# NON-IONIC SURFACTANT CARRIER ANTI-BACTERIAL GEL OF ERYTHROMYCIN

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***ABSTRACT: Niosomes are one of the most promising novel drug delivery systems. Niosomes are widely known for their drug targeting of specific organs and tissues when compared to other drug delivery systems. In the present endeavor, Erythromycin in non-ionic surfactant vesicle gel, were attempted to reduce the frequent dosing, side-effects and improve bioavailability and residence time of drug. Erythromycin, a macrolide antibiotic drug was selected for the experiment having bacteriostatic action, binds to the 23S ribosomal RNA molecule in the 50S subunit of bacteria which inhibits the protein synthesis of bacteria ultimately causing inhibition of bacterial growth. We prepared different F1 to F6 formulations of erythromycin. Niosomal formulations were developed by using different proportions of cholesterol (Penetrating enhancer) and maintaining constant proportions of remaining ingredients such as tween 80(non-ionic surfactant, Preservative) Ethanol(solvent), phosphate buffer (pH adjuster). All formulations from F1 to F6 were evaluated for different parameters like particle size, Drug Entrapment efficiency and In-vitro drug release studies. Among of all the six formulations F2 formulation was the most satisfactory formulation with 92.56% of drug release. The Particle size was found to be 270nm with 84.98% drug entrapment efficiency. Maximum bioavailability of drug was after 8hours of administration.***

***KEYWORDS: Erythromycin, Niosomes, Niosomal gel, Thin Film Hydration method, Rotatory evaporator, Entrapment efficiency, In-vitro drug release.***

## I. INTRODUCTION

Niosomes are microscopic, non-ionic surfactant vesicle/ carrier that are either unilamellar or multilamellar. These are generally prepared by using synthetic non-ionic surfactants by hydration method with or without cholesterol. The size range of Niosomes varies from 10 to 1000nm. Niosomes consists of both hydrophobic tails and hydrophilic heads facing each other forming a bilayer. When we focus on the topical issues, skin is the largest organ in the body and is easily prone to bacterial infections. To overcome these issues, we have selected the anti-bacterial drug erythromycin. Bacteria requires protein synthesis in-order-to replicate, erythromycin gives its action by inhibition of protein synthesis. Generally, bacteria consist of 70S ribosome composed of two asymmetric 30S and 50S subunit. Here, erythromycin binds to the 23S ribosomal RNA molecule in the 50S subunit and inhibits the transpeptidation/translocation step of protein synthesis followed by inhibition of assembly of 50S ribosomal subunit which results in bacteriostatic action. Therefore, controls various bacterial infections. The main aim for choosing the non-ionic surfactant drug delivery through topical route is erythromycin gets deactivated by gastric acid when administered through oral route. Whereas, in case of topical route, it directly shows its action at the site of administration reducing the dose frequency, dose dumping, side effects and increased bioavailability. Erythromycin is considered as hydrophobic drug as it is practically insoluble in water. So, it can be entrapped within the hydrophobic tail bilayer of Niosomal structure. Cholesterol influences the nature of Niosomes in aspects such as thickness, fluidity, and helps in stabilization of the structure. On the other hand, tween 80 a non-ionic surfactant has the action as emulsifier, wetting agent, penetrating agent, diffusant. There are various methods to formulate the Niosomes, such as thin film hydration method, sonication method, ether injection method, heating method, reverse phase evaporation method, bubble method etc. In this experiment, we followed thin film hydration method and formulated erythromycin incorporated Niosomes. These Niosomes were mixed with gel base to obtain the desired Niosome based antibacterial gel. We chose non-ionic-surfactant carrier drug delivery system over other drug delivery systems as it is advantageous in the aspects of stability, control release, non-immunogenic, less toxic in nature, improves entrapped drug stability, osmotically active etc.

