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Research Article

DEVELOPMENT AND CHARACTERIZATION OF  
GANCICLOVIR-LOADED ETHOSOMAL GEL WITH IN  
VITRO EVALUATION<sup>1</sup>Dr. Y. Ganesh Kumar, <sup>2</sup> P. Sreeya Laxmi, <sup>3</sup>P. Lavanya, <sup>4</sup>P. Sai Nandhini, <sup>5</sup>P. Sumanth,  
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Ibrahimpattanam (M), R.R. Dist - 501510, Telangana.<sup>2,3,4,5,6</sup> Bharat School of Pharmacy, Mangalpally (V), Ibrahimpattanam (M), R.R. Dist - 501510,  
Telangana.**Abstract:**

The present study was aimed at formulating and evaluating Ganciclovir-loaded ethosomes to enhance drug delivery and improve therapeutic performance through a vesicular carrier system. Ganciclovir-loaded ethosomes were prepared using phosphatidylcholine and ethanol by the cold method. Eight formulations (F1–F8) were developed with varying concentrations of phosphatidylcholine and ethanol and evaluated for physicochemical characteristics, drug-excipient compatibility, vesicle size, zeta potential, entrapment efficiency, in vitro drug release and stability. Preformulations studies including organoleptic evaluation, melting point determination, solubility studies, UV spectroscopic analysis and FTIR studies were carried out. The  $\lambda_{max}$  of Ganciclovir was found to be 252 nm, and the calibration curve showed good linearity in the concentration range of 10–50  $\mu\text{g/mL}$  with a correlation coefficient ( $R^2$ ) of 0.997. FTIR studies confirmed the compatibility of Ganciclovir with the selected excipients. The particle size of the ethosomal formulations ranged from 163 to 238 nm, while zeta potential values ranged from –21 to –32 mV, indicating good stability of the vesicles. SEM analysis confirmed the spherical morphology and uniform distribution of ethosomes. Drug entrapment efficiency ranged from 70.80% to 85.50%, with formulation F4 exhibiting the highest entrapment efficiency. In vitro drug release studies demonstrated sustained drug release over 8 hours, with formulation F4 showing a cumulative drug release of 97.48%. Stability studies conducted under accelerated conditions for three months indicated no significant changes in the formulation characteristics, confirming good stability. Based on particle size, zeta potential, entrapment efficiency, drug release profile and stability studies, formulation F4 was identified as the optimized formulation. The study concluded that ethosomal delivery of Ganciclovir is a promising approach for improving drug delivery, enhancing stability and achieving sustained release.

**Keywords:** Ganciclovir, Ethosomes, FTIR Studies, In vitro drug release studies, Stability studies**Corresponding author:****Dr. Y. Ganesh Kumar,**Professor & HOD, Department of Pharmaceutics, Bharat Institute of  
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**INTRODUCTION:****Defination of Ethosomes**

Ethosomes are soft, malleable, phospholipid-based vesicular drug delivery systems that contain a high concentration of ethanol (usually 20–45%) along with water. They are modified liposomes in which ethanol acts as a penetration enhancer, increasing the flexibility of the vesicles and improving their ability to deliver drugs through the skin. Ethosomes are

designed primarily for **topical and transdermal drug delivery**, as their unique composition allows them to penetrate deeply into the skin layers more effectively than conventional liposomes. The presence of ethanol disrupts the lipid structure of the stratum corneum and enhances vesicle deformability, thereby facilitating improved drug permeation.

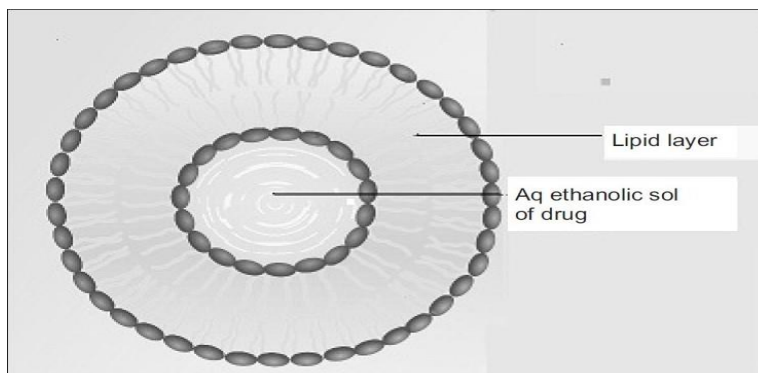


**Fig 1: Structure of Ethosomes**

**Advantages of Ethosomal Drug Delivery****1. Enhanced Skin Penetration**

Ethosomes contain a high concentration of ethanol, which disrupts the lipid structure of the stratum corneum and increases membrane fluidity. This allows deeper penetration of the drug into the skin layers.

