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Formulation and Evaluation of Ethosomal Gel Containing Clarithromycin for the Treatment of Acne Vulgaris

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Abstract:
Ethosomes are a novel lipid carrier, used as a transdermal drug delivery. The ethosomal approach was selected to enhance the permeability of clarithromycin that increases bioavailability, reduce side effects, reduce large doses and increases the therapeutic efficiency. Ethosomal gel of clarithromycin was prepared using cold method by taking different concentration of ethanol and phospholipid. The prepared formulations were evaluated for optical microscopy, drug entrapment efficiency, drug content, pH, viscosity, homogeneity and grittiness. The spreadability and in vitro drug release studies were also carried out. In vitro drug release studies were performed by using Franz Diffusion Cell for 12 h. The results of FTIR analysis showed that there was no physical and chemical interaction between drug and other excipients. The formulation F4 was considered as best formulation. The data obtained from in vitro release study were fitted into various mathematical models like zero order, first order, Higuchi and Peppas. The results of mathematical modelling obtained indicated that it was best explained by zero order kinetics and followed diffusion type of drug transport mechanism. The study concluded that the ethosomal gel of clarithromycin can effectively improve the bioavailability of drug by penetration enhancement, reduce the frequency of administration, given better patient compliance and also followed a sustained drug release mechanism. The ethosomal gel could be successfully prepared in a cost effective manner and had better drug release than the conventional dosage forms.

Keywords: Clarithromycin, ethanol, phospholipid, ethosome, sustained release.

INTRODUCTION

Novel drug delivery system is the advance drug delivery system which improve drug potency & control drug release to give a sustained therapeutic effect, provide greater safety, and able to target a drug specifically to a desired tissue. This system gives a new life to the existing drug molecule by solving the problems related towards the release of the drug at specific site with specific rate. The aim of the novel drug delivery system is delivering drugs to patients efficiently with fewer side effects. Liposomes, niosomes, liposomes, polymeric nanoparticles, and microspheres are the novel vesicular carriers used to entrap therapeutic molecule for better results in prolonged systemic bioavailability.

Topical drug delivery system is considered as one of the most convenient route for treating skin diseases and also an alternative route for delivery of drug into systemic circulation. As compared to traditional drug delivery, topical drug delivery achieve a constant plasma level for prolonged period of time and also requires less frequent dosing regimen. It has advantages such as self administration, better patient compliance, avoid first pass metabolism, GIT disturbance of drug molecoule and reduction in systemic adverse effect. Some restrictions of transdermal drug delivery system are slow diffusion across the stratum corneum and barrier property of the skin limits the delivery of the drug molecule through skin. To overcome these restrictions and novel non-invasive vesicular carrier, ethosomes are used which contain high concentration of ethanol, which act as a penetration enhancer to the skin. This system have the capacity of prolonging the existence of drug in stratum corneum and also have the capacity to target organ and tissues. Most of the ethosomal drugs are administered in semisolid form (gel or cream).[1,2]

Ethosomes were developed by Touitou, 1997. They are mainly used for the delivery of drug molecoule through transdermal route. Ethosomes are soft, highly flexible vesicle efficiently penetrate through skin and carry this molecule to the deep layers and systemic circulation. Ethosomal system consist of drug in a matrix of lipids, ethanol and water. Ethanol act as a penetration enhancer by dissolving skin lipid there by enhances the permeation of drug molecule through skin. Ethosomes overcome the disadvantage of liposomes and proliposomes such as less stability, leakage of drug, fusion of vesicle and breakage of vesicle. The size of the ethosome will be in the range of tens of nanometer to microns(μ).[3]

Acne vulgaris or simply known as acne is a human skin disease characterized by skin with scaly red skin (seborrhea), blackheads and whiteheads (comedones), pinheads (papules), large papules (nodules), pimples and scarring. Acne affects skin having dense sebaceous follicles in areas including face, chest and back. It is a chronic inflammatory disease. Acne is usually caused by increase in androgen level like testosterone mainly during puberty in both males and females. Antibiotics are used to treat acne vulgaris. Various topically active agents are available for treating bacterial infection.[4]

Clarithromycin is a novel macrolide antibiotic with broad spectrum of activity. It is better absorbed than erythromycin, is well tolerated and is to be administered less frequently. Clarithromycin is used to prevent and treat certain infections caused by bacteria. Oral administration of clarithromycin cause liver or kidney problems along with disturbance of heart rhythm. So the drugs are formulated for topical use to avoid gastro-intestinal irritation, to overcome first pass effect and to maximize the drug concentration at the site of action.[5,6]

MATERIALS AND METHODS

Materials: Clarithromycin, soya lecithin, ethanol, propylene glycol, carbopol 934, methyl paraben, and triethanolamine was obtained from Yarrow Chem products, Mumbai, India. All other chemicals and reagent were of analytical grade used for the development of topical gel.

Methods:[7,8]

Preparation of ethosomes:

Cold method: Ethosomal formulations were prepared by using cold method. This vesicular system is composed of phospholipid, ethanol, propylene glycol, drug and distilled water. Phospholipid was dissolved in ethanol and heated upto 30 ℃ on a magnetic stirrer. Drug solution in propylene glycol which is previously heated upto 30 ℃ and was added slowly in a fine stream to the above ethanolic lipid solution with continuous mixing using mechanical stirrer at 700 rpm in a closed container. Further warm water, heated up to 30 °C was added drop wise. The preparation was left to cool at room temperature for 30 min and then it was sonicated for 3 cycles, each cycle of 5 min to get nanosized ethosomes by using probe sonicator.

