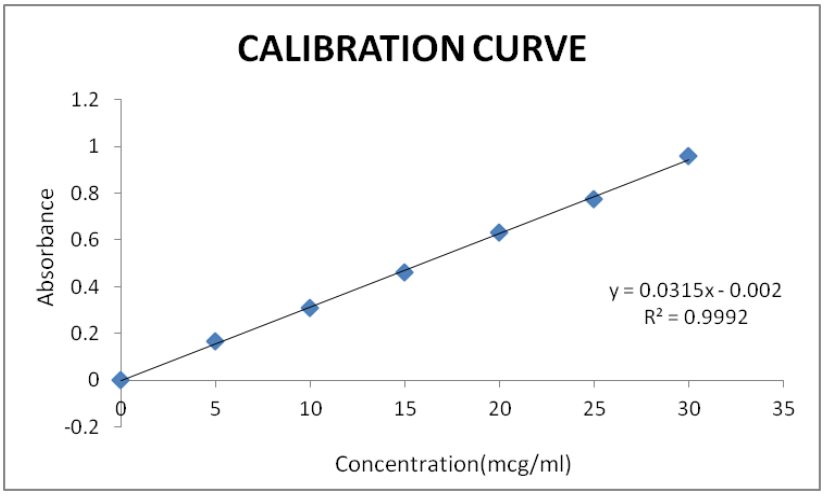

Fig-V: calibration curve.

DISCUSSION

Metronidazole beer's range concentration was found to be in the range of 5-30 µg/ml using 7.4 pH buffer as buffer solution. The regression value was closer to 1 indicating the method obeyed Beer-lamberts' law as it was linear.

6.5 Drug content

The drug content was found to being the range of 89.6-98.5% for all the formulations indicating uniform distribution of drug.

Table-VII: Drug content values.

Formulation code	Drug content
MF1	89.6
MF2	86.5
MF3	90.5
MF4	94.35
MF5	91.4
MF6	98.5

PH Measurement Measurement of pH is very important for oral preparations measurement of pH is very important for oral preparations; otherwise it leads to irritation to the throat. All the formulation has a pH around neutral or slightly alkali. The pH of formulations was found in the range of 6.0-6.8.

Table-VIII: pH values.

Formulation Code	pH
MF1	5.8
MF2	6.2
MF3	6.0
MF4	6.6
MF5	6.4
MF6	6.8

Viscosity studies

The formulation should have an optimum viscosity that will allow ease of administration and swallowing as a liquid and produces satisfactory gel strength for use as a delivery vehicle. The formulations showed a viscosity order of Carbopol 934 < HPMCK4M < Xanthan gum. In addition to the influence of the type of viscosity enhancing polymer added, it was observed that increasing the concentration of the viscosity enhancing polymer in the formulation simultaneously increased the viscosity for all polymer types studied.

Table IX: Viscosity data.

Formulation Code	Viscosity(CPs)
MF1	140
MF2	156
MF3	163
MF4	165
MF5	172
MF6	181

Spreadability

The spreadability of Carbopol based emulgel formulations & and of Xanthan gum based formulation is depicted in table. From the combined graph of all formulation it was concluded that all the developed formulation showed acceptable spreadability (Fig.). Carbopol based formulations showed better spreadability than HPMCK4M and Xanthan gum based.

Table X: Spreadability of emulgel formulations.

Formulations.	Spreadability (gm.cm/sec.)
MF1	**18.6**
MF2	**15.8**
MF3	**19.7**
MF4	**20.5**
MF5	**17.3**
MF6	**23.5**

TABLE XI: Swelling index (%).

Formulation	S.I at 2Hrs	S.I at 4Hrs	S.I at 8Hrs	S.I at 12Hrs
MF1	18	22	24	28
MF2	24	26	29	39
MF3	32	36	38	47
MF4	48	51	46	58
MF5	52	58	58	69
MF6	58	62	69	76

Invitro drug release study

The *in vitro* release study of Metronidazole from all formulations in 7.4pH was conducted for a period of 12 hours. The highest drug release of 99.19 % was observed with formula MF6.

Table XII: invitro drug release.