**2. Improved Drug Entrapment Efficiency**

Ethosomes can encapsulate both hydrophilic and lipophilic drugs effectively, resulting in higher drug loading capacity compared to conventional liposomes.

**3. Increased Vesicle Flexibility**

The presence of ethanol makes the vesicles soft and deformable, enabling them to pass through narrow skin pores and intercellular spaces.

**4. Sustained and Controlled Drug Release**

Ethosomal formulations provide prolonged drug release, reducing the frequency of application and improving therapeutic effectiveness.

**5. Reduced Systemic Side Effects**

By delivering the drug locally and efficiently to the target site, ethosomes minimize systemic absorption and related adverse effects.

**Disadvantages****1. Skin Irritation**

High concentration of ethanol (20–45%) may cause skin dryness, irritation, or burning sensation, especially in sensitive individuals.

**2. Limited Stability**

Ethosomal formulations may undergo vesicle aggregation, fusion, or drug leakage during long-term storage if not properly stabilized.

**3. Cost of Phospholipids**

Phospholipids used in formulation can be expensive, increasing the overall production cost.

**4. Ethanol Evaporation**

Loss of ethanol during storage may affect vesicle structure, size, and drug entrapment efficiency.

**5. Limited Drug Loading for Some Drugs**

Although entrapment efficiency is generally good, certain drugs with poor solubility may show lower encapsulation.

**MATERIALS**

Ganciclovir was procured from Hetero drugs, Hyderabad, Phosphatidyl choline and Ethanol were obtained from Synpharma Research Labs,

Hyderabad. Other chemicals and the reagents used were of analytical grade.

**METHODOLOGY:****Formulation development****Table-1: Composition of Ganciclovir Ethosomes (F1 to F8)**

| S.No. | Ingredients               | F1  | F2  | F3  | F4  | F5  | F6  | F7  | F8  |
|-------|---------------------------|-----|-----|-----|-----|-----|-----|-----|-----|
| 1     | Ganciclovir (mg)          | 5   | 5   | 5   | 5   | 5   | 5   | 5   | 5   |
| 2     | Phosphatidyl choline (mg) | 200 | 300 | 400 | 500 | 600 | 700 | 800 | 900 |
| 3     | Ethanol (ml)              | 2   | 2.5 | 3.0 | 3.5 | 4.0 | 4.5 | 5.0 | 5.5 |
| 4     | P.Water (ml)              | 10  | 10  | 10  | 10  | 10  | 10  | 10  | 10  |

**Procedure**

- ☐ Weigh phospholipid accurately.
- ☐ Dissolve phospholipid in ethanol under magnetic stirring (700 rpm).
- ☐ Dissolve Ganciclovir in distilled water separately.
- ☐ Add aqueous phase slowly into alcoholic phase under continuous stirring.
- ☐ Stir for 30–45 minutes at room temperature.
- ☐ Sonicate for 5–10 minutes to reduce vesicle size.
- ☐ Store in refrigerator (4°C).

**Formation of Ethosomes**

The aqueous phase was slowly added to the alcoholic phase in a fine stream under constant stirring using a magnetic stirrer. Stirring was continued for 30–45 minutes, resulting in the formation of a milky ethosomal dispersion.

**Size Reduction**

The formed ethosomal dispersion was subjected to probe sonication or bath sonication for 5–10 minutes to reduce vesicle size and obtain a uniform distribution.

**Maturation of Vesicles**

The prepared ethosomal suspension was allowed to stand at room temperature for 30 minutes to ensure complete vesicle formation.

**Storage**

The final Ganciclovir ethosomal formulation was transferred into a clean, amber-colored glass container and stored at 4°C until further evaluation.

**CHARACTERIZATION****1. Vesicle Size**

The average vesicle size and polydispersity index (PDI) were determined using Dynamic Light Scattering (DLS) after suitable dilution with distilled water.