Preparation of gel base: 1% carbopol gel base was prepared by dispersing 1 g of carbopol 934 in a distilled water. The mixture was then allowed to hydrate under stirring for 60 min. Accurately weighed amount of methyl paraben was added into it. Again the mixture was stirred until thickening occurred and then neutralised by adding triethanolamine to achieve a transparent gel.

Incorporation of ethosomes in gel base: Ethosomal formulation was slowly dispersed into hydrated carbopol 934 slurry under mild stirring. Finally, the ethosomal gel was mixed using mechanical stirrer for 5 min.

Analytical methods:[6,9,10]

Determination of λmax for Pure drug Clarithromycin:

Preparation of stock solution: Accurately weighed quantity of 10 mg of clarithromycin was taken in 100 ml volumetric flask and was dissolved by using 3 ml of ethanol, finally the volume was made up with 5.5 pH phosphate buffer upto 100 ml to produce 100 µg/ml of solution.

Determination of λmax: The solution containing 10 µg/ml in phosphate buffer (pH 5.5) was scanned between 200-400 nm by using UV-Visible spectrophotometer against phosphate buffer pH 5.5 as blank.

Preparation of standard calibration curve of clarithromycin: From the above stock solution, aliquots of 1, 2, 3, 4, and 5 were transferred to 100 ml volumetric flask and diluted with pH 5.5 phosphate buffer. The absorbance of the solution was measured spectrophotometrically at 288 nm by using phosphate buffer pH (5.5) as blank. A calibration curve was plotted by taking concentration on X-axis and absorbance on Y-axis.

Preformulation studies:[11,12]

Organoleptic characters: The colour, odour and taste of the pure drug were recorded using descriptive terminology.

Solubility: Solubility test of clarithromycin was performed by using various solvents such as water, ethanol, methanol, acetonitrile, and acetone as solvent.

Melting point: Melting point of clarithromycin was determined by capillary method. Filled the capillary tube with the sample and was inserted into the melting point apparatus. The temperature at which sample gets melted gives the value for melting point of the sample.

Drug – Excipient compatibility studies:

FTIR: Integrity of the drug in the formulation was checked by taking an IR spectrum of the selected formulation along with the drug and other excipients. The spectra were taken by using Shimadzu IR Prestige-21 Spectrophotometer and compared with standard spectra. In this study, palletisation of potassium bromide (KBr) was employed. Before forming the pellets of potassium bromide, it was completely dried at 100 ℃ for 1 h and after drying it was thoroughly mixed with the sample in the ratio of 1 part of sample and 100 parts of KBr. The mixture was compressed to form a disc using dies. This disc was placed in the sample chamber and a spectrum was obtained through the software program which is further subjected to interpretation.

Characterization of ethosome vesicles:[13-25]

Optical microscopy: The Ethosomal dispersion was first spreaded on the glass slide and examination was conducted using optical microscope with magnification of 40x and 10x.

Drug entrapment efficiency: Entrapment efficiency of clarithromycin ethosomal vesicles was determined by centrifugation. The total volume of the ethosomal suspension was measured. 5 ml of this formulation was diluted with distilled water upto 8 ml and centrifuged at 15,000 rpm for 45 min at 40 ℃ using a cooling centrifuge. After centrifugation, the supernant and sediment were recovered, their volume was measured. Then sediment was lysed using n-propanol and filtered through a 0.45 µm nylon disk filter. The concentration of clarithromycin in the supernatant and sediment was analysed by UV spectroscopic method at 288 nm against phosphate buffer pH 5.5 as blank. The percentage drug entrapment was calculated using the following equation:

$$\%\ entrapment\ efficiency = \frac{amount\ of\ entrapped\ drug\ recovered}{total\ amount\ of\ drug} * 100$$

In vitro **drug release:** The diffusion studies of formulation containing clarithromycin ethosomal gel was carried out in Franz diffusion cell through dialysis membrane. Weight equivalent to 0.5 gm of the optimized formulation F4 was transferred to the diffusion cell and the temperature was maintained at 37 ± 0.5° C by using 24 ml phosphate buffer (pH 5.5) as the dissolution medium. 1 ml of sample was withdrawn at regular time intervals (1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, & 12 h) and equal volume of fresh buffer was replaced to maintain sink condition. The withdrawn samples were filtered through a whatmann filter paper (No. 41) and made the volume upto 10 ml and analysed by using UV spectrophotometer (Schimadzu, UV-1800) at 288 nm against phosphate buffer pH 5.5 to determine the percentage release of clarithromycin ethosomal gel.

Characterization of clarithromycin loaded ethosomal gel:[26-35]

Drug content: 1 g of each gel formulation was taken in 100 ml of volumetric flask containing 20 ml of phosphate buffer (pH 5.5) and stirred for 30 min. The volume was made up to 100 ml & 1 ml of the above solution was further diluted to 50 ml with phosphate buffer (pH 5.5). The resultant solution was filtered through Whatsman paper no.41. The absorbance was recorded by using UV spectrophotometer at 288 nm against phosphate buffer pH 5.5 as blank. Drug content was determined from the standard calibration curve of clarithromycin.

pH: pH of the ethosomal gel formulations was determined by using digital pH meter. 1 g of clarithromycin gel was mixed in 100 ml distilled water by using homogenizer. Then the electrode was immersed in the prepared gel solution and readings were recorded in triplicate and average value was calculated.

