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Aswathy.B
Associate professor
KTN College of pharmacy
Kerala, India

Remya Raveendran
Associate professor
KTN College of pharmacy
Kerala, India

Madhav.H
Student
KTN College of pharmacy
Kerala, India

Sreeroopa.C
Student
KTN College of pharmacy
Kerala, India

Shabhana.Tm
Student
KTN College of pharmacy
Kerala, India

Rohith.K
Student

KTN College of pharmacy
Kerala, India

Correspondence:
Aswathy.B
Associate professor
KTN College of pharmacy
Kerala, India

Formulation and In Vitro Evaluation of Clindamycin Liquid Crystalline Gel in the Topical Skin Infection

Aswathy.B, Remya Raveendran, Madhav.H, Sreeroopa.C, Shabhana.Tm, Rohith.K

Abstract
Present study was focused on the formulation and invitro evaluation of novel gel containing clindamycin liquid crystalline gel. Aim of our study to devolope clindamycine in the treatment of topical skin infection in liquid crystalline gel form. This is prepared by using tween 80, cetosteryl alcohol and glycerol. Formulation G1 to G4 differs in the ratio of tween 80 and cetosteryl alcohol. Preformulation studies for pure drug was conducted formulation were evaluated on the basis of viscosity, encapsulation efficiency and invitro drug release study using Trans diffusion cell. FTIR study of pure drug, polymer and the formulation proves to have no chemical interaction. Formulation G2 had appropriate viscosity 1738.34 and highest encapsulation efficiency 94.45±0.4 .The invitro release study found to have zero order release profile compare to all other formulation that indicates diffusion as drug release mechanism. Invitro comparative evaluation of the liquid crystalline gel with that of 3 marketed samples proves that liquid crystalline gel formulation has the sustained release capability compare to other.

Keywords: Clindamycine, liquid crystalline gel, Tween80, Cetosteryl alcohol

Introduction
Clindamycin gel form is available in the market and can be used mainly for topical skin and bacterial vaginal infections. These formulations are available with short half-life. By adopting the drug, clindamycin to a liquid crystalline form the half-life can be increased with sustained release action. Due to high viscosity of the liquid crystalline gel, the contact time of the drug with that of the infected area can also increase. Thus this formulation can be more effective in topical skin or vaginal infections.
The main aim of any type of drug delivery system is to deliver a therapeutic amount of drug to the proper site of the body to get a proper outcome of a drug. The drug application to the skin mainly aims to treat dermatological disorder and to treat deep tissues such as muscles and vein.
A gel is a solid jelly-like substance whose consistancy range from soft and weak to hard and tough. Gels are defined as a dilute cross- linked system, which exhibits no flow property at steady-state. Liquid crystals (LCs) have the properties between those of conventional liquids and those of solid crystals. Liquid crystals can be divided in to thermotropic, lyotropic and metallotropic phase.

2. Methodology
2.1 Preformulation of Clindamycin
2.1.1 Organoleptic property
The drug was visually inspected to find the organoleptic property like colour odour and appearance

2.1.2 Determination of solubility of clindamycin
Excess drug(100 mg) was added to 15ml of each fluid taken in a 25ml Stoppered conical flask and the mixtures were shaken for 24hrs at room temperature(28+-1) on rotary flask

shaker for 24 hrs. 2ml sample were withdrawn at 2 hr. interval and filtered immediately using a 0.45 disc filter. The filtered sample were diluted and the amount of clindamycin determined by measuring absorbance at 241nm. Shaking was continued until two consecutive estimations results are same.

2.1.3 Melting point determination
The melting point of clindamycin was determined by using melting point apparatus.

2.1.4 Determination of partition coefficient
30ml n-octanol and30 ml of water solution were taken to the separating funnel. 100mg of drug (clindamycin) was added to it and shake for 1 hour. From this 1ml of aqueous layer was removed and transferred into a 100ml standard flask and make up the volume with water. The absorbance was measured using UV at 241nm by taking water as blank.

2.1.5 UV spectroscopy:
Determination of λ max
Weighed sample is dissolved in distilled water and make 1mg/ml. The solution was then diluted to 100ml using distilled water of 100µm/ml concentration. UV spectrum was measured in the wavelength range 200-400nm.

Preparation of calibration curve for clindamycin
Stock solution of clindamycin (100µg/ml) was prepared in water. The solution of clindamycin was transferred into 5 different 10ml volumetric flask upto the mark with water to get the concentration in the range of 10-50µg/ml. The absorbance of the resulting solutions was measured at 241nm.