**2. Zeta Potential**

Zeta potential was measured using a zeta sizer to assess the surface charge and physical stability of the ethosomal vesicles.

**3. Entrapment Efficiency (%)**

Entrapment efficiency of Ganciclovir in ethosomes was determined by separating the untrapped drug using centrifugation followed by estimation of drug content in the supernatant using a suitable analytical method.

**4. Surface Morphology**

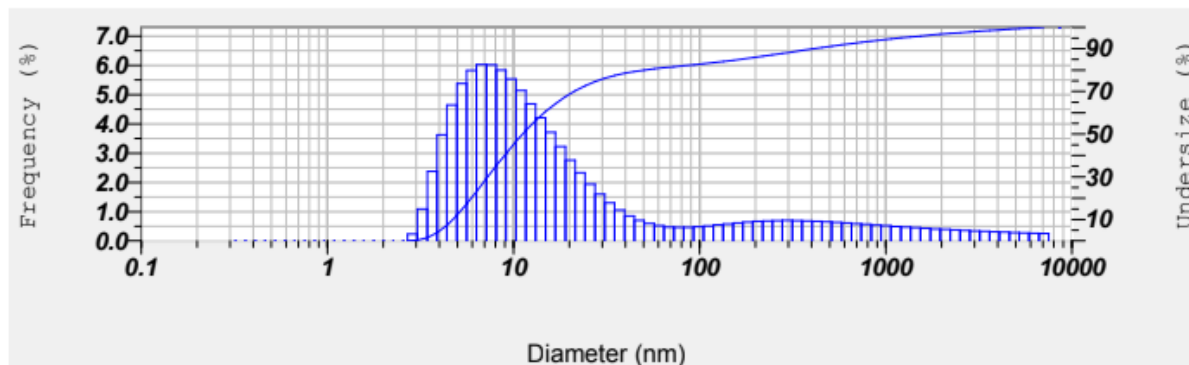
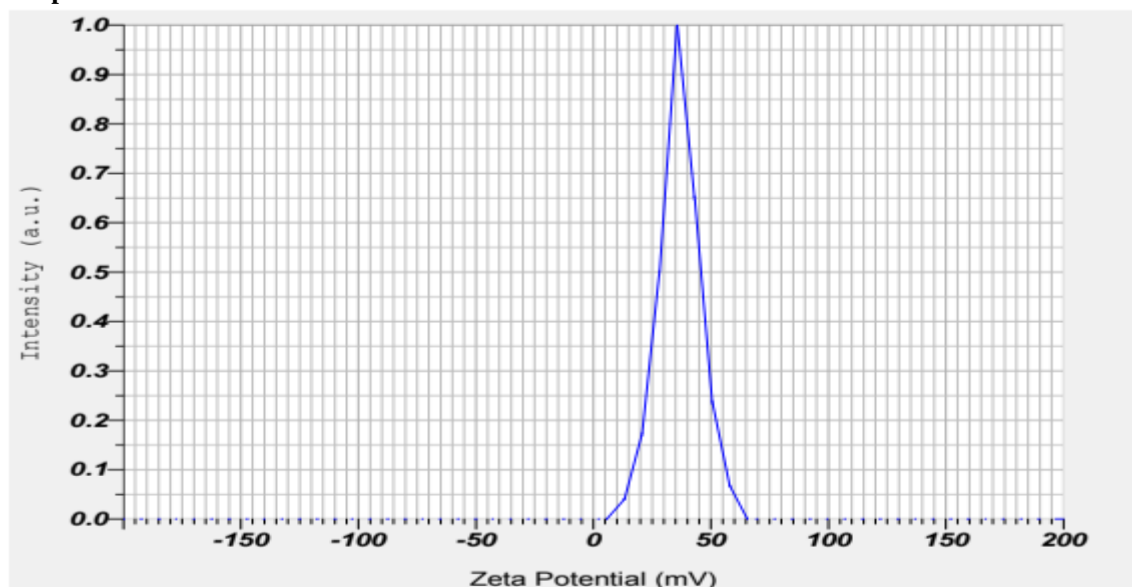
The shape and surface morphology of ethosomal vesicles were examined using Scanning Electron Microscopy (SEM).