Viscosity: Viscosity of the gel is to be such that the preparation should be easily removed from the container and can be easily applied to the skin. Viscosity measurements were done on Brookfield viscometer by selecting suitable spindle number S-7 at 60 rpm.

Spreadability: Spreadability is the term expressed to denote the extent of area to which gel readily spreads on application to skin or affected part. The therapeutic efficacy of a formulation depends upon its spreading value. Spreadability is expressed in terms of time in seconds taken by two slides to slip off from gel and placed in between the slides under the way of certain load. Smaller the time taken for separation of two slides better will be the spread ability of the formulations. It is then calculated by using the formula:

$$S = \frac{ML}{T}$$

Where, M = Wt. tied to upper slide

L = Length of glass slides

T = Time taken to separate the slides.

0.1 g of ethosomal gel was pressed between two slides (divided into squares of 5 mm sides) and left for about 5 min where no more spreading was expected. Diameters of spreaded circles were measured in cm and were taken as comparative values for spreadability. The standardized weight tied on the upper slide was 125 g. The results were obtained are average of three determination.

Homogeneity and grittiness: A small quantity of ethosomal gel was pressed between the thumb and the index finger. The consistency of the ethosomal gel was noticed (whether homogeneous or not), if there was any coarse particles appeared on fingers. Also, the homogeneity could be detected when a small quantity of the ethosomal gel was rubbed on the skin of the back of the hand. The grittiness of prepared ethosomal gel was also observed in the same manner.

Extrudability: A good gel extrude optimally with slight pressure applied. The Extrudability of the formulations determined with aluminium collapsible tubes by applying pressure at the crimp end. The formulation extruded until the pressure dissipated. Extrudability of formulation was determined in terms of weight in grams required to extrude a 0.5 cm ribbon of gel in 10 seconds.

***In vitro* drug release:** The diffusion studies of formulation containing clarithromycin ethosomal gel was carried out in Franz diffusion cell through dialysis membrane. Weight equivalent to 0.5 gm of the selected formulation was transferred to the diffusion cell and the temperature was maintained at 37 ± 0.5 °C by using 24 ml phosphate buffer (pH 5.5) as the dissolution medium. 5 ml of sample was withdrawn at regular time intervals (1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, & 12 h) and equal volume of fresh buffer was replaced to maintain sink condition. The withdrawn samples were filtered through a whatmann filter paper (No. 41) and made appropriate dilution and analysed by using UV spectrophotometer (Schimadzu, UV-1800) at 288 nm against phosphate buffer (pH 5.5) as blank to determine the percentage release of clarithromycin ethosomal gel.

Dug release kinetics

Release kinetics of drug from the dosage form was determined by various mathematical models such as zero order, first order, koresmeyer- peppas and higuchi model.

1. Cumulative percent drug released Vs time (zero order plots)
2. Log cumulative percent drug remaining Vs time (first order plots)
3. Cumulative percent drug release Vs square root of time (Higuchi plots)
4. Log cumulative percent drug release Vs log time (korsmeyer – peppas plots)

RESULTS AND DISCUSSIONS

The present study was carried out to develop the ethosomes of clarithromycin by cold method. Six formulations were prepared using different concentration of phospholipid and ethanol. Phospholipid was used as vesicle forming agent. Propylene glycol is used as penetration enhancer. Ethanol is used for softening the vesicle. Distilled water is used as vehicle **(table 1)**. Carbopol 934 is used as gelling agent. Methyl paraben is used as preservative and triethanolamine is used as neutralizing agent **(table 2).**

Table 1 Composition of different ethosomal formulations

INGREDIENTS	F1	F2	F3	F4	F5	F6
Clarithromycin (mg)	100	100	100	100	100	100
Soyalecithin(mg)	100	200	300	400	200	300
Ethanol(ml)	10	20	10	20	15	20
Propylene glycol(ml)	10	10	10	10	10	10
Distilled water	q.s	q.s	q.s	q.s	q.s	q.s

Table 2 Composition of gel base

Ingredients	Concentration
Carbopol 934	1 %
Methyl paraben	0.02 %
Triethanolamine	0.3 %
Distilled water	Upto 100%

Analytical methods:

Standard calibration curve: λ_{max} of clarithromycin by spectrophotometric method in phosphate buffer pH 5.5 was found to be 288nm.

Calibration curve data of clarithromycin:

The obtained results on **table 5** were used to plot a graph of absorbance v/s concentration. The calibration curve was linear between the concentration 0 – 40 µg/ml was shown in **fig 1**. The measurement was done at 288 nm against phosphate buffer (pH 5.5) as blank.

