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FORMULATION AND EVALUATION OF CLARITHROMYCIN LOADED EMULGEL FOR TOPICAL DELIVERY

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ABSTRACT

Emulgel is wastly growing field of topical drug delivery system and up till emulgels has limited marketed products. Gel and emulsion are combined to form the emulgels. Emulgels has many advantages as drug delivery system. Emulgel has property of gel and emulsion both and thus it has dual control release system. Emulgels have high patient compliance as it has advantages of both the gel and emulsion. Clarithromycin is BCS class II drug and hence hydrophobic in nature and has only 50% of bioavailability. Hence, it was necessary to improve the therapeutic effectiveness of drug. In the present study, an attempt was made to formulate and evaluate the emulgel of clarithromycin for topical delivery. All the emulgel formulations were evaluated for physical appearance, pH, viscosity, drug content and *in-vitro* drug release study. Emulgel prepared with menthol and 2% xanthan gum showed highest spreadability coefficient. In the in-vitro drug release study F3 formulation showed highest drug release 79.17% after 8 hours. Emulgel formulation showed better antimicrobial activity. From all the results obtained from the study, F3 was found as an optimized formulation. So, the results of the current study are encouraging, there is a potential for more pharmacokinetic research.

Keywords: Emulgel, Controlled release, Antibiotic, Permeation enhancers, Diffusion

1. INTRODUCTION

Topical drug delivery systems are the systems in which formulations are directly applied to the skin to get the localized effect. Topical drug delivery system has wide advantages like more selectivity and site specificity, bypasses first pass metabolism, improved bioavailability as well as consistency in the delivery of drug for an extended period **[1]**.

Topical formulations are available in various forms like solid, liquid and semisolids. If the drug substance is in liquid or solution form, it has enhanced absorption through the skin. Skin is the largest organ of human body. Due to large surface area and easy accessibility, it provides multiple sites for administration of drugs for both systemic and local effect. Semisolids are the most commonly used and popular products for topical drug delivery. Within the semisolid preparations, the gels have expansion in both pharmaceutical and cosmetic preparations. Gels have high aqueous composition and thus allows greater drug dissolution.

Despite of having so many advantages, gels exhibit predominant limitation in the delivery of poorly water soluble or hydrophobic drugs **[2]**. To overcome this flaw, emulgels are prepared.

Emulsion + Gel = Emulgel

Emulgels are emulsions gelled by using gelling agents.

Emulgel is wastly growing field of topical drug delivery system and up till emulgels has limited marketed products.

Gel and emulsion are combined to form the emulgels. Emulgels has many advantages as drug delivery system **[3]**.

Emulgels are either oil-in-water type (direct system) or water-in-oil type (reverse system). Oil-in-water type is employed for entrapment of hydrophobic drugs and water-in-oil type is for entrapment of hydrophilic drugs.

Emulgel has property of gel and emulsion both and thus it has dual control release system. Emulgels have high patient compliance as it has advantages of both the gel and emulsion **[4]**.

Clarithromycin is a macrolide antibiotic used to treat many bacterial infections. Macrolides inhibits protein synthesis. This are substances that stop proteins from being synthesized. This effect is mostly bacteriostatic, but at high doses, it can also be bactericidal **[6, 7]**.

In the present study, Emulgel of clarithromycin was prepared by using 3 different gelling agents: Xanthan gum, Carbopol 940 and HPMC K100M. Clove oil and menthol were used as permeation enhancers.

2. MATERIALS AND METHODS

2.1 Chemical and Reagents:

Clarithromycin was received as a gift sample from Cipla R&D Centre, Mumbai. Xanthan gum, clove oil and menthol were obtained from Research lab, Mumbai. Carbopol 940 was obtained from Loba chemicals, Mumbai. HPMC K100M was obtained from Centaur Pharma, Pune. All the other chemicals were used of analytical grade and without any further chemical modifications.

2.2 Preparation of emulgel:

The four emulgel formulations F1, F2, F3 and F4 were comprised of xanthan gum gel base, F5, F6, F7 and F8 were comprised of Carbopol 940 gel base, F9, F10, F11 and F12 were comprised of HPMC K100M gel base. Each formulation contained 1% w/w clarithromycin as the active ingredient. All the ingredients were weighed and prepared as illustrated in Table 1.

The gel base was prepared by adding weighed amount of gelling agent in required quantity of water with continuous stirring. This dispersion was cooled and then left overnight. pH was adjusted by adding triethanolamine.

The oil phase of o/w emulsion was prepared by adding all the oil soluble excipients into oil phase. Span 80 was dissolved in light liquid paraffin stirred well. Then clove oil / menthol also added into it. Clarithromycin was added into this oil phase as it is hydrophobic in nature.

Tween 80 was dissolved into distilled water to prepare the aqueous phase of the emulsion. Methyl paraben was dissolved in propylene glycol and then mixed with the aqueous phase.

Both the oil and aqueous phases were heated separately to 75ºC. Afterword, oil phase was added into the aqueous phase by continuous stirring until it comes to room temperature.

The o/w emulsion was incorporated into gel base in 1:1 ratio at room temperature with gentle stirring to obtain the homogeneous emulgel.

3. CHARACTERIZATION OF EMULGEL FORMULATION

3.1 Physical Examination:

The prepared emulgel formulations were inspected for the colour, consistency, phase separation, grittiness and homogeneity **[2]**.

3.2 pH Measurement:

The pH of emulgel formulations was measured by using auto digital pH meter. The calibration of pH meter was done by using standard buffer solutions of pH 4 and 7. The electrode of pH meter was directly dipped into the beaker containing emulgel formulation. The measurement of pH of each emulgel formulation was done in triplicate. Average values were then calculated **[7]**.

3.3 Viscosity Measurement:

Viscosity of F1-F12 emulgel formulations were determined by using Brookfield

viscometer. T bar type of spindle TF-96 was used at 50 RPM **[8]**.

3.4 Spreadability Studies:

Emulgel should have good spreadability. Spreadability is defined as extent of area which on application of gel to skin spread easily.

Special apparatus was designed for the study of spreadability. Two glass slides of length 7.5cm were selected. Then emulgel formulation was placed on one slide which is fixed to ground. Then on this slide another slide was deposited. Thus, the formulation of emulgel was sandwiched amid these two slides. Then this formulation was consistently squeezed to form a slight layer. To obtain this slight layer, a weight (100 gm) was put on the upper slide. The excess formulation was scrapped off after the removal of weight. The upper slide was tied to a string and lower slide was placed on the surface of apparatus. The load (20 gm) was applied to this string by using a pulley. Then the time taken by upper slide to travel the distance and separate from the lower slide was noted. The experiment was repeated for three times and average was calculated **[9]**.

3.5 Extrudability Study:

This is an empirical test also called as Tube test. It measures the force required to extrude the emulgel from a collapsible tube of aluminium. 10 gm of emulgel formulation was filled in a collapsible aluminium foil and then then by applying uniform force the emulgel extruded was weighed and % extrudability was calculated of each formulation **[10]**.

3.6 Globule Size Determination:

Globule size of the emulgel formulations were determined by using electronic microscope. The emulgel was spread uniformly on a glass slide and observed under electronic microscope (at magnification 45×). The globule size of about 100 globules were measured and then average size was calculated **[11]**.