**5. In-Vitro Drug Release Study**

In-vitro drug release studies were carried out using a Franz diffusion cell fitted with a dialysis membrane. Phosphate buffer pH 7.4 was used as the receptor medium and maintained at  $37 \pm 0.5^\circ\text{C}$  under continuous stirring.

**6. Stability Studies**

The optimized formulation was subjected to accelerated stability studies for a period of three months at  $40 \pm 2^\circ\text{C}$  and  $75 \pm 5\%$  RH.

**RESULTS AND DISCUSSION:****Particle Size Analysis****Fig-2: Particle size analysis of Optimized ethosomes****Zeta potential****Fig-3: Zeta potential of Optimized formulation****Table-2: Evaluation Studies of particle size and Zeta potential of ethosomes**

| F. No | Particle size (nm) | Zeta potential |
|-------|--------------------|----------------|
| F1    | 228                | -21            |
| F2    | 198                | -24            |
| F3    | 176                | -28            |
| F4    | 163                | -32            |
| F5    | 238                | -23            |
| F6    | 180                | -26            |
| F7    | 227                | -23            |
| F8    | 198                | -24            |

The particle size of ethosomal formulations ranged from 163 to 238 nm. Formulation F4 exhibited the smallest particle size (163 nm) and highest zeta potential (-32 mV), indicating better stability and uniform vesicle distribution.

#### SEM Analysis

Zeta potential values ranged from -21 to -32 mV. The higher negative zeta potential of F4 indicated good electrostatic repulsion between vesicles and enhanced physical stability of the formulation.

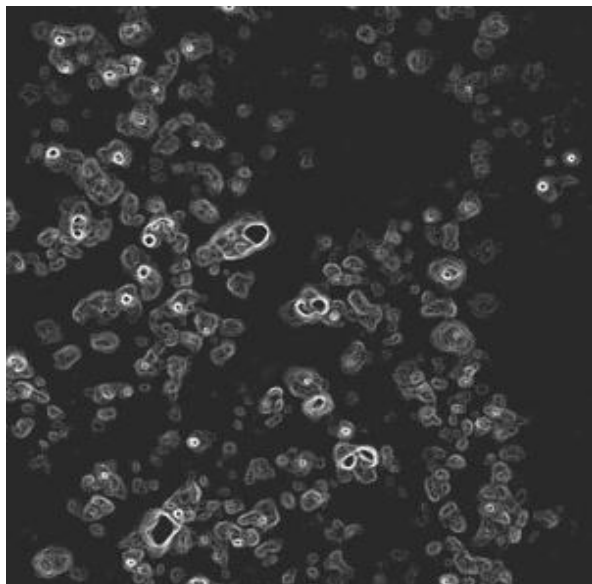


**Fig-4: SEM Analysis of Ethosomes**

SEM analysis revealed that the prepared ethosomes were spherical in shape with smooth surface morphology. No significant aggregation was

observed. The vesicle size observed in SEM images was consistent with the particle size analysis, confirming successful formation of ethosomal vesicles.

#### Entrapment Efficiency:

**Table-3: Drug entrapment efficiency**

| F. code | Drug entrapment efficiency |
|---------|----------------------------|
| F1      | 70.80                      |
| F2      | 72.30                      |
| F3      | 78.60                      |
| F4      | 85.50                      |
| F5      | 71.86                      |
| F6      | 80.15                      |
| F7      | 81.24                      |
| F8      | 79.20                      |