**Materials:** Erythromycin, Cholesterol, Tween 80, Ethanol, Phosphate buffer, Carbopol 940.

## II. METHODOLOGY

**Table-1: Formulation of Erythromycin Niosomes**

| Ingredients | F1 | F2 | F3 | F4 | F5 | F6 |
|---|---|---|---|---|---|---|
| Erythromycin(mg) | 400 | 400 | 400 | 400 | 400 | 400 |
| Cholesterol(mg) | 400 | 800 | 1200 | 1600 | 2000 | 2400 |
| Tween 80 (ml) | 10 | 10 | 10 | 10 | 10 | 10 |
| Solvent (Ethanol)(ml) | 10 | 10 | 10 | 10 | 10 | 10 |
| Phosphate buffer(ml) | 10 | 10 | 10 | 10 | 10 | 10 |

**Preparation Of Niosomes:**

Niosomes were prepared by the thin film hydration method. Measured amount of non-ionic surfactant (Tween 80), Cholesterol dissolved in 10 ml of ethanol. The mixture was then transferred into a round bottom flask. Then by using rotary evaporator, at 40°c, 100 rpm and with vacuum, the solvent was evaporated until a thin layer is formed. Hydration of film was carried out by using drug incorporated 7.4 phosphate buffer at 40°c, 100rpm and without vacuum for 30 minutes. This results in formation of Niosomal dispersion, which was sonicated for 15 min by using bath Sonicator.

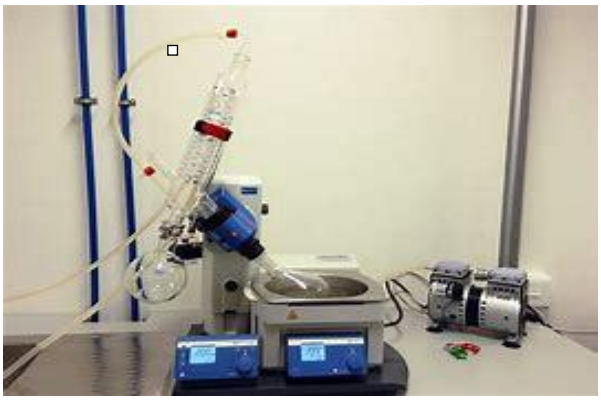


Fig.1. Rotary Evaporator

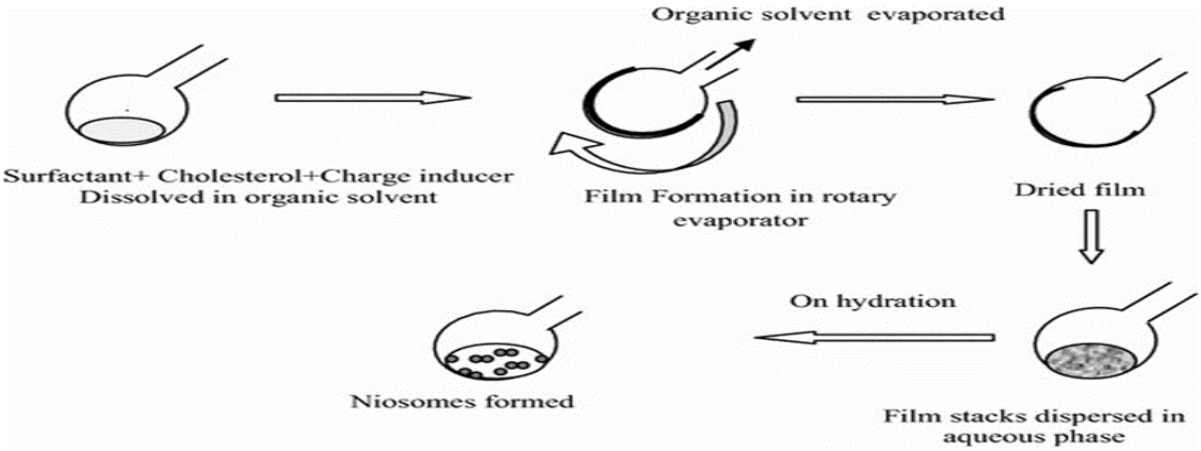



Fig.2. Thin film Hydration Method

Fig.3. Niosomal dispersion

**Preparation Of Niosomal Gel:**

Gel base was prepared by using Carbopol 940. Then, the prepared Niosomal dispersion was incorporated into Carbopol gel on the magnetic stirrer.