3.7 Drug Content Determination:

UV spectrophotometer was used to determine the drug content. 100 mg of emulgel formulation was dissolved in 100 ml freshly prepared PBS 5.5 solution using Ultra sonicator and then filtered by using Whatman filter paper. After suitable dilutions the absorbance was measured in UV spectrophotometer at 265 nm and from calibration curve the drug content of each formulation was determined **[12]**.

3.8 Microbiological Assay:

Cup and plate technique were used for determination of microbiological assay of emulgel formulations. Petri plates of nutrient agar were prepared and inoculated with bacterial culture of Staphylococcus aureus. Calculated amount of emulgel formulation was placed in each well and standard and control also added in separate wells. Petri plates were then incubated for

16-24 hours at 37ºC and then the zone of inhibition was measured **[13]**.

3.9 *In-Vitro* Drug Release Study:

The in-vitro drug release study of emulgel formulations were carried out by using Franz Diffusion Cell and Egg membrane. Franz diffusion cell of 16.5 ml of volume, 1.7 cm of diameter and 2.27 cm^2 of area was used.

Egg membrane was prepared by dissolving the eggshell in hydrochloric acid then the membrane was separated and washed using distilled water. The egg membrane was then soaked in PBS 5.5 solution for 12 hours. This egg membrane is then placed onto the receptor chamber facing upward into donor chamber. The emulgel formulation was spread uniformly onto the egg membrane. The donor chamber was mounted onto it. The PBS 5.5 was used as receptor medium to maintain the sink condition. The PBS 5.5 was added from the side arm up to the volume of the diffusion cell and magnet was also placed into it. The cell was then placed on a magnetic stirrer to maintain 100 RPM. After every 30 min. the 5ml sample was withdrawn from cell and replaced with fresh PBS 5.5 solution. After suitable dilution absorbance was measured by using UV spectrophotometer at 265 nm. Then cumulative drug release was calculated **[12]**.

3.10 Permeability Coefficient:

Permeability coefficient of emulgel formulations was determined from drug release data. Flux was determined by plotting the graph of cumulative amount permeated per cm^2 Vs time (in hours). From the value of flux and area of diffusion cell, permeability coefficient was determined **[14]**.

3.11 Release Kinetics of Optimized Formulation:

Drug Release Kinetic Study:

The data obtained from the *in-vitro* drug permeation study of optimized formulation F3 was used to determine the drug release kinetics and mechanism. The obtained data was converted into drug release data and put into the kinetic equations of:

- Zero Order
- First Order
- Higuchi Model
- Korsmeyer-Peppas Model
- Hixon-Crowell Model **[15]**.

4. RESULT AND DISCUSSION

4.1 PREFORMULATION STUDIES:

a) Identification Study:

The sample of clarithromycin was studied for organoleptic characters such as colour, odour, and appearance. The results obtained were reported in **Table 2**.

b) Solubility:

The solubility of clarithromycin was determined in Water, Methanol, Phosphate buffer 5.5 and Acetone.

Clarithromycin was found to be insoluble in water, sparingly soluble in methanol and phosphate buffer 5.5, soluble in acetone.

c) Melting Point:

The melting of Clarithromycin was determined by capillary method. The observed melting point value was in accordance with the reported melting point value 217-220ºC. Therefore, it was confirmed that the given sample of Clarithromycin was pure form.

d) FTIR Spectroscopy:

FTIR spectrum of Clarithromycin implied that the observed peaks of received drug were corresponding with reported peaks from the results (**Figure 2** and **Table 4)** of drug authentication study, it was concluded that the sample of clarithromycin obtained was pure and complied with the standards. It was concluded that the sample of clarithromycin was pure.

e) Determination of λ max:

The λ max of Clarithromycin was found to be 265 nm in PBS 5.5. This study confirmed that sample of Clarithromycin was pure as shown in **Figure 3**.

f) Calibration curve of Clarithromycin by using UV spectrophotometer:

The calibration curve of clarithromycin was prepared in phosphate buffer 5.5. **Table 5** showed the absorbance at absorption maxima (λmax) 265 nm for 5 different concentrations of clarithromycin and **Figure 4** shows calibration curve of Clarithromycin with the regression coefficient 0.9992 for concentration range of 0-10 µg/ml. The results indicated that there was a linear relationship between concentration and absorbance and followed Bears-Lambert law in range of 0-10 µg/ml.

4.2 Drug and Excipients Compatibility Study:

The Drug-Excipients compatibility studies were performed to confirm the compatibility of drug with the excipients used in the emulgel formulation. This study mainly includes physical appearance and FTIR studies.

a) Physical appearance:

Physical appearance of the physical mixture of drug and excipients was observed after a one month. The physical mixture was found as white in colour and odourless.

b) FTIR Spectroscopy studies:

IR spectrums of physical mixture of clarithromycin with Xanthan Gum, Carbopol 940 and HPMC K100M were recorded in **figure 5A, 5B, 5C** and **5D** respectively.

1. **FTIR spectrum of physical mixture of clarithromycin & xanthan gum**

From the spectra of physical mixture, the major peaks of clarithromycin were retained. These results obtained shows that there was no any evidence for the interaction between clarithromycin and xanthan gum material. In that FTIR values of the

clarithromycin shows no change or slight change from the standard value which was reported in **Table 6A**. These results clearly indicated that the xanthan gum can be used without any interaction for the preparation of clarithromycin emulgel.

2. **FTIR spectrum of physical mixture of clarithromycin & Carbopol 940**

From the spectra of physical mixture, the major peaks of clarithromycin were retained. These results obtained shows that there was no any evidence for the interaction between clarithromycin and carbopol 940 material. In that FTIR values of the clarithromycin shows no change or slight change from the standard value which was reported in **Table 6B**. These results clearly indicated that the carbopol 940 can be used without any interaction for the preparation of clarithromycin emulgel.

3. **FTIR spectrum of physical mixture of clarithromycin & HPMC K100M**

From the spectra of physical mixture, the major peaks of clarithromycin were retained. These results obtained shows that there was no any evidence for the interaction between clarithromycin and HPMC K100M material. In that FTIR values of the clarithromycin shows no change or slight change from the standard value which was reported in **Table 6C**. These results clearly indicated that the HPMC K100M can be used without any interaction for the preparation of clarithromycin emulgel.