2.2 Formulation of Clindamycin Liquid Crystaline Gel
Liquid crystals (LC) gel was prepared by melting cetosteryl alcohol and tween 80 together and water is added to approximately same temperature followed by cooling slowly and mixing at 500rpm stirrer. Clindamycine was mixed in mixture of cetosteryl alcohol and tween80 and glycerol in different ratio.

2.3 Comparison of Liquid Crystalline Gel with Three Other Marketed Products
We are comparing in vitro release study of liquid crystalline gel (sample) with the marketed products like (Gel and Ointment)
These drugs are mainly used for the treatment of vaginal infection.

Formulation Table of Clindamycin

Table 1: formulation table of clindamycine

SLN CODE	DRUG (mg)	TWEEN 80 (ml)	CETOSTEARYL ALCOHOL (mg)	GLYCEROL (ml)	WATER (ml)
G1	100	5	5	0.5	15
G2	100	2.5	7.5	0.5	15
G3	100	7.5	2.5	0.5	15
G4	100	5	10	0.5	15

G-Liquid crystalline gel

2.4 Evaluation of Gel
2.4.1 Gel pH and viscosity
The pH of the sample is measured using pH meter and viscosity by brook field viscometer

2.4.2 Determination of %entrapment efficiency
The % entrapment efficiency (%EE) of clindamycin in SLN s formulations ere determined by trifugation of centrifuging the colloidal sample at 14000 rpm at 25ºC for 30 min. The free clindamycin in the supernatant is sample was estimated by UV spectroscopy at 241nm.

$$EE\% = \frac{\text{Amount of clindamycin found in liquid crystalline}}{\text{Amount of clindamycin added during preparation of liquid crystalline gel}} \times 100$$

2.4.3 Invitro release study.
In vitro release studies of clindamycin was performed using diffusion cell whose receptor compartment haves a surface area of permeation 3.14sq cms. The cellophane membrane (semipermeable) was placed between the donor and the receptor compartment. A weighed amount of gel is at one side of the membrane and the receptor medium filled with phosphate buffer pH 7.4 on other side. The receptor compartment is surrounded by a jacket in order to maintain the temperature of 37± 0.5 ºC. Heat is provided to this through a thermostatic hot plate with a magnetic stirrer. The receptor fluid is stirred by using a Teflon coated magnetic bead fitted to a magnetic stirrer. Sample is withdrawn at each time interval and the amount of sample present in it was calculated.

2.4.4 FTIR Spectra of clindamycin phosphate: IR spectra of physical mixture containing **drug** and excipients were determined by Fourier Transform Infrared Spectrophotometer using potassium bromide. A base line correction was made using dried pellet. The pellet of about l mm diameter was prepared by grinding about 3-5 mg of physical mixture of drug-excipients with 100-150 mg of potassium bromide in pressure compression machine. The sample pellet was placed in IR compartment and scanned at wavelengths 4000 cm-1 to 400 cm-1

3. Result and Discussion
3.1 Pre Formulation Studies Of Clindamycin
3.1.1 Organoleptic property
Colour: White to off- white
Odour: odourless
Taste: bitter

Appearance: powder
Nature: hygroscopic and crystalline

3.1.2 Determination of solubility of clindamycin

The solubility of the sample of clindamycin was examined in various solvents. The results shows that it was freely soluble in water, slightly soluble in methanol, very slightly soluble in acetone and insoluble in chloroform.

3.1.3 Melting point determination

The melting point of pure clindamycin determined by melting point determining apparatus was found out to be 115ºc.

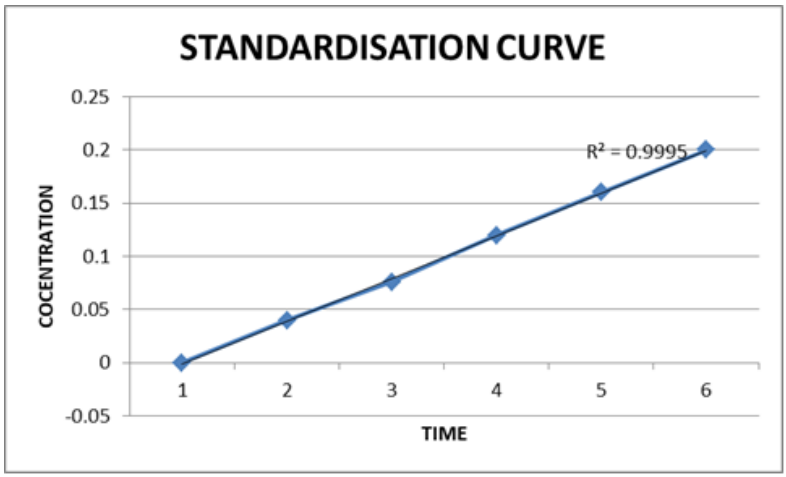
3.1.4 Determination of Partition coefficient

Partition coefficient of clindamycin determined by using water and n-octanol as solvents was found out to be 3.5.