Fig.4. Niosomal Gel

## III. RESULTS AND DISCUSSION

**Physical Appearance:**

The prepared gel was observed for color, odour, homogeneity, texture.

**Particle Size Of Niosomes:**

The particle size of niosomes in gel base of all formulations from F1 to F6 were determined by the Scanning Electron Microscope.

| Batch No | Particle size (nm) |
|---|---|
| F1 | 250 |

| | |
|---|---|
| F2 | 270 |
| F3 | 262 |
| F4 | 272 |
| F5 | 268 |
| F6 | 272 |

**Table-2: Particle size of Niosomes.**

**pH:**

Accurately weighed gel was taken and dissolved in required amount of distilled water which resulted in formation of dispersion. By using a digital pH meter, pH was determined. The pH of F2 formulation was found to be 7.2 ± 0.15

**VISCOSITY:**

Brookfield viscometer was used to determine the viscosity of all the prepared formulations. Viscosity is one of the important physical parameters of gels which affects the rate of drug release. The Niosomal gel formulation F2 showed a maximum viscosity of 123300cps.

**SPREADABILITY:**

Spreadability is defined as the extent of ability of gel to spread on the skin on application. It is determined using the following formula –

$$\text{Spreadability} = \frac{m.l}{t}$$

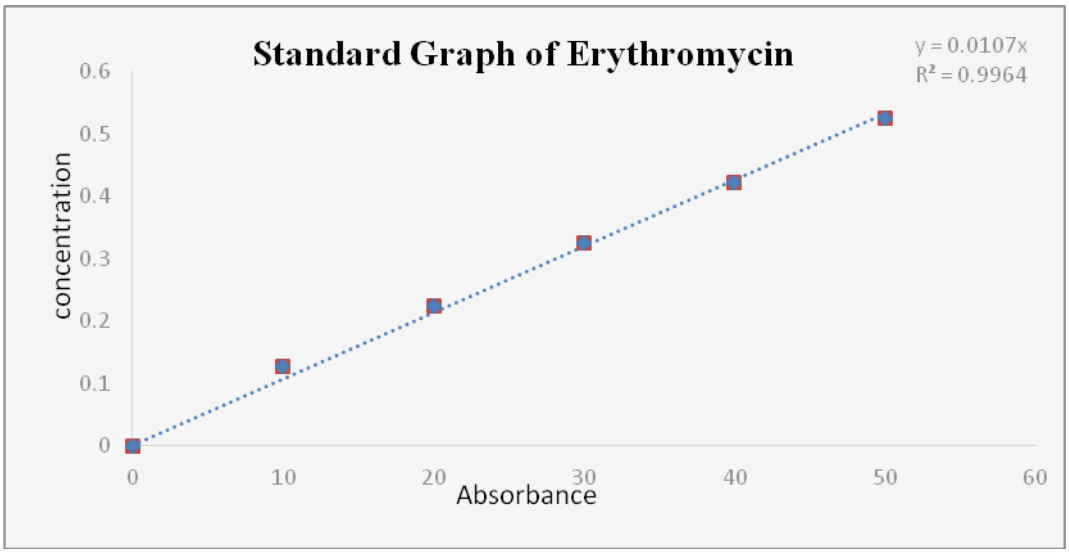
Where, S=Spreadability
m=weight tied to the slide
l=length of the slide
t= time taken in sec.