Table 3: Calibration curve data of clarithromycin

SL.No	Concentration (µg/ml)	Absorbance (nm) (Mean ± SD)*
1	0	0.071 ± 0.12
2	10	0.135 ± 0.18
3	20	0.208 ±0.13
4	30	0.275 ± 0.11
5	40	0.334 ±0.15
6	50	0.394 ± 0.11

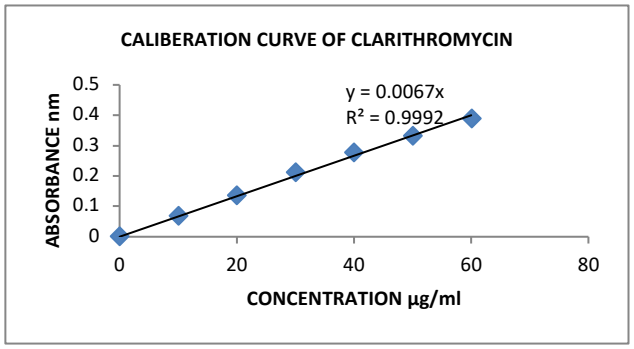

Fig 1: Calibration curve plot of clarithromycin

Pre formulation study:

Organoleptic characters: Colour, odour and taste of clarithromycin was found to be white, odourless and bitter in taste.

Melting point: Melting point of clarithromycin was found to be 218 ℃ and which was found to be in the range of 217 – 220 ℃.

Solubility: Clarithromycin is sparingly soluble in ethanol, methanol and acetonitrile and freely soluble in acetone. Insoluble in water.

Drug polymer compatibility:

FTIR studies: The drug excipient compatibility study was done by using SHIMADZU FT/IR spectrometer. The IR spectra of pure drug and drug – excipients mixtures were shown in **figures 2-8**. The spectrum of the pure drug and excipients suggests that there were no interaction between drug and excipients and were compatible with each other.