4.3 Evaluation of Clarithromycin Emulgels:

a) Physical Examination:

The prepared emulgel formulations were inspected visually for the colour, consistency, phase separation, grittiness and homogeneity. The results are depicted in **Table 7**.

b) pH Measurement:

The pH of emulgel formulations was measured by using auto digital pH meter. The pH of all the emulgel formulations were found between the 6.0-6.5 which fits into the desired range of pH shown in the Table. Formulation F11 found to have the lowest pH value and F8 found to have the highest pH value. All the formulations had the optimal pH value and thus no any formulation will cause any skin irritation.

c) Viscosity Measurement:

Viscosity of F1-F12 emulgel formulations were determined by using Brookfield viscometer. T bar type of spindle TF-96 was used at 50 RPM. The results obtained are depicted in **Table 9**. Viscosity of the emulgel formulations was found between 12400-38800 cp. F1 showed the lowest viscosity and F8 showed the highest value of viscosity. Formulations prepared with xanthan gum gel base showed low viscosity and those with carbopol 940 showed highest viscosity. It was observed that as the

concentration of gelling agent increased, the viscosity of formulation also found to be increased.

d) Spreadability Studies:

Spreadability of emulgel formulations were performed by using two slide method and results obtained are illustrated in **Table 10**. F12 showed the lowest spreadability and F3 showed highest spreadability. Formulations with 2% gelling agent showed higher spreadability coefficient than formulations with 3% of gelling agents. It was observed that as the concentration of gelling agent increased the spreadability coefficient was decreased. High spreadability coefficient means emulgel can be applied easily.

e) Extrudability Study:

This was performed by using aluminium collapsible tubes. The results obtained are illustrated in Table. Percent extrudability was found between 68%-88%. F6 showed the lowest extrudability while F11 showed highest extrudability. It was observed that there is an inverse relationship between extrudability and gelling agent concentration. Extrudability increased with reduced concentration of gelling agent. Extrudability was in the range of F11>F9>F3>F1>F12>F10>F4>F2>F7>F5 >F8>F6.

f) Globule Size Determination:

Globule size of the emulgel formulations were determined by using electronic microscope. The microscopy study showed the presence of globules in formulation which indicates that emulsion is formulated in gel base. This demonstrated the success of the technique used in the formulation of emulgel. The globule size was found between 12-15.68 µm.

g) Drug Content Determination:

UV spectrophotometer was used to determine the drug content of all emulgel formulations. The percentage drug content was found between 95.2% - 98.97%. F3 formulation found to contain highest drug and F10 formulation showed lowest drug content. All the formulations showed the % drug content in the desired range given in IP. Results obtained are illustrated in **Table 13** and **Figure 11**.

h) Microbiological Assay:

Cup and plate technique were used for determination of zone of inhibition of emulgel formulations. Well with control formulation showed no any activity against S. aureus strain.

The antimicrobial activity of clarithromycin in emulgel formulation and commercial antimicrobial agent is shown below. Zone of inhibition was measured for the determination of antimicrobial activity. The highest antimicrobial activity was observed in F3 formulation (25mm) whereas F9 formulation showed the lowest antimicrobial activity (12mm).

i) *In-Vitro* Drug Release Study:

The cumulative percentage of clarithromycin that permeated is illustrated in **Table 15** and **Figure 13.** The order of release of drug from formulation from highest to lowest as follows: F3>F4>F1>F5>F7>F8>F2>F6>F9>F11>F 10>F12, respectively. F3 formulation containing 2% xanthan gum and menthol showed highest drug release of 79.17% after 8 hours.

j) Permeability Coefficient:

Permeability coefficient of emulgel formulations were calculated using the data obtained from *in-vitro* drug release study. F3 formulation showed highest permeability coefficient through the egg membrane.

4.4 Optimization of Clarithromycin Emulgel:

From the results of drug diffusion study, microbiological assay, spreadability and permeation coefficient, it was concluded that F3 is optimized formulation.

4.5 Drug Release Kinetics:

The data obtained from drug release kinetic study of optimized formulation is shown in **Table 17**.

R^2 value is the correlation coefficient for the zero order, first order, Higuchi mode, Korsmeyer-Peppas model and Hixon-Crowell model. The diffusion release data of formulation F3 was fitted to zero order, first order, Higuchi, Korsmeyer-Peppas and Hixon–Crowell models. The coefficient of determination (R^2) value was used as criteria to choose the best model to describe drug release from emulgel formulation. The R^2 values of various models are given in **Table 17**. In the case of diffusion release kinetic of F3 emulgel formulation the R^2 value was in zero order model indicating that the drug release from the formulation followed Zero order model.

Table 1: Composition of different Clarithromycin emulgel formulations (%w/w)

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Clarithromycin	1	1	1	1	1	1	1	1	1	1	1	1
Clove Oil	8	8	-	-	8	8	-	-	8	8	-	-
Menthol	-	-	8	8	-	-	8	8	-	-	8	8
Span 80	5	5	5	5	5	5	5	5	5	5	5	5
Tween 80	5	5	5	5	5	5	5	5	5	5	5	5
Light Liquid Paraffin	12	12	12	12	12	12	12	12	12	12	12	12
Acetone	2	2	2	2	2	2	2	2	2	2	2	2
Methyl Paraben	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Propylene Glycol	15	15	15	15	15	15	15	15	15	15	15	15
Xanthan Gum	2	3	2	3	-	-	-	-	-	-	-	-
Carbopol940	-	-	-	-	2	3	2	3	-	-	-	-
HPMC K100M	-	-	-	-	-	-	-	-	2	3	2	3
Water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

Table 2: Identification tests of clarithromycin with the reported standards

Identification Test	Observation
Appearance	Crystalline Powder
Color	White to off white
Odor	Odorless

Figure 1: Clarithromycin Powder

Table 3: Melting Point of Clarithromycin

Sr. No	Method	Reported Melting Point	Observed Melting Point
1	Capillary Method	217-220°C	217-220°C

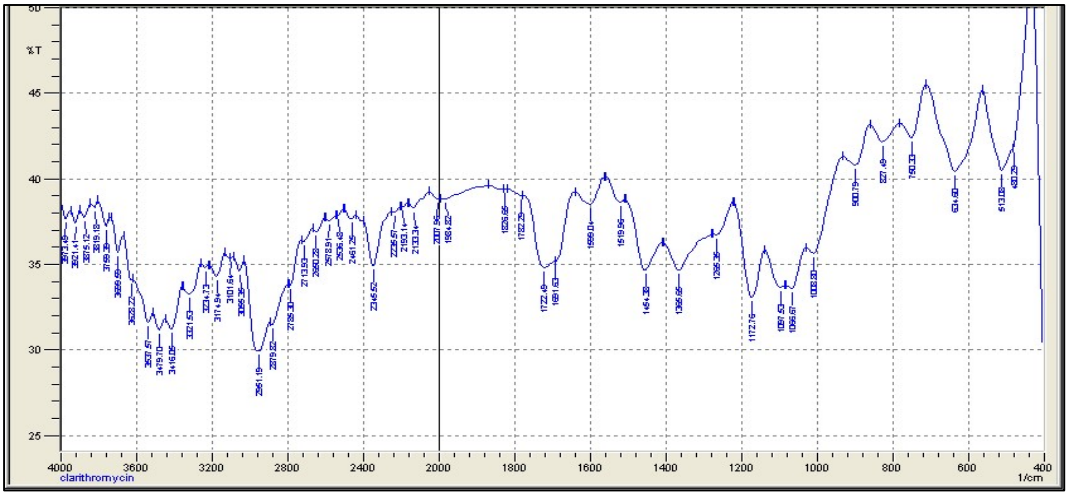

Figure 2: FTIR spectrum of Clarithromycin

Table 4: Interpretation FTIR spectra of Clarithromycin

Functional groups	Reported Peak Frequencies (cm^{-1})	Observed peak frequencies (cm^{-1})
C=O Stretching	1800-1650	1691
-C-O-C- Stretching	1200-1160	1172
CH_2 Bending	1465-1405	1454
Lactone Carbonyl	1900-1700	1722
Alkane Stretching Peaks	~3000	2951
OH Stretching	3600-3200	3479