**CALIBRATION CURVE:**

The analytical wavelength and calibration data for erythromycin in 7.4 phosphate buffer was determined. The λ max was found to be 238nm, which was selected as the analytical wavelength for further analysis. The calibration curve for erythromycin is given in graph 1. Linearity range was obtained in the concentration between 10,20,30,40&50 µg/ml.

| Concentration(µg/ml) | Absorbance |
|---|---|
| 10 | 0.128 |
| 20 | 0.224 |
| 30 | 0.325 |
| 40 | 0.423 |
| 50 | 0.525 |

**Table-3: Standard graph of Erythromycin**




**Graph-1:** Linear regression analysis for standard curve

**Entrapment Efficiency:**

Entrapment efficiency is the parameter in which the amount of drug entrapped is Niosomal vesicles can be determined. For this, first untrapped drug is needed to be separated from the Niosomal dispersion which was achieved by following centrifugation method. Centrifugation was done at 1200rpm for 15 minutes. Entrapment efficiency was calculated by using the following formula-

$$\text{Entrapment Efficiency} = \frac{\text{Total drug - Diffused drug}}{\text{Total drug}}$$

| Batch No. | Entrapment Efficiency (%) |
|---|---|
| F1 | 80.12 |
| F2 | 84.98 |
| F3 | 79.28 |
| F4 | 82.17 |
| F5 | 78.24 |
| F6 | 80.31 |

**Table-4:** Entrapment Efficiency

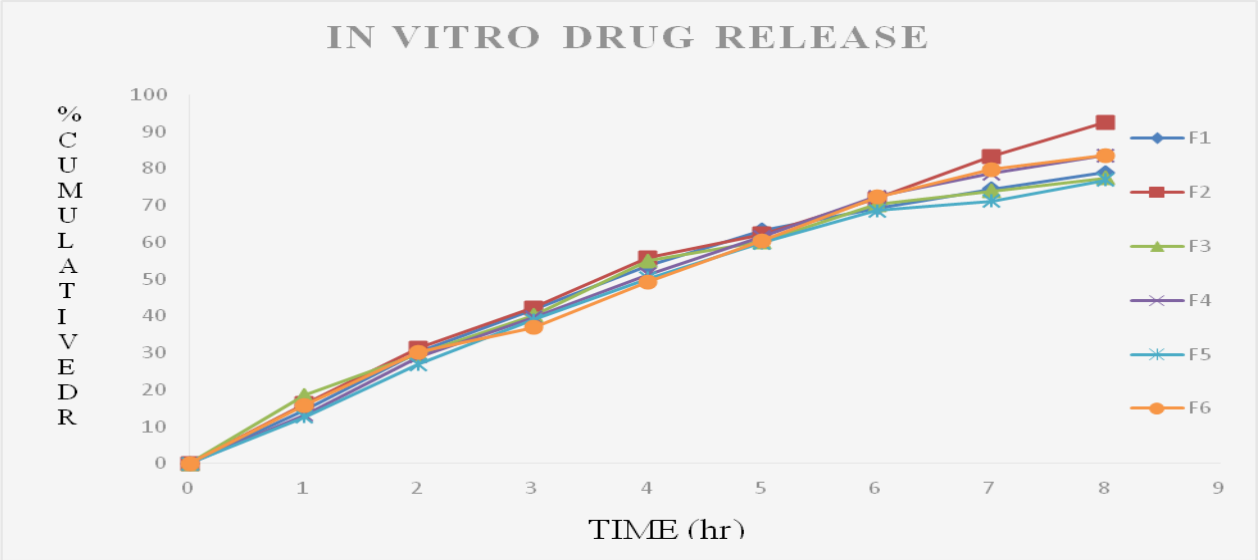
**In Vitro Drug Release Studies:**

In vitro drug release studies were carried out by following the Franz Diffusion method. In this method, Franz diffusion cell was used in which the niosomal gel was dialyzed against 7.4 phosphate buffer at room temperature, with the help of dialysis membrane. At regular time intervals, samples were withdrawn and analyzed for the determination of drug content.