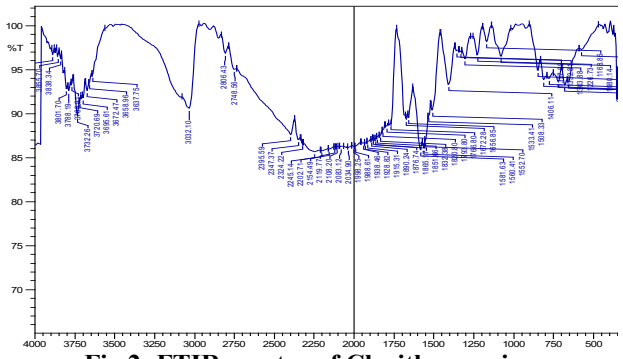

Fig 2: FTIR spectra of Clarithromycin

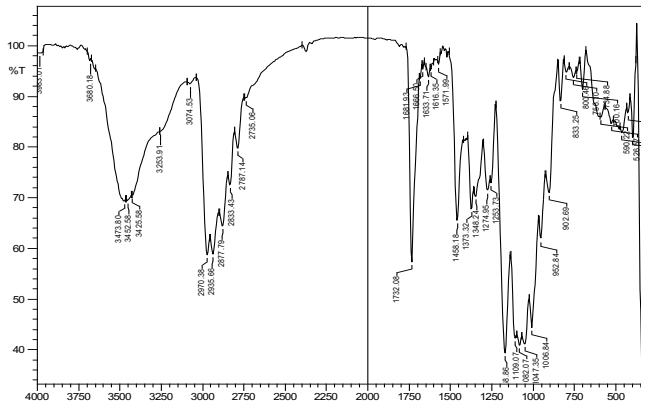

Fig 3: FTIR spectra of Clarithromycin + Soyalecithin

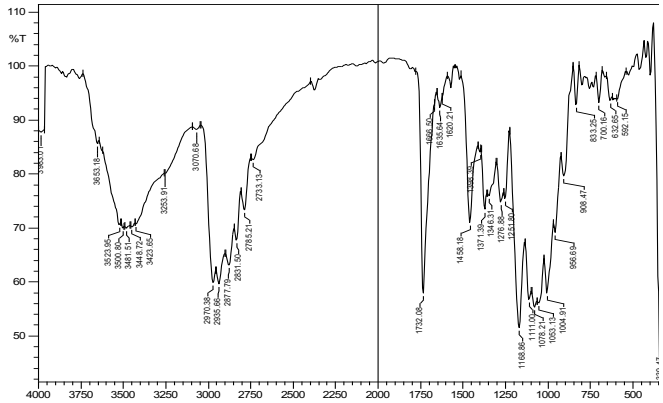

Fig 4: FTIR spectra of Clarithromycin + Ethanol

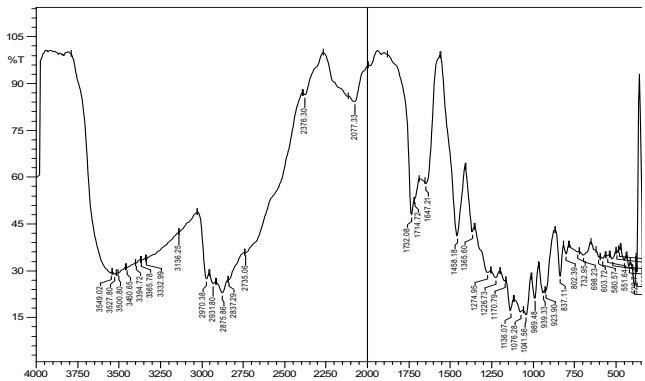

Fig 5: FTIR spectra of Clarithromycin + Propylene glycol

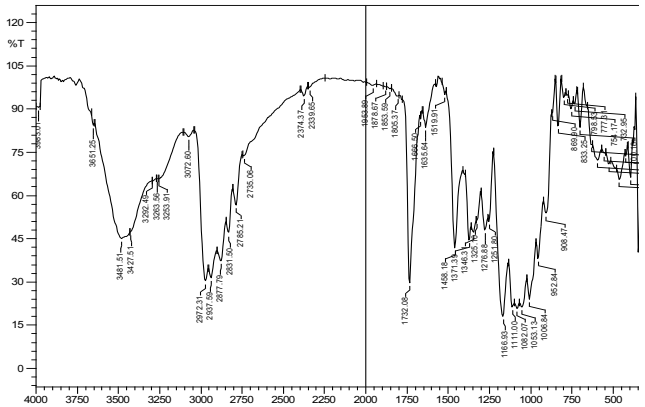

Fig 6: FTIR spectra of Clarithromycin + Carbopol 934

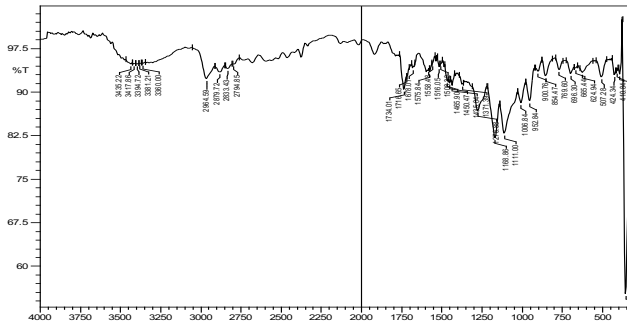

Fig 7: FTIR spectra of Clarithromycin + Methyl paraben

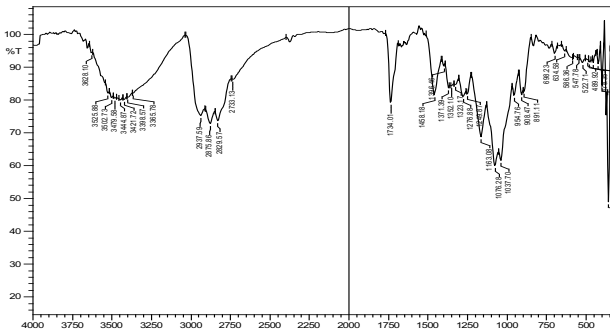

Fig 8: FTIR spectra of Clarithromycin + Triethanolamine

Characterisation of ethosome vesicles:

Optical Microscopy: The visual examination of ethosomes was confirmed by using optical microscope. The particles were observed as spherical globules.

Drug entrapment efficiency: Percentage entrapment of clarithromycin ethosomes was found to be in the range of 71.6 % to 91.4 % was shown in **table 4**. Higher entrapment efficiency was observed with F4 (91.4 %) and lower entrapment efficiency was noted in F1 (71.6%). Amount of ethanol and lecithin used for ethosomes preparation seemed to influence the entrapment efficiency.

Table 4: Entrapment efficiency of ethosome

SL.No	Formulation Code	Entrapment efficiency (%) (Mean ± SD)*
1	F1	71.6 ± 0.17
2	F2	82.58 ± 0.12
3	F3	83.5 ± 0.23
4	F4	91.4 ± 0.14
5	F5	72.6 ± 0.26
6	F6	88.5 ± 0.10

***In vitro* drug release Study:** The percentage release of the drug was observed with F4 (95.15 %) at the end of 12 h, and less percentage of drug release was noted in F1 67.40 %) at the end of 12 h. It is concluded that concentration of soya lecithin and ethanol gave predominant effect in drug release. The percentage cumulative drug release of all the ethosome formulations was summarized in **table 5** and the percentage cumulative drug release with time was shown in **figures 9 &10**.

Table 5: *In vitro* drug release study data of ethosome

SL.No	Time (h)	Percentage of drug released (%)					
		F1	F2	F3	F4	F5	F6
		0	0	0	0	0	0
1	0.5	13.29	7.10	3.99	5.23	4.45	5.32
2	0.25	20.95	12.58	10.32	12.35	10.44	9.97
3	1	30.31	19.45	18.22	18.52	15.93	15.17
4	2	40.91	27.32	25.67	26.91	20.67	24.98
5	3	51.32	44.40	38.34	37.55	32.78	33.48
6	4	55.15	60.10	46.21	45.21	45.93	45.37
7	5	58.44	60.87	55.22	57.88	56.64	48.77
8	6	63.48	61.18	64.45	71.24	58.34	60.35
9	7	63.95	61.32	67.41	75.17	62.22	63.54
10	8	64.32	61.88	68.22	80.31	65.31	68.37
11	9	65.10	62.25	70.18	85.74	67.38	68.81
12	10	65.23	64.43	71.14	85.89	70.21	72.12
13	11	65.78	64.72	71.82	90.13	75.45	72.95
14	12	67.40	67.84	72.11	95.15	80.88	73.54