3.1.5 Determination of λmax

The λ max of clindamycin determined by using UV spectrophotometer was found to be 241 nm.

Graph: 1 Calibration curve of clindamycin



3.1.6 Colour and appearance

The formulation shows white in colour with semisolid consistency. It was observed that gel formulation shows good spread ability and viscosity.

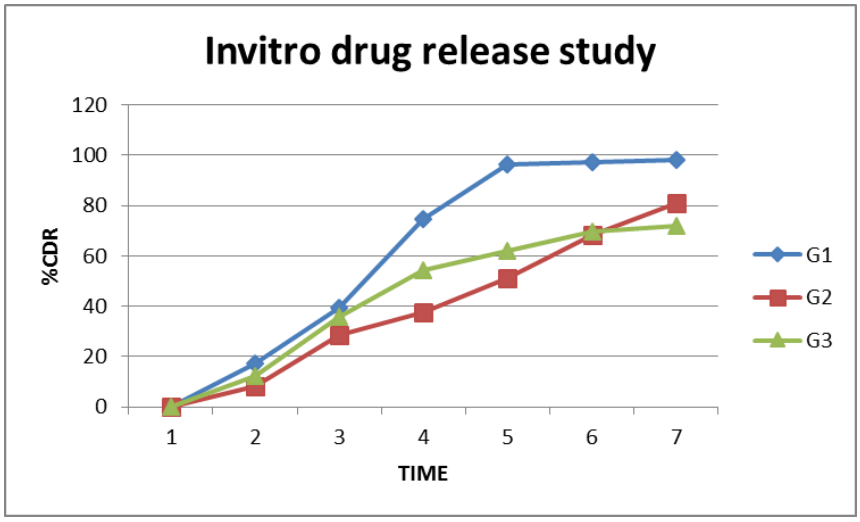
3.2 Evaluation Test

Table 2: The formulation are subjected to various evaluation test and results are tabulated.

S. NO	Formulation Code	PH	Viscosity (CPS)	Encapsulation Efficiency
1	G1	8.12	1354.67	88.46±0.16
2	G2	6.52	1738.34	94.45±0.4
3	G3	8.06	1452.78	87.82±0.56
4	G4	7.82	982.25	62.34±0.24