| Time(hrs) | F1 (%) | F2 (%) | F3 (%) | F4 (%) | F5 (%) | F6 (%) |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 14.52 | 16.85 | 18.55 | 13.25 | 12.68 | 15.84 |
| 2 | 30.25 | 31.24 | 29.63 | 28.96 | 26.89 | 30.15 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | 41.82 | 42.18 | 40.18 | 39.65 | 38.96 | 36.93 |
| 4 | 53.60 | 55.80 | 54.98 | 51.25 | 50.18 | 49.25 |
| 5 | 63.28 | 62.18 | 60.16 | 61.55 | 59.86 | 60.38 |
| 6 | 69.25 | 71.80 | 70.18 | 72.42 | 68.59 | 72.25 |
| 7 | 74.40 | 83.35 | 73.96 | 78.71 | 71.15 | 79.80 |
| 8 | 78.92 | 92.56 | 77.45 | 83.63 | 76..94 | 83.55 |

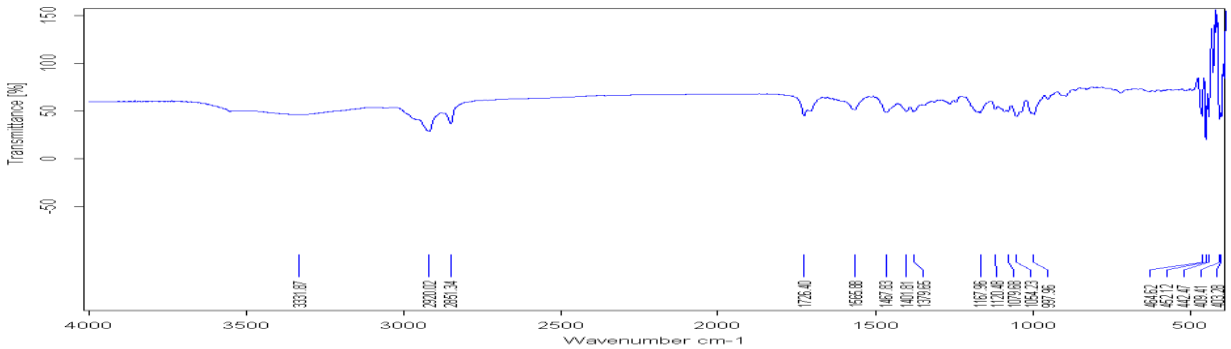
**Table-5:** In- Vitro drug release



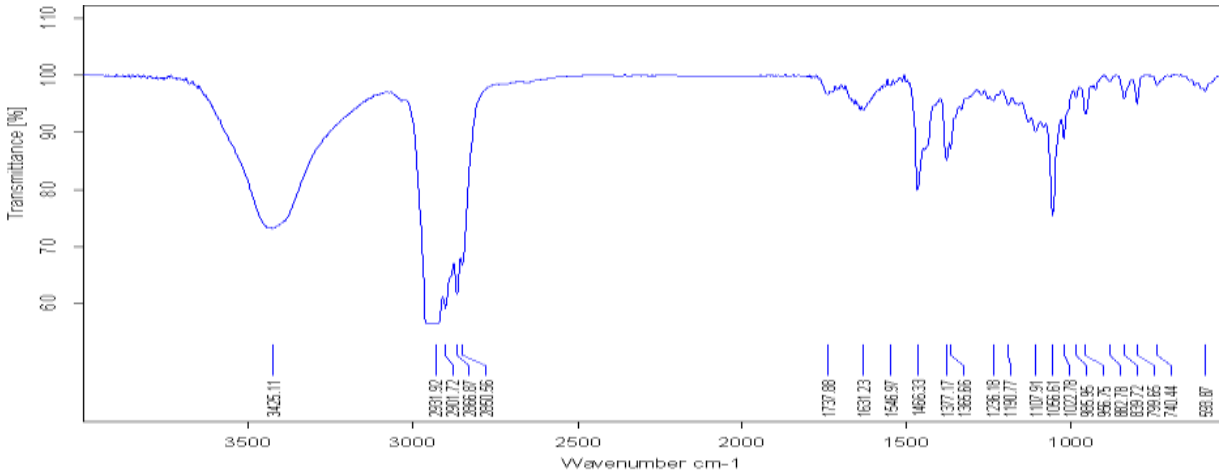

**Graph-2: In vitro drug release**

**FTIR SPECTROSCOPY:**

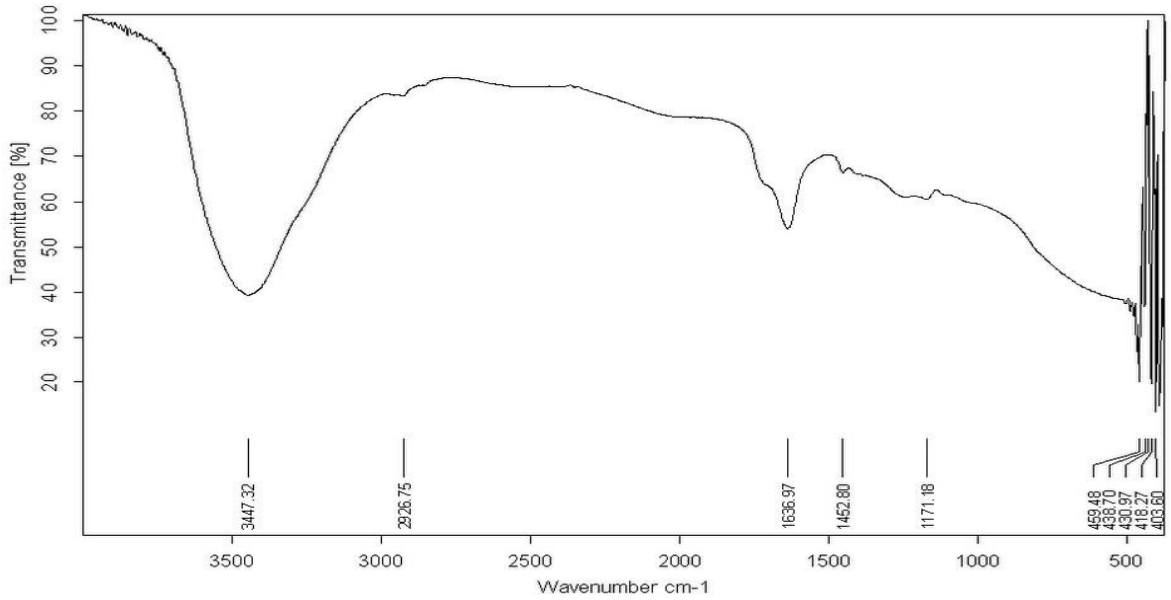
FTIR spectroscopy stands for 'Fourier transform infrared spectroscopy. FTIR works on the principle that when infrared radiation passes through the sample, some of the radiation is absorbed and the radiation which passes through the sample is recorded. Generally, FTIR is, used for quick and definite identification of compounds plastics, fillers, coatings, resins, paints, blends, and adhesives. It is also useful for monitoring that there are no interactions between API and Excipients used for formulation of Niosomal gel. For Erythromycin incorporated Niosomal gel FTIR data revealed that there are no considerable changes observed in the IR peak of API and excipients with which it has been formulated. Therefore, as there is no unvarying data it is considered as there is no presence of chemical interaction between the API and excipients. FTIR data results is given as follow,