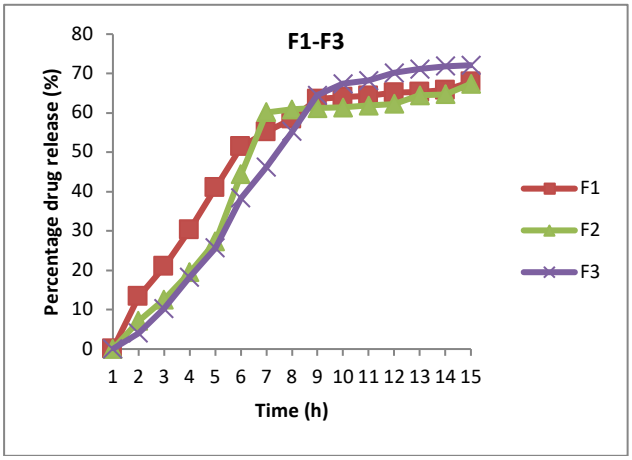

Fig 9: *In vitro* drug release study data of formulations F1-F3

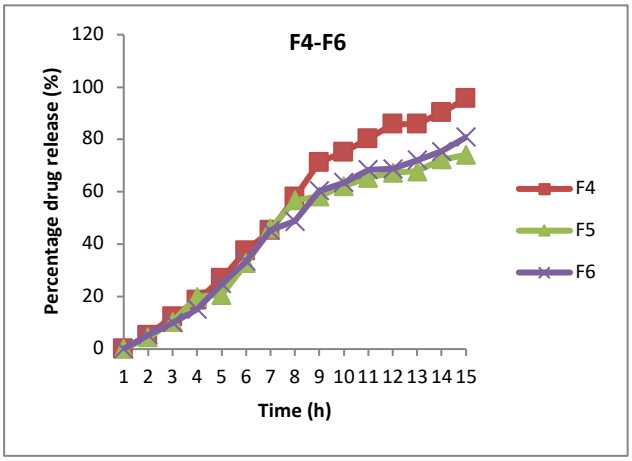

Fig 10: *In vitro* drug release study data of formulations F4-F6

Characterisation of clarithromycin loaded ethosomal gel:

Drug Content: Drug content of ethosomal gel was found to be in the range of 71.64 % to 92.51 %. The drug content was found to be higher in F4 (92.51 %) and the least drug content was observed with F1 (71.64 %). Concentration of Soyalecithin has a great influence in drug loading. The results were tabulated in **table 6**.

Table 6: Drug content of ethosomal gel

SL.No	Formulation Code	Drug Content (%) (Mean ± SD)*
1	F1	71.64 ± 0.21
2	F2	83.58 ± 0.14
3	F3	86.56 ± 0.13
4	F4	92.51 ± 0.21
5	F5	74.62 ± 0.28
6	F6	89.55 ± 0.12

pH Determination: pH determination of the different formulations found to be in the range of 6.98 to 7.56 which states that the prepared gels are non-irritant to the skin. The pH of the optimized formulation F4 was 6.56 and the formulation code F1 was noted with lowest pH of 5.98. The results were tabulated in **table 7**.

Table 7: pH Values of ethosomal gel

SL.No	Formulation Code	pH (Mean ± SD)*
1	F1	5.98 ± 0.18
2	F2	5.61 ± 0.12
3	F3	6.14 ± 0.25
4	F4	6.56 ± 0.16
5	F5	5.81 ± 0.13
6	F6	7.11 ± 0.21

Viscosity measurement: Viscosity of various formulated gels were found in range of 5634 to 8994 centipoises was shown in **fig 11**. High viscosity was observed at F4 (8994 cps) and less viscosity was noted in F1 (5634 cps). This satisfying viscosity of the prepared ethosomal gel further confirm the reasonable skin retention time.

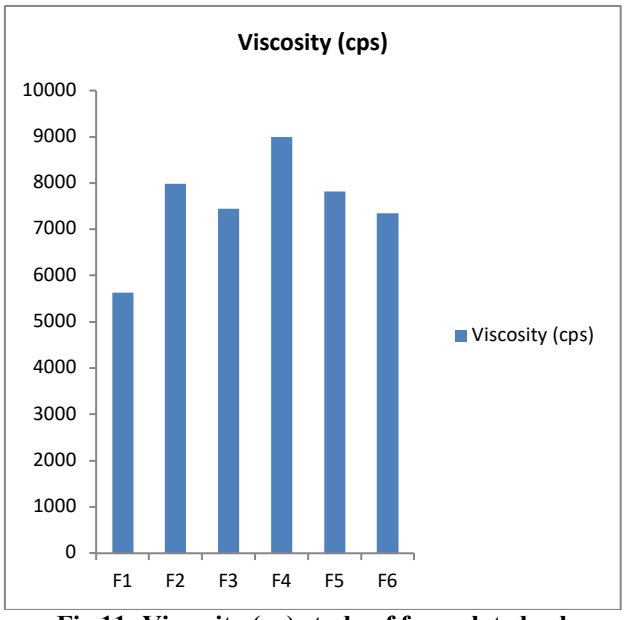

Fig 11: Viscosity (cp) study of formulated gel preparation

Spreadability: The spreadability results were found to be most effective using ethosomal gel. This indicated that the gel was easily applicable. The results were tabulated in **table 8**.