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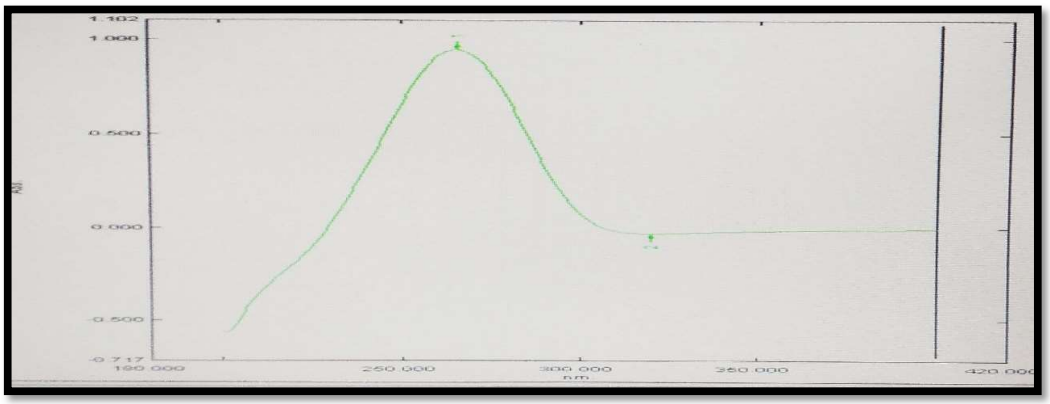

Figure 3: UV spectra of clarithromycin showing $\lambda_{max.}$

Table 5: Data for calibration curve of Clarithromycin

Sr. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.234
3	4	0.438
4	6	0.614
5	8	0.823
6	10	1

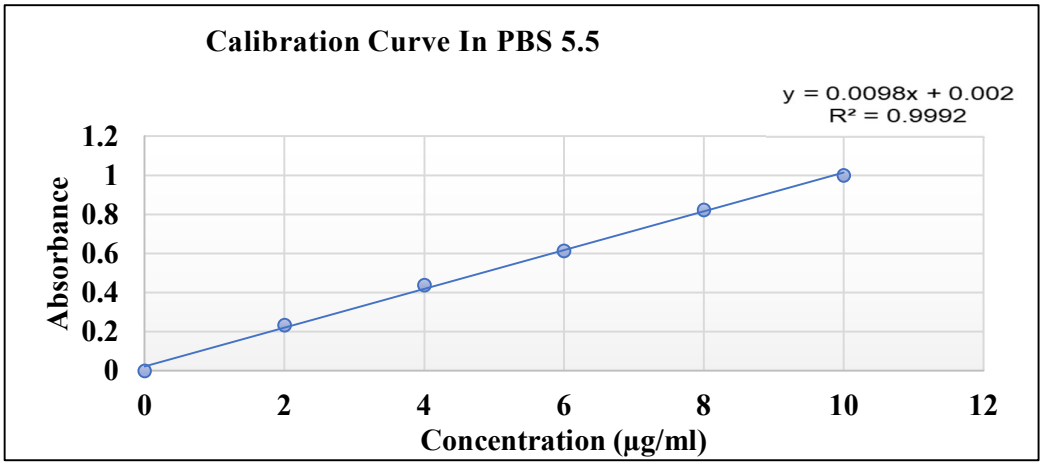

Figure 4: Calibration curve of clarithromycin in phosphate buffer 5.5

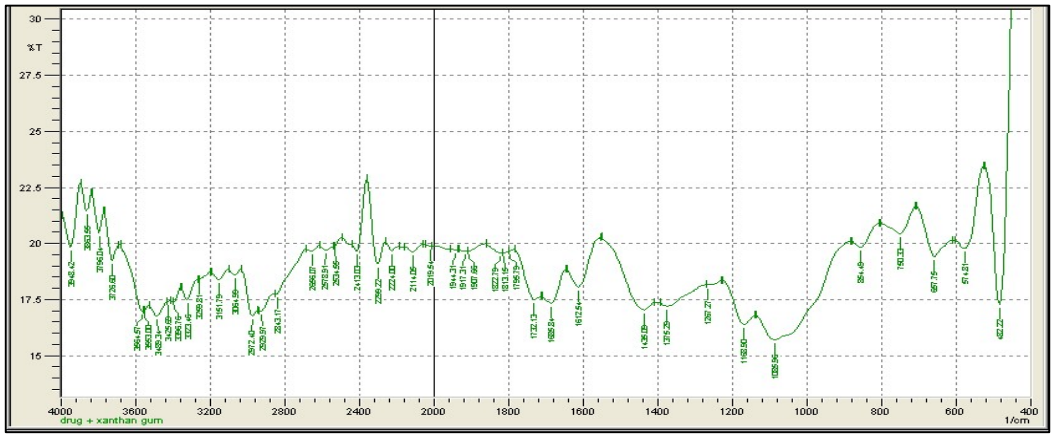

Figure 5A: IR spectrum of Clarithromycin + Xanthan Gum

Table 6A: Interpretation of FTIR Spectrum peak of Clarithromycin and Xanthan gum

Functional groups	Reported Peak Frequencies (cm^{-1})	Observed peak frequencies (cm^{-1})
C=O Stretching	1800-1650	1685
-C-O-C- Stretching	1200-1160	1168
CH_2 Bending	1465-1405	1435
Lactone Carbonyl	1900-1700	1732
Alkane Stretching Peaks	~3000	2972
OH Stretching	3600-3200	3489

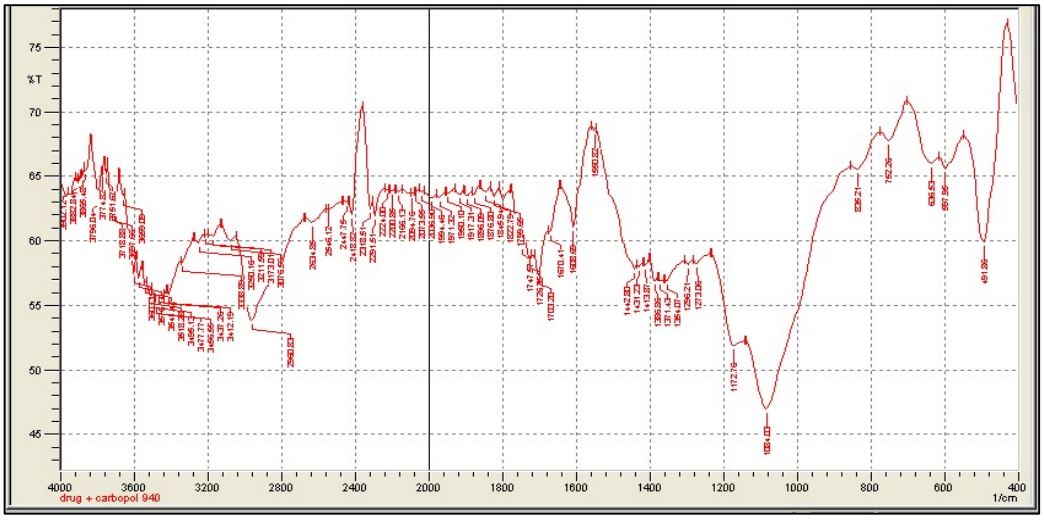

Figure 5B: IR spectrum of Clarithromycin + Carbopol 940

Table 6B: Interpretation of FTIR Spectrum peak of Clarithromycin and Carbopol 940