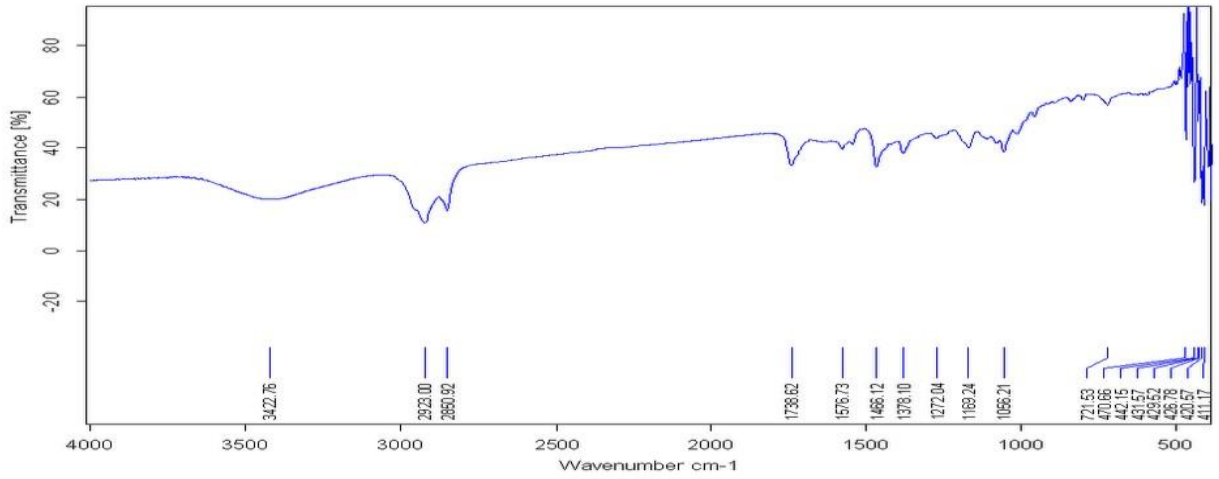

**Graph-3:** FTIR spectra of pure Erythromycin




**Graph-4**: FTIR Spectra of Cholesterol




**Graph-5:** FTIR Spectra of Carbopol 940




**Graph-6:** FTIR of optimized Niosomal gel formulation

**STABILITY STUDIES:**

There is no significant change in physical and chemical properties of the formulation F2 after 3 months. Parameters quantified at various time intervals were shown below,

| Formulation code | Parameter | Initial | 1st month | 2nd month | 3rd month | Limits as per specifications |
|---|---|---|---|---|---|---|
| **F2** | **25 C/60%RH % Release** | 92.56 | 91.32 | 89.89 | 87.83 | Not less than 85% |
| **F2** | **30 C/75%RH %Release** | 92.56 | 90.63 | 89.55 | 87.50 | Not less than 85% |
| **F2** | **40 C/75%RH %Release** | 92.56 | 90.05 | 89.31 | 86.66 | Not less than 85% |

**Table-6:** Results of stability studies of F2 formulation

## IV. CONCLUSION

The purpose of this research was to formulate Erythromycin incorporated niosomal gel for topical anti-bacterial action to reduce the side effects and increase the local action of the drug. By employing thin film hydration technique F1 to F6 formulations were prepared. Formulations were developed by using constant concentrations of non-ionic surfactant(tween 80) and different concentrations of cholesterol. Among all the six formulations F2 formulation was found to be most satisfactory formulation with 92.56% drug release. The FTIR studies shows that there are no interactions between the cholesterol, non-ionic surfactant(tween 80) and drug. Formulation is composed of cholesterol which acts as a stabilizer of niosomal membrane and tween 80 is non-immunogenic, biocompatible and biodegradable - the vesicles composed of them can be used as an appropriate drug delivery system. Niosomes were incorporated in gel for topical route of administration the second thick layer of epidermis of skin which is stratum lucidum is tough layer for any particle to cross through it but with niosomes it is possible to penetrate into the deeper layers of skin. The present study concludes that niosomal based gel containing erythromycin, enhances the drug penetration and release by reducing the side effects and frequency of administration as it helps in control release of drug.

## REFERENCE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