Table 8: Spreadability of ethosomal gel

SL.No	Formulation Code	Spreadability (g/cm/sec) (Mean ± SD)*
1	F1	9.52 ± 0.13
2	F2	13.85 ± 0.21
3	F3	11.33 ± 0.18
4	F4	15.22 ± 0.20
5	F5	14.21 ± 0.12
6	F6	10.88 ± 0.17

Homogeneity and grittiness: All the formulations showed homogenous property with smoothness in texture and the results were shown in **table 9.**

Table 9: Homogeneity and grittiness of ethosomal gel

SL.No	Formulation Code	Homogeneity	Grittiness
1	F1	Homogenous	No
2	F2	Homogenous	No
3	F3	Homogenous	No
4	F4	Homogenous	No
5	F5	Homogenous	No
6	F6	Homogenous	No

Extrudability: The optimized formulation F4 was subjected to determine its Extrudability property and the results were shown in **table 10.**

Table 10: Extrudability of optimized gel

	Extrudability
F4	Good
	Good
	Good

***In vitro* drug release study**: The optimized ethosomal gel showed high percentage drug release in F4 (95.64 %) at the end of 12 h, and a lesser percentage of drug release was observed with F1 (79.90 %). Concentration of soyalecithin, ethanol and polymer influenced the drug release from the formulation. The percentage cumulative drug release of all the ethosome formulations was summarized in **table 11** and the percentage cumulative drug release with time was shown in **figures 12 & 13**.

Table 11: *In vitro* drug release study data of ethosomal gel

SL.No	Time (h)	Percentage of drug released (%)					
		F1	F2	F3	F4	F5	F6
		0	0	0	0	0	0
1	0.25	4.56	5.34	3.45	6.25	5.11	5.23
2	0.5	10.44	9.36	9.74	11.24	10.44	10.42
3	1	16.02	16.48	16.44	18.45	15.94	15.61
4	2	24.02	21.65	24.55	24.11	24.36	24.47
5	3	35.87	30.73	32.83	35.74	35.65	35.56
6	4	45.22	43.16	40.67	46.38	46.23	45.02
7	5	56.76	52.38	51.68	57.87	54.18	55.78
8	6	62.48	61.97	58.44	71.09	65.48	68.65
9	7	68.44	68.34	62.46	74.55	70.82	74.12
10	8	72.34	76.44	65.74	79.74	74.34	74.88
11	9	74.44	78.22	70.30	85.31	74.95	78.28
12	10	76.12	78.95	74.45	88.66	78.43	78.95
13	11	78.22	79.94	78.52	91.32	80.12	80.12
14	12	79.90	81.02	82.31	95.64	84.11	83.78

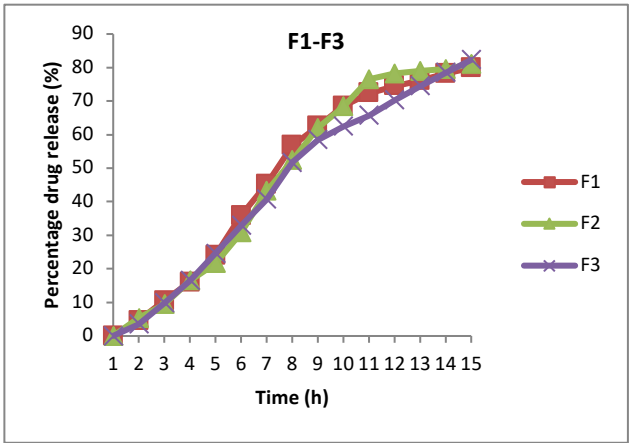

Fig 12: *In vitro* drug release study data of formulations F1-F3

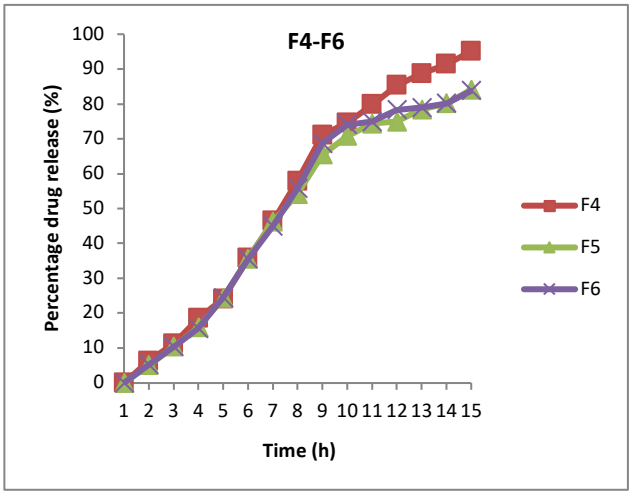

Fig 13: *In vitro* drug release study data of formulations F4-F6

Kinetic modelling of F4: The data of *in vitro* release study were fitted in different kinetic models and the values were showed in **table 12** and **figures 14, 15, 16 & 17**. The best fit with highest regression value R was observed in higuchi model. So the optimized formulation shows diffusion mechanism and the release profile of drug from the ethosome was explained by first order kinetics.