3.2.1 Invitro release study (%CDR of clindamycin from liquid crystalline gel)

Graph: 2 In Vitro release study of 3 formulation G1, G2, G3



3.2.2 FTIR study

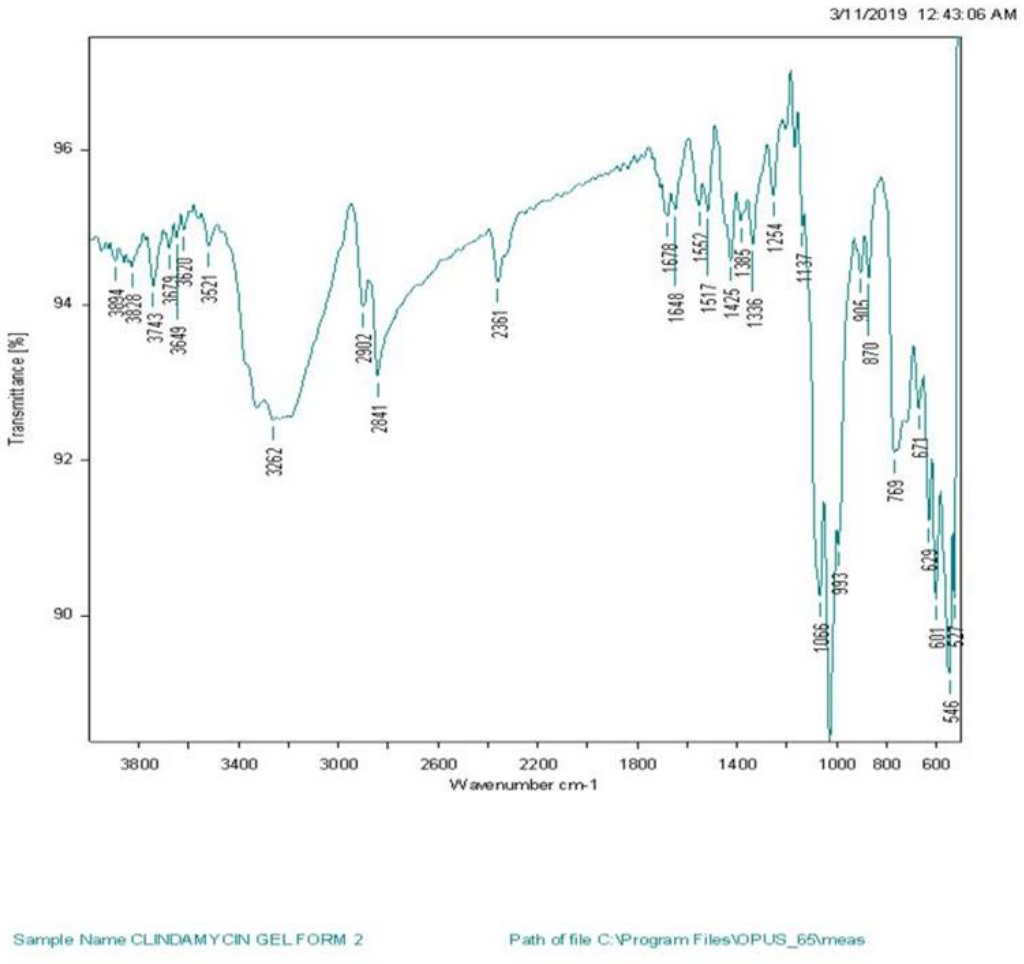


Fig. 1: IR study of clindamycine pure drug

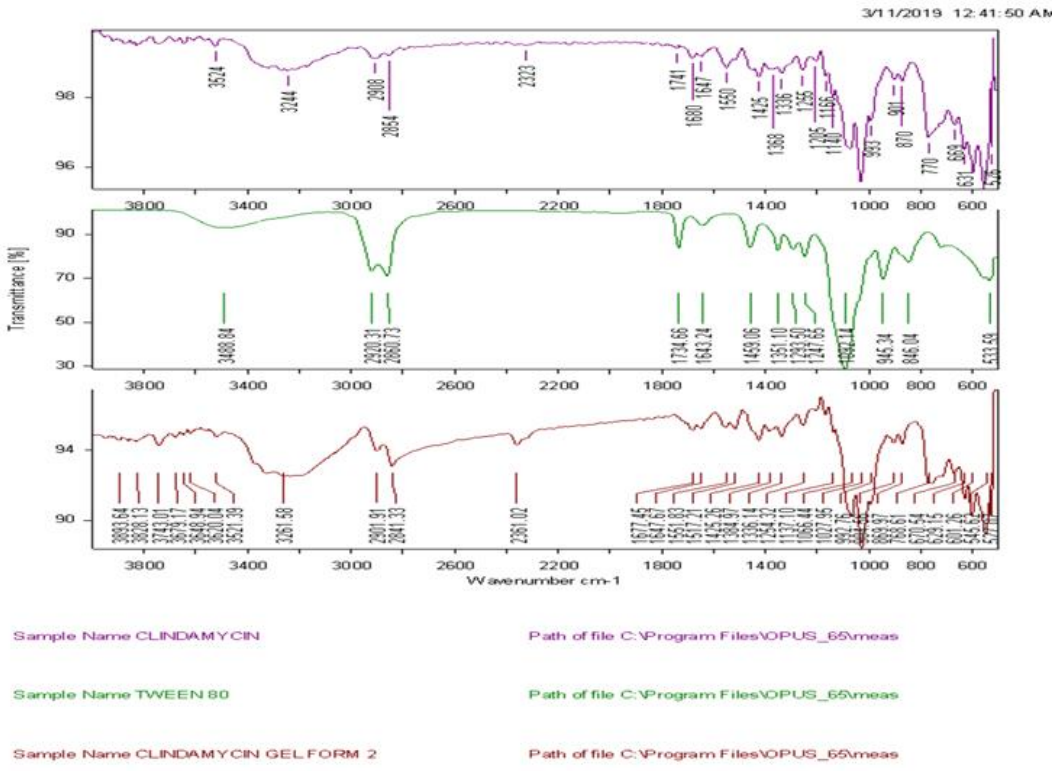


Fig. 2: polymer interactive study of LC gel

The FTIR sectra of clindamycine HCL, tween 80, clindamycine liquid crystalline gel are depicted in figures. FTIR spectra of pure clindamycine HCL shows characteristic peaks at 1095cm C-O stretching, 1755cm C-