Functional groups	Reported Peak Frequencies (cm^{-1})	Observed peak frequencies (cm^{-1})
C=O Stretching	1800-1650	1670
-C-O-C- Stretching	1200-1160	1172
CH_2 Bending	1465-1405	1442
Lactone Carbonyl	1900-1700	1726
Alkane Stretching Peaks	~3000	2960
OH Stretching	3600-3200	3477

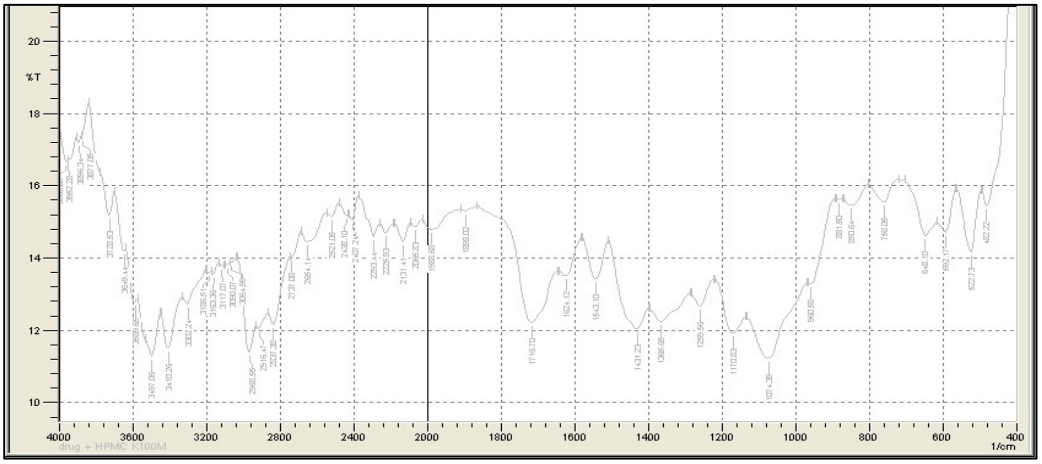

Figure 5C: IR spectrum of Clarithromycin + HPMC K100M

Table 6C: Interpretation of FTIR Spectrum peak of Clarithromycin and HPMC K100M

Functional groups	Reported Peak Frequencies (cm^{-1})	Observed peak frequencies (cm^{-1})
C=O Stretching	1800-1650	1716
-C-O-C- Stretching	1200-1160	1170
CH_2 Bending	1465-1405	1431
Lactone Carbonyl	1900-1700	1716
Alkane Stretching Peaks	~3000	2968
OH Stretching	3600-3200	3497

Table 7: Physicochemical characteristics of Emulgel formulations

Formulation	Color	Phase Separation	Grittiness	Homogeneity	Consistency
F1	Off White	No	-	Excellent	+++
F2	Off White	No	-	Excellent	+++
F3	Off White	No	-	Excellent	+++
F4	Off White	No	-	Excellent	+++
F5	White	No	-	Excellent	++
F6	White	No	-	Excellent	++
F7	White	No	-	Excellent	++
F8	White	No	-	Excellent	++
F9	Transparent	No	-	Good	+
F10	Transparent	No	-	Good	+
F11	Transparent	No	-	Good	++
F12	Transparent	No	-	Good	++

Table 8: pH of clarithromycin emulgel formulations

Formulation	Viscosity (cp)
F1	12400
F2	20000
F3	12800
F4	20100
F5	30600
F6	38800
F7	30700
F8	38000
F9	17300
F10	24000
F11	17400
F12	24100

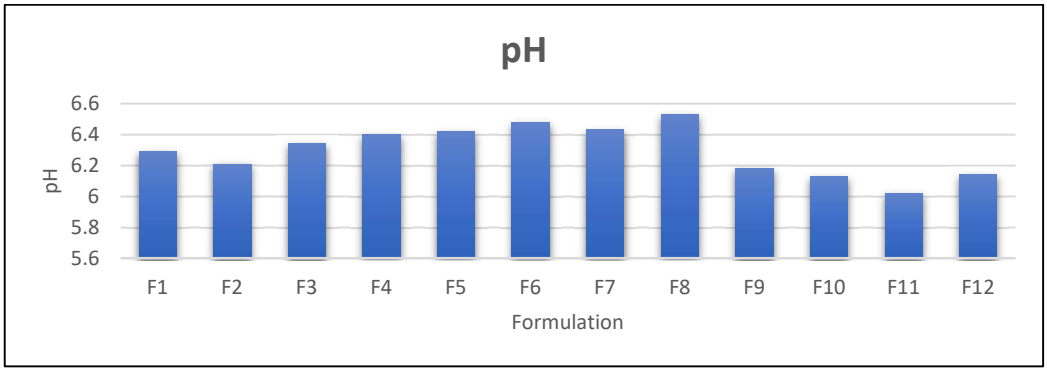

Figure 6: pH of clarithromycin emulgel formulations

Table 9: Viscosity of emulgel formulation

Formulation	F1	F2		F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
pH	6.29	6.21		6.34	6.40	6.42	6.48	6.43	6.50	6.18	6.13	6.02	6.14

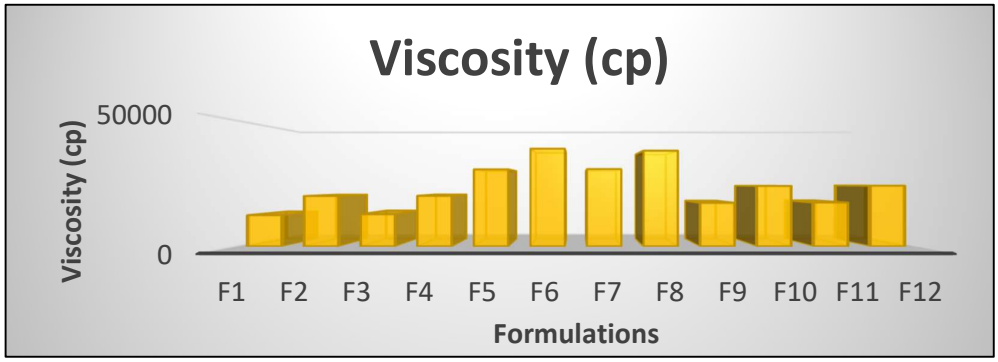

Figure 7: Viscosity of formulated emulgels

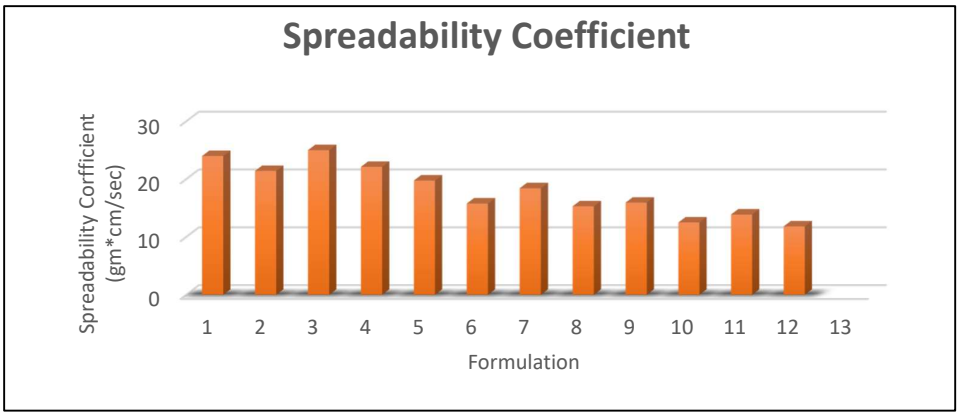

Figure 8: Spreadability coefficient of emulgel formulation of clarithromycin

Table 10: Spreadability coefficient of clarithromycin emulgel formulation

Formulation	Spreadability Coefficient (gm*cm/sec)
F1	24
F2	21.42
F3	25.01
F4	22.12
F5	19.75
F6	15.78
F7	18.42
F8	15.3
F9	15.93
F10	12.5
F11	13.88
F12	11.83