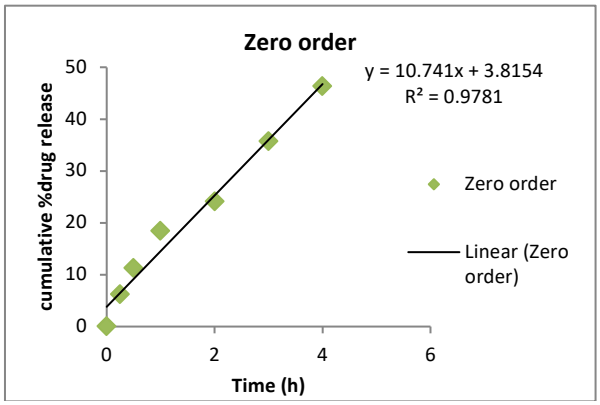

Fig 14: Zero order plot of F4

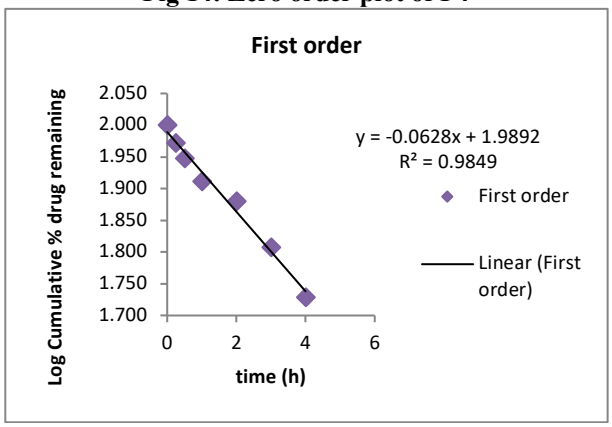

Fig 15: First order plot of F4

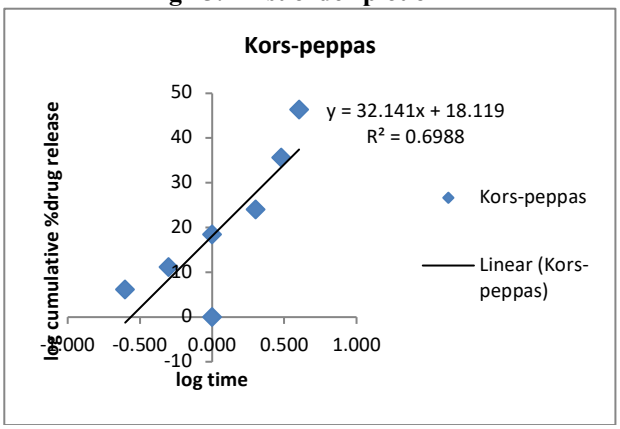

Fig 16: Korsmeyer-peppas model

Table 12: Kinetic modelling of F4

Time (h)	Cumu % drug release	% drug remaining	Square root time	Log cumu % drug remaining	Log time	Log Cumu % drug released	% drug released	Cube root of % drug remaining (w)
0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
0.25	93.75	0.500	1.972	-0.602	0.796	6.25	4.543	0.099
0.5	88.76	0.707	1.948	-0.301	1.051	4.99	4.461	0.181
1	81.55	1.000	1.911	0.000	1.266	7.21	4.337	0.305
2	75.89	1.414	1.880	0.301	1.382	5.66	4.234	0.408
3	64.26	1.732	1.808	0.477	1.553	11.63	4.005	0.637
4	53.62	2.000	1.729	0.602	1.666	10.64	3.771	0.871
5	42.13	2.236	1.625	0.699	1.762	11.49	3.480	1.162
6	28.91	2.449	1.461	0.778	1.852	13.22	3.069	1.573
7	25.45	2.646	1.406	0.845	1.872	3.46	2.941	1.701
8	20.26	2.828	1.307	0.903	1.902	5.19	2.726	1.916
9	14.69	3.000	1.167	0.954	1.931	5.57	2.449	2.193
10	11.34	3.162	1.055	1.000	1.948	3.35	2.247	2.395
11	8.68	3.317	0.939	1.041	1.961	2.66	2.055	2.587
12	4.85	3.464	0.686	1.079	1.978	3.83	1.693	2.949

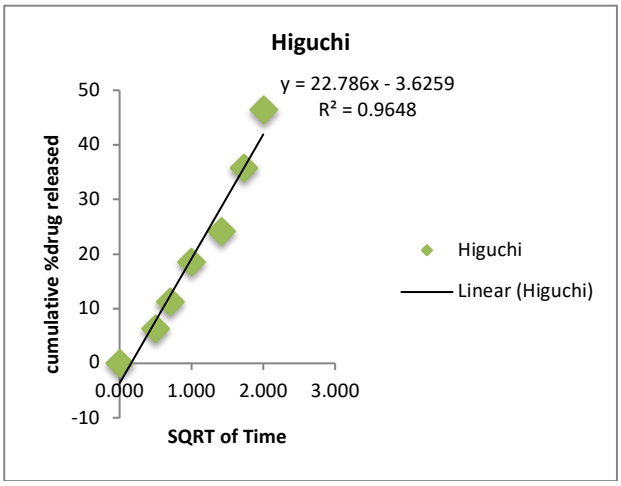

Fig 17: Higuchi plot

CONCLUSION

In the present study, ethosomal formulations were prepared as a new attempt to enhance the bioavailability of the drug clarithromycin for the treatment of acne vulgaris. Ethosomal suspensions were prepared by cold method using different concentration of phospholipid. Formulation F4 was found to be the best formulation among others based on some characteristic parameters such as drug entrapment, drug content, percentage drug release and in-vitro drug release data. FTIR studies showed that absence of incompatibility between drug and excipients. The present research proved that the ethosomal gel reduce the frequency of administration, give better patient compliance and also follows a sustained drug release mechanism.

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