TIME	MF1	MF2	MF3	MF4	MF5	MF6
0min	0	0	0	0	0	0
1hr	12.81	17.25	14.16	9.67	20.16	6.81
2hr	21.92	24.2	23.61	17.33	32.04	13.24
3hr	36.07	38.37	35.67	25.11	45.73	20.06
4hr	50.81	52.92	49.59	31.86	55.02	25.12
5hr	61.23	67.47	55.93	50.74	62.97	40.89
6hr	66.5	76.1	73.46	56.86	73.37	52.25
7hr	82.08	86.4	83.4	66.41	79.47	63.11
8hr	90.23	98.23	93.35	78.22	88.28	74.97
10hr	96.18		99.26	86.28	94.86	86.46
12hr				98.23	99.19	96.56

Invitro dissolution profile graphs

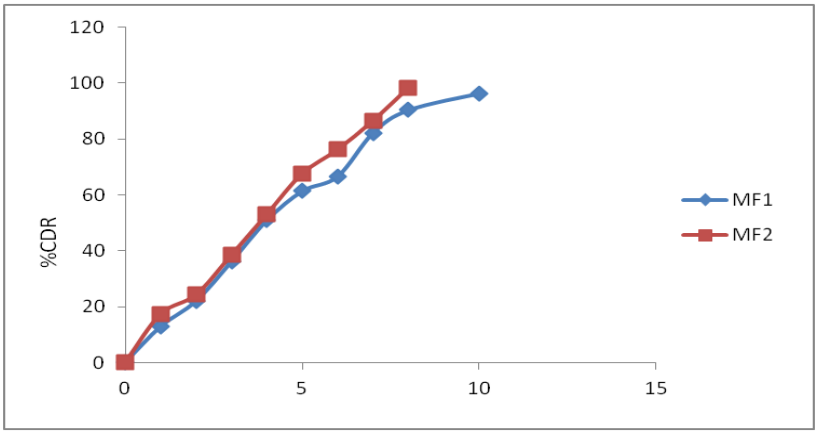

Fig V: Invitro dissolution profile of MF1-MF2.

DISCUSSION: MF1 formulation containing HPMC K4M shows 96.18% drug release at 10 Hours. Where as MF2 containing xanthan Gum shows 98.23% drug release at 8 hours. So the concentrations of the polymers were further increased to get sustained release.

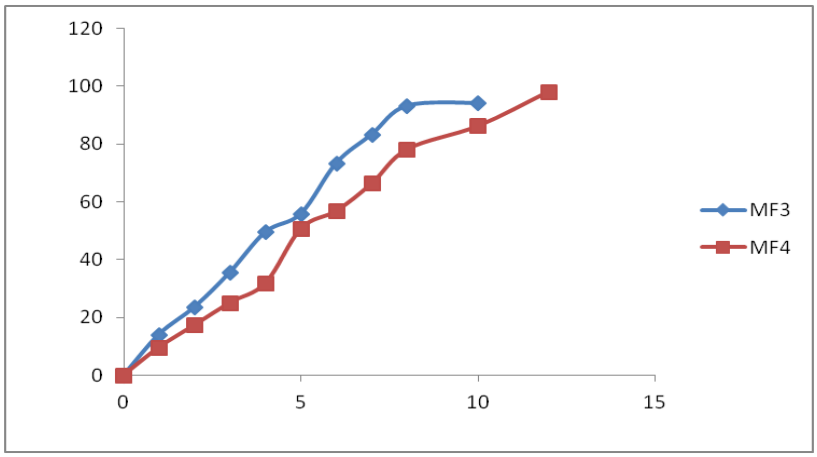

Fig VI: Invitro dissolution profile of MF3-MF4.

DISCUSSION: MF3 formulation containing carbopol 940 shows 99.26% drug release at 10 Hours. So the concentration of carbopol 940 was further increased to attain sustained release. where as MF4 containing HPMC K4M shows 98.23% drug release at 12 hours but not in a sustained manner.

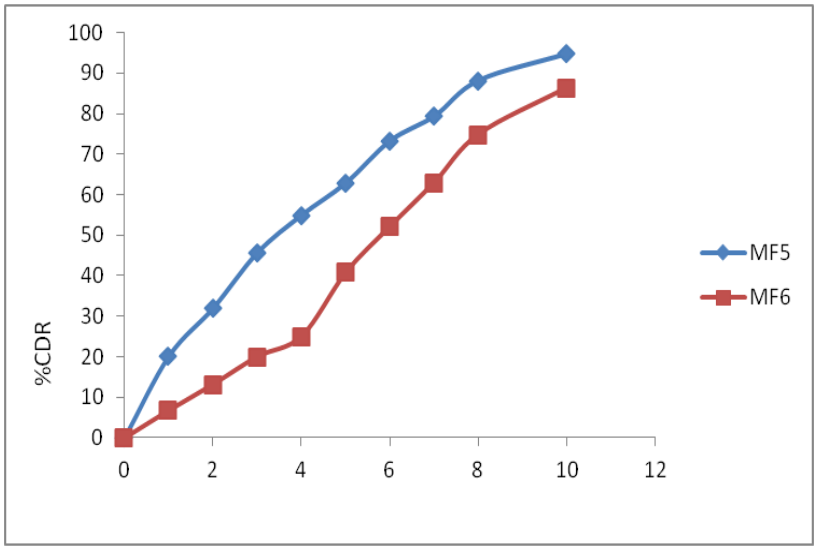

Fig VII: Invitro dissolution profile of MF5-MF6.