Table 11: Extrudability of clarithromycin emulgel formulations

Formulation	Extrudability (%)
F1	82.5
F2	75.2
F3	85.2
F4	78.3
F5	72.4
F6	68.6
F7	74.9
F8	70.2
F9	87.3
F10	81.01
F11	88.5
F12	82.31

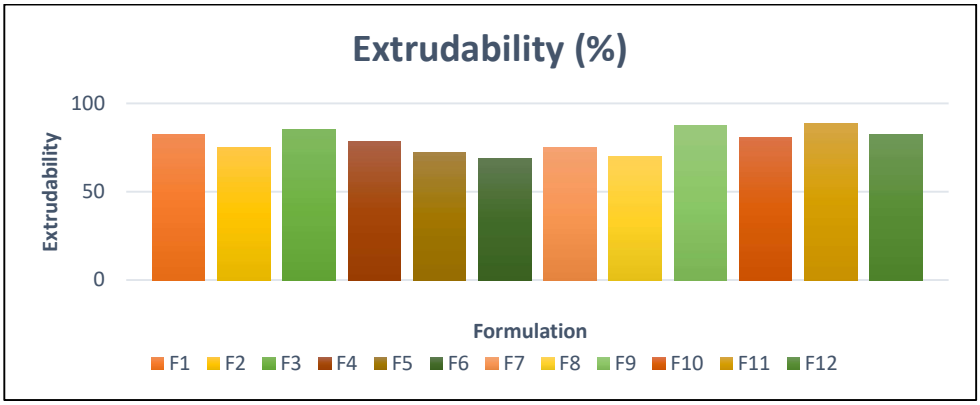

Figure 9: Extrudability of emulgel formulations of clarithromycin

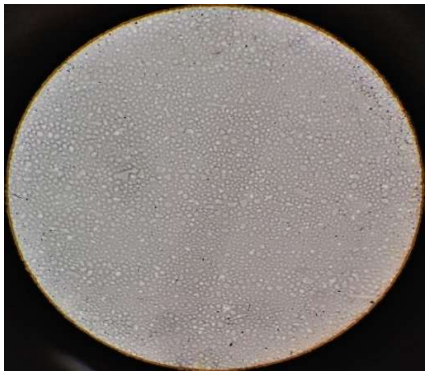

Figure 10A: Photograph of globules of emulgel under electronic microscope (magnification 45×)

Table 12: Globule size of clarithromycin emulgel formulation

Formulation	Globule Size (µm)
F1	12.88
F2	15.68
F3	13.58
F4	15.12
F5	14.84
F6	14.7
F7	14.98
F8	13.86
F9	12.88
F10	13.72
F11	13.44
F12	13.3

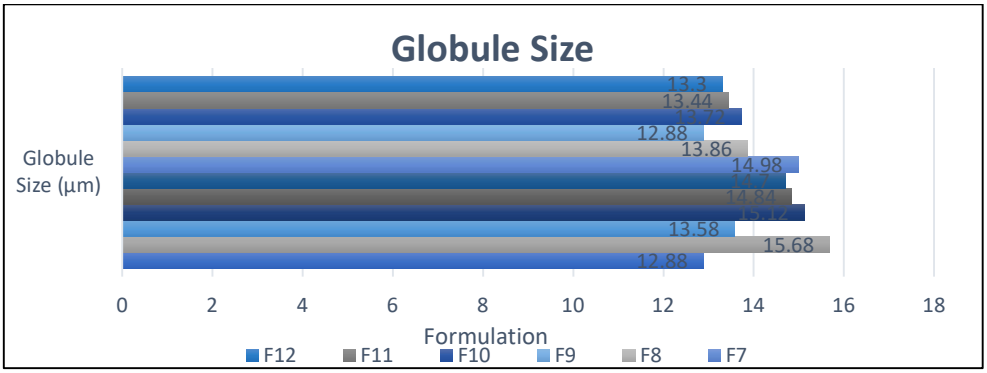

Figure 10B: Globule size of clarithromycin emulgel formulations

Table 13: Percent Drug content of emulgel formulations of clarithromycin

Formulation	Drug Content (%)
F1	97.55
F2	97.95
F3	98.97
F4	98.57
F5	96.53
F6	97.24
F7	97.14
F8	97.44
F9	96.53
F10	95.2
F11	95.51
F12	96.9

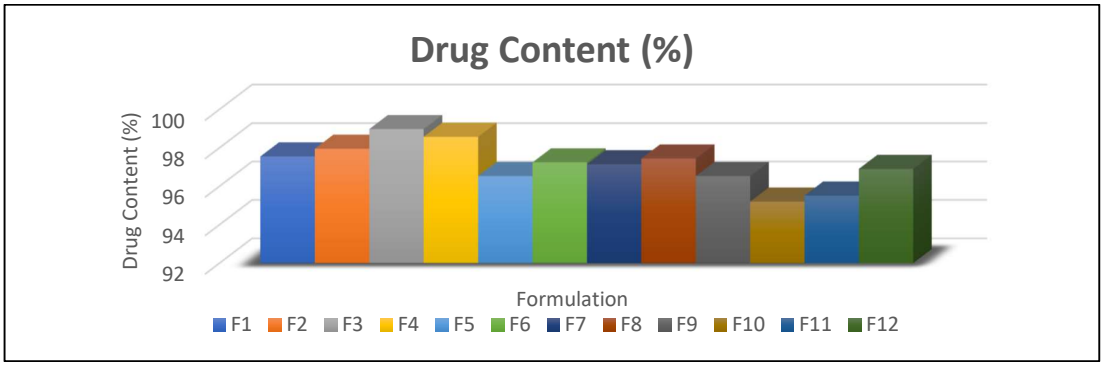

Figure 11: Percent Drug content of emulgel formulations of clarithromycin

Figure 12A: Photograph of microbiological assay of emulgel showing zone of inhibition

Table 14: Zone of inhibition clarithromycin emulgel formulation

Formulation	Zone of Inhibition (mm)
F1	21
F2	19
F3	25
F4	20
F5	20
F6	19
F7	21
F8	19
F9	12
F10	17
F11	18
F12	19