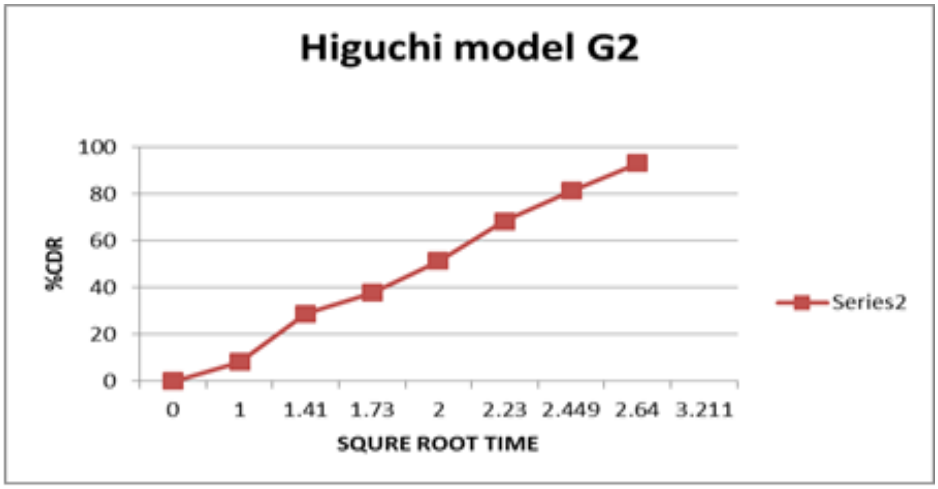
O stretching, 1516cm C-C stretching, 2941cm C-H stretching.
From the FTIR spectra of clindamycin and the polymer it is evident that there is no chemical intraction between the drug and polymer in the formulation

3.3 Optimization of Best Gel
Out of three formulations G2 exhibited good release pattern.G1 release 90% of drug with in 4hr and show saturation effect.G3 release only 75% of drug of drug in 7 hrs and 71% drug in 6 hrs and show that G3 have sustained action. So G2 had been optimized as the best formulation. To describe the exact mechanism and order of drug release, curve fitting analysis was done with G2.

3.4 Curve Fiting Analysis

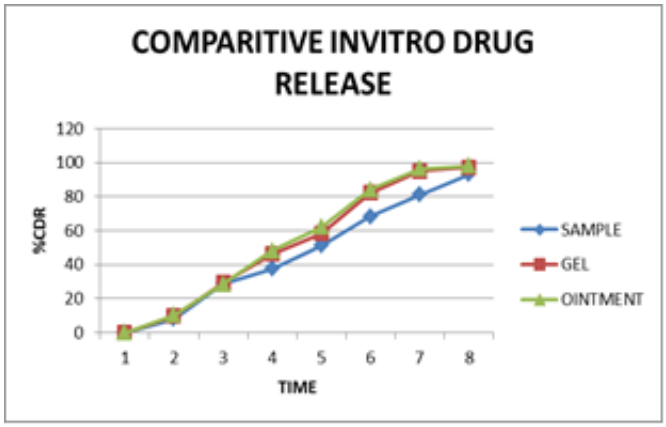
Graph 3: zero order kinetics of G2

Graph 4: First order kinetics of G2



Graph 5: Higuchi model of G2

3.5 Invitrocomparison of Formulated Drug with Marketed Formulations.



3.6 Discussion

3.6.1 Preformulation studies

Preformulation studies of clindamycine were found to be white to off white crystalline powder of hygroscopic in nature. The drug was found to have odourless bitter in taste. Considering solubility, the drug is freely soluble in water. From FTIR studies proves to have no chemical intraction between drugs and polymer.

3.6.2 Liquid crystalline gel

Liquid crystalline was prepared from the formulation and whose encapsulation efficiency was determined. The G2 have EE 94.45% and G3 have EE 87.8%.

For more optimizing these formulation the invitro release study was conducted G2 have release of 93.15% in about 7 hours.G3 release only 75% of drug in 7 hours. G3 was not suitable for inserting gel into cosmetic cream because of sustained action so G2 has been optimized as the best formulation. The invitro release profile of liquid crystalline gel Vs marketed products are plotted by time in x axis and % CDR in y axis. Invitro comparison of the sample with that of marketed product founds that liquid crystalline formulation has sustained action compares to other formulation.

3.7 Conclusion

The preformulation studies were performed using the pure drug and was found to be useful for the formulation.

The formulation was prepared using fusion method. The formulation were subjected to evaluation procedures and found that this formulation was having high drug releasing ability of about 93.15% in 7 hour. This is also having high encapsulation efficiency.

Zero order plot of optimized formulation (G2) indicated that its release mechanism is concentration independent (R^2 = 0.995). Higuchi's plot for the formulation revealed that the predominant mechanism of the drug release is diffusion (R^2=0.898).

Optimized formulation shows sustained action compares to other marketed formulation.

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