DISCUSSION: MF5 formulation containing xanthan Gum shows 99.19% drug release at 12 Hours but not in a sustained manner. Where as MF4 containing carbopol 940 shows 96.56% drug release at 12 hours in a sustained manner. So MF6 was considered as optimized formulation. Further drug release kinetics studies were performed for MF6 formulation.

6.11 drug release kinetic studies

Zero order release kinetics

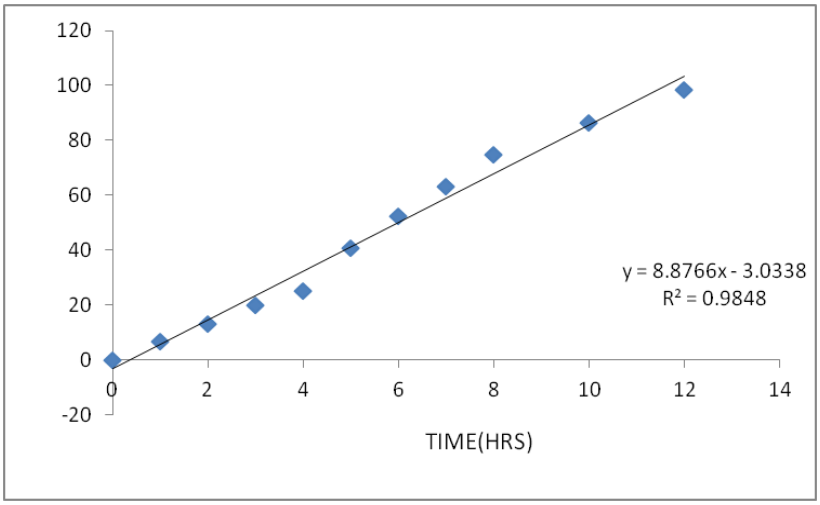

Fig VIII: Zero order release graph.

First order release kinetics

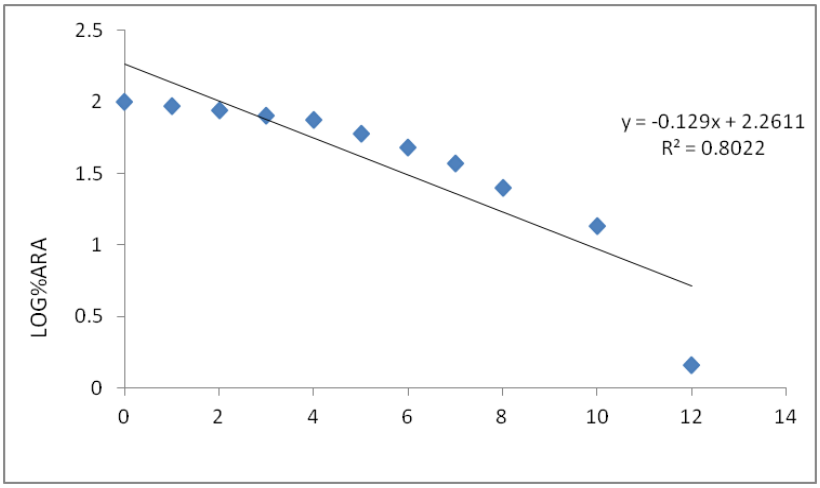

Fig IX: First order release graph.

Higuchi release plot

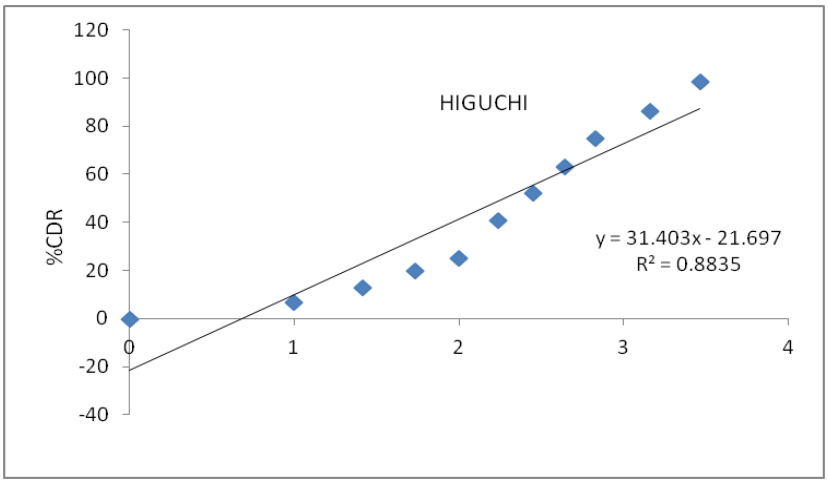

Fig X: Higuchi release graph.