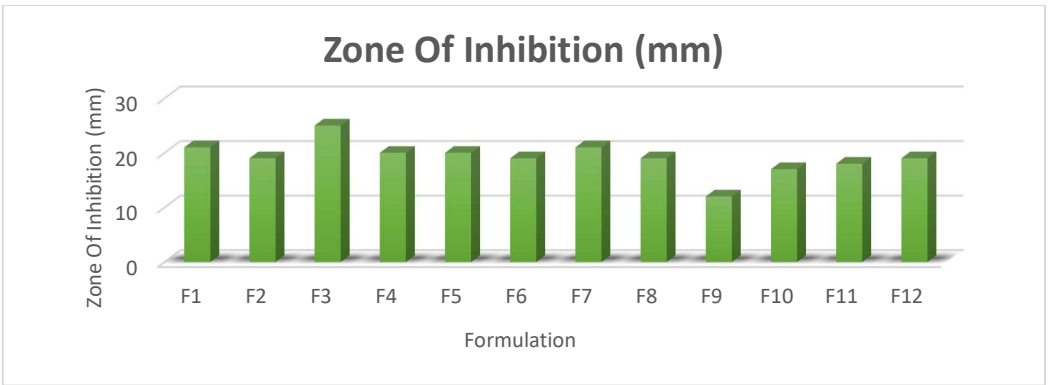

Figure 12B: Zone of inhibition shown by emulgel formulations (in mm)

Table 15: *In vitro* drug release study of emulgel formulations

Time (Hrs.)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
00	0	0	0	0	0	0	0	0	0	0	0	0
0.5	0.71	0.17	0.57	0.86	0.70	0.26	0.81	0.57	0.01	0.008	0.64	0.32
1.0	1.94	0.98	1.87	1.78	1.58	0.81	1.78	1.36	1.13	1.01	1.55	1.32
1.5	2.97	2.04	3.59	2.76	2.58	5.71	2.99	2.85	2.51	2.43	2.96	2.65
2.0	4.44	3.69	5.64	3.99	4.25	9.03	4.57	4.68	4.41	4.18	4.70	4.29
2.5	6.32	5.64	8.32	5.56	6.58	12.48	6.40	7.00	6.72	6.07	6.83	6.38
3.0	8.49	8.32	11.3	7.84	9.80	15.96	9.29	10.2	9.56	8.24	9.23	8.85
3.5	11.8	11.7	15.5	11.1	13.9	19.92	13.0	13.6	12.8	11.1	12.3	11.6
4.0	16.3	15.3	20.8	15.2	18.4	23.93	17.1	17.2	16.8	14.2	16.1	15.3
4.5	21.2	19.3	26.2	20.8	23.4	28.17	21.7	21.5	21.2	17.9	20.3	19.4
5.0	27.1	24.2	32.2	26.5	28.6	32.66	26.9	26.2	25.8	22.3	24.9	24.0
5.5	33.5	29.8	38.7	32.4	34.1	37.27	32.4	31.2	30.8	27.1	29.8	29.1
6.0	40.2	35.9	45.6	38.5	39.7	42.16	38.2	36.8	36.3	32.4	35.0	34.4
6.5	47.3	42.4	53.3	45.0	45.6	47.34	44.5	42.7	42.1	38.1	40.8	40.3
7.0	54.6	49.1	61.7	52.1	52.3	52.80	51.3	49.4	48.3	44.5	46.9	46.5
7.5	62.1	56.3	70.3	59.8	59.3	58.30	58.6	57.2	54.8	52.1	53.5	52.9
8.0	67.8	64.3	79.1	68.3	66.3	63.93	65.8	65.2	61.8	60.0	60.3	59.7

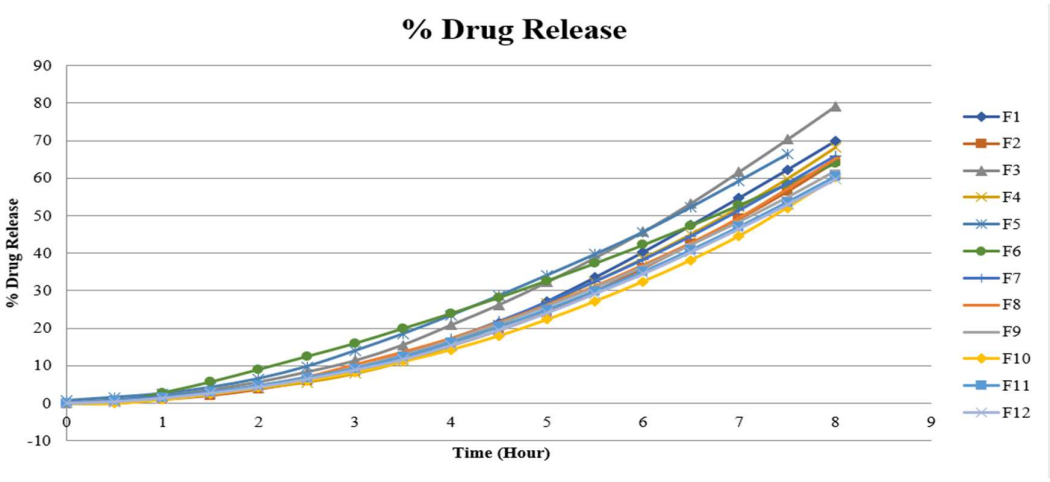

Figure 13: Percent Drug Release data from *in vitro* diffusion study as a function of time

Table 16: Permeability coefficient of emulgel formulations

Formulation	Permeability coefficient (cm/hour)
F1	0.130
F2	0.124
F3	0.148
F4	0.131
F5	0.118
F6	0.096
F7	0.145
F8	0.125
F9	0.112
F10	0.080
F11	0.111
F12	0.067

Table 17: Data for Diffusion Kinetic Study

Model/ Parameter	R^2 values for formulations FC4
Zero Order	0.93
First Order	0.82
Higuchi Model	0.76
Korsmeyer-Peppas Model	0.72
Hixon Crowell Model	0.87
Best Fitted Model	Zero order

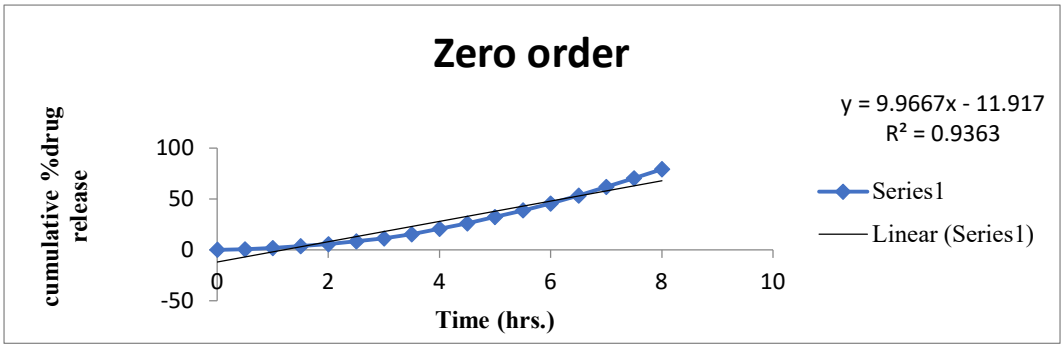

Figure 14A: Zero order graph of drug release data

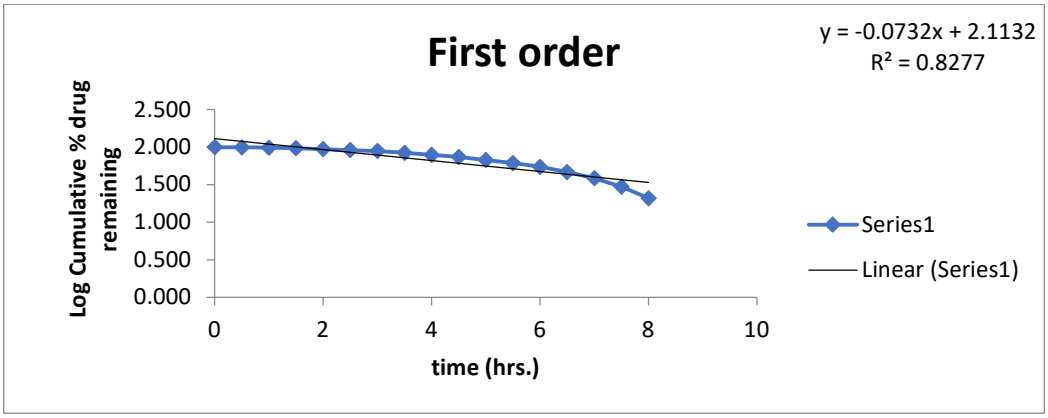

Figure 14B: First order graph of drug release data

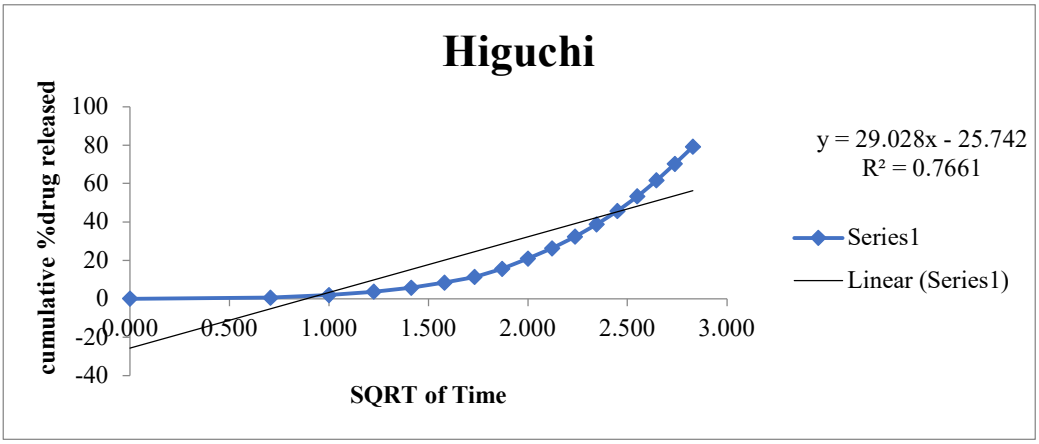

Figure 14C: Higuchi plot of drug release data

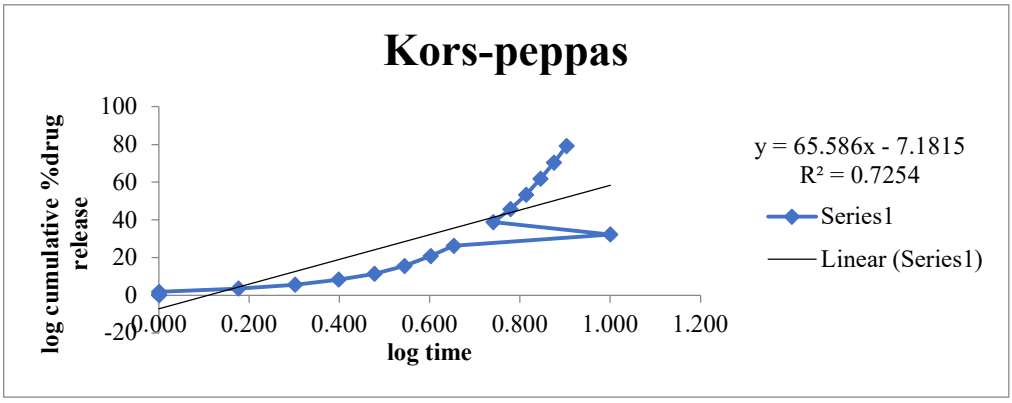

Figure 14D: Korsmeyer-Peppas plot of drug reiease data

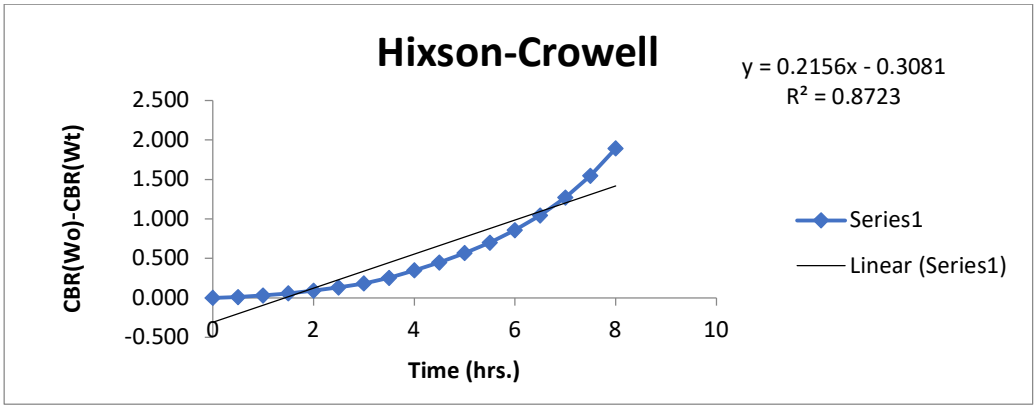

Figure 14E: Hixon-Crowell plot of drug reiease data

Stability Study:

Optimized formulation F3 was stored at room temperature for one month. Formulation is visually checked for its appearance, colour change, phase separation, and homogeneity after a month of preparation. pH, drug content and spreadability. No any phase separation was observed and results shows no any significant variation from initial test results.

Table 18: Evaluation of emulgel after stability study

Test Parameter	Colour	pH	Drug Content (%)	Spreadability (gm*cm/sec)
Initial	Off white	6.34	98.97	25.01
After 1 Month	Off white	6.33	98.96	25.02

5. CONCLUSION

Clarithromycin is a macrolide antibiotic. Clarithromycin is BCS class II drug and hence hydrophobic in nature and has only 50% of bioavailability. Hence, it was necessary to improve the therapeutic effectiveness of drug. Topical drug delivery system is selected to avoid GI irritation, first pass metabolism and to increase the concentration of drug at the site of action. Due to the barrier nature of skin permeation enhancers are added into the formulation.

In the present study, an attempt was made to formulate and evaluate the emulgel of clarithromycin for topical delivery. All the emulgel formulations were evaluated for physical appearance, pH, viscosity, drug content and *in-vitro* drug release study. Emulgel prepared with menthol and 2% xanthan gum showed highest spreadability coefficient. In the in-vitro drug release study F3 formulation showed highest drug release 79.17% after 8 hours. Emulgel formulation showed better antimicrobial activity. From all the results obtained from the study, F3 was found as an optimized formulation. So, the results of the current study are encouraging, there is a potential for more pharmacokinetic research.

6. REFERENCES

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