Peppas release plot

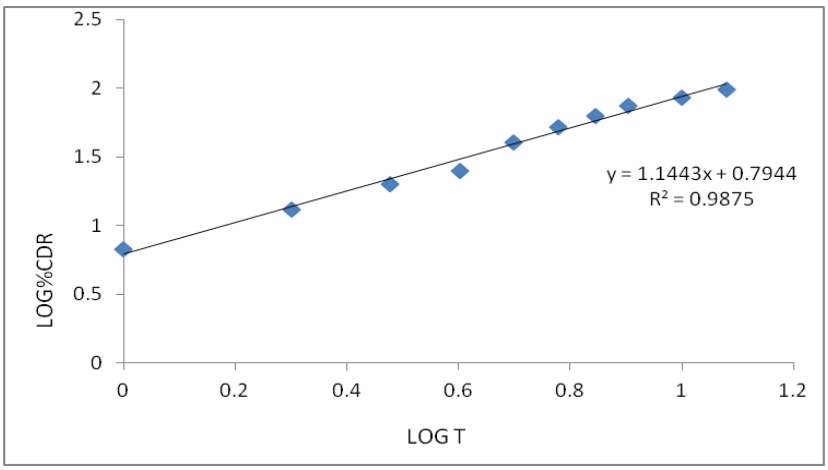

Fig XI: Peppas release graph.

R^2 values					n values
Formulation	**Zero order**	**First order**	**Higuchi**	**Korsmeyer - Peppas**	**Korsmeyer-Peppas (n)**
VF8	0.9848	0.8022	0.883	0.987	1.143

The invitro dissolution data for best formulation MF6 were fitted in different kinetic models i.e, zero order, first order, Higuchi and korsemeyer-peppas equation. Optimized formulation MF6 shows R^2 value 0.984. As its value nearer to the '1' it is conformed as it follows the Zero order release. The mechanism of drug release is further confirmed by the korsmeyer and peppas plot, if n = 0.45 it is called Case I or Fickian diffusion, 0.45 < n < 0.89 is for anomalous behavior or non-Fickian transport, n = 0.89 for case II transport and n > 0.89 for Super case II transport.

The 'n' value is 1.487 for the optimised formulation(MF6) i.e., n value was >0.89 this indicates case II suoer transport. The release kinetics for the optimized formula are shown in table.

CONCLUSION

Metronidazole emulgels were prepared by using polymers like HPMCK4M, Xanthan gum, Carbopol 940, Tween 20, SPAN 20, Propylene glycol, Methyl paraben, Benzalkonium chloride, Methanol and water. (MF1 to MF6) formulations were prepared and MF6 was found to be the best formulation. Drug and polymers was subjected for compatibility study using FTIR studies, which revealed that there was no interaction between drug and polymers. The prepared formulations were evaluated for drug content, Ph, viscosity, gelling nature, visual appearance & invitro release studies were also performed. The invitro release studies of all the formulations were discussed formulation MF1 containing HPMC K4M(0.5g) shows drug release of 96.18% by the end of 10hrs, MF2 containing Xanthan Gum (0.5g) shows drug release of 98.23% by the end of 8hrs, MF3 containing Carbopol 940 (0.5g) shows drug release of 99.26% by the end of 10hrs, MF4 containing HPMC K4M (1g) shows drug release of 98.23% by the end of 12hrs, MF5 containing Xanthan Gum (1g) shows drug release of 99.19% by the end of 12hrs, MF6 containing Carbopol 940 shows drug release of 96.56% by the end of 12hrs, optimized formula MF6 (Carbopol highest concentration) has 96.56% drug release. Since the formulation containing coarbopol with highest concentration shows drug release in a sustained manner whereas the other polymers didn't show sustained release. So the MF6 formulation was considered as the optimized formulation. So the drug release kinetics were performed for the optimized formulation. The release kinetics of the optimized

formulation was best fitted into peppas model (R^2 =0.987) and showed zero order (R^2 =0.984) drug release with super case II mechanism.

From the above experimental results it can be concluded that,

- Metronidazole was chosen as the model candidate for development of emulgels, since they possesses near ideal characteristics that these drugs must have formulating sustained drug delivery system.
- The results of study demonstrate that carbopol 940 was suitable to develop sustained release emulgels.

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