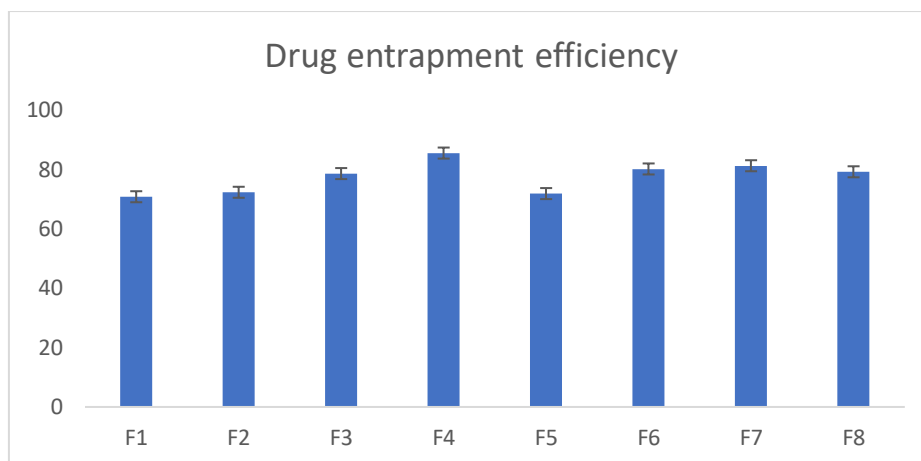


**Fig-5: Drug entrapment efficiency of all formulations**

Drug entrapment efficiency (EE) ranged from 70.80% to 85.50%. Higher EE indicates effective incorporation of Ganciclovir into the lipid bilayer of ethosomes. F4 (85.50%) showed the highest entrapment, possibly due to an optimal lipid-to-drug ratio. Higher EE% contributes to improved drug stability and controlled release.

#### **In vitro release study:**

Phosphate buffer pH 7.4 was used as medium for the release studies and good linearity was observed in the plotted standard graph with a correlation coefficient of 0.998.

**Table-4: In vitro drug release profiles of Ganciclovir Ethosomal gel (F1-F8)**

| Time | F1    | F2    | F3    | F4    | F5    | F6    | F7    | F8    |
|------|-------|-------|-------|-------|-------|-------|-------|-------|
| 0    | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
| 1    | 14.89 | 16.13 | 18.10 | 16.97 | 15.69 | 17.58 | 14.69 | 15.98 |
| 2    | 26.65 | 28.19 | 28.93 | 27.46 | 28.10 | 27.82 | 25.35 | 26.35 |
| 3    | 34.52 | 36.82 | 38.59 | 35.48 | 36.18 | 37.17 | 35.96 | 34.50 |
| 4    | 46.98 | 48.19 | 48.53 | 43.50 | 45.27 | 47.35 | 45.10 | 44.21 |
| 5    | 58.49 | 57.58 | 59.28 | 56.98 | 55.69 | 58.10 | 57.58 | 52.31 |
| 6    | 65.55 | 68.55 | 71.25 | 67.84 | 65.83 | 69.85 | 70.26 | 71.25 |
| 7    | 79.88 | 81.29 | 83.65 | 85.32 | 83.69 | 82.35 | 80.39 | 82.35 |
| 8    | 92.20 | 96.30 | 95.51 | 97.48 | 95.15 | 95.58 | 94.69 | 93.66 |

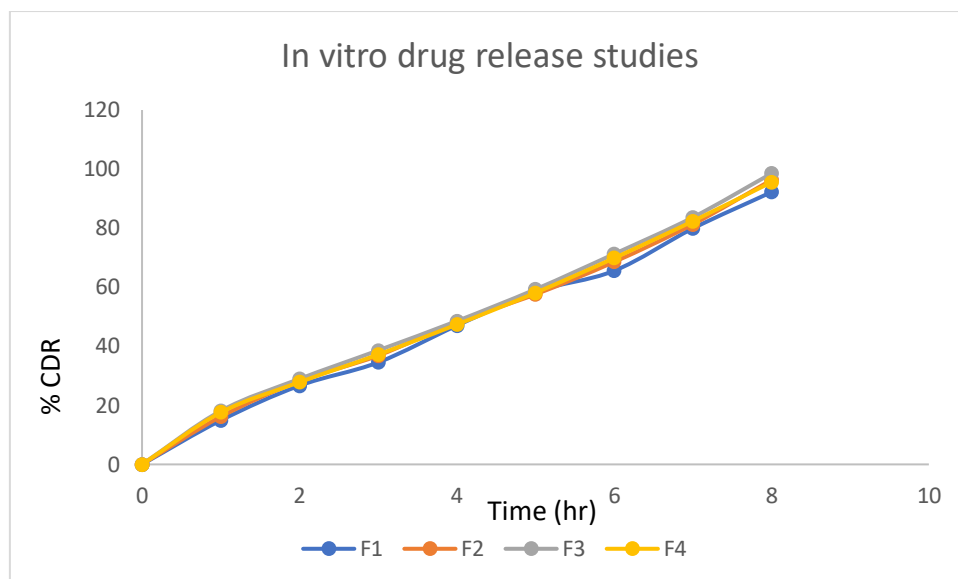


**Fig-6: In vitro drug release studies of F1-F4 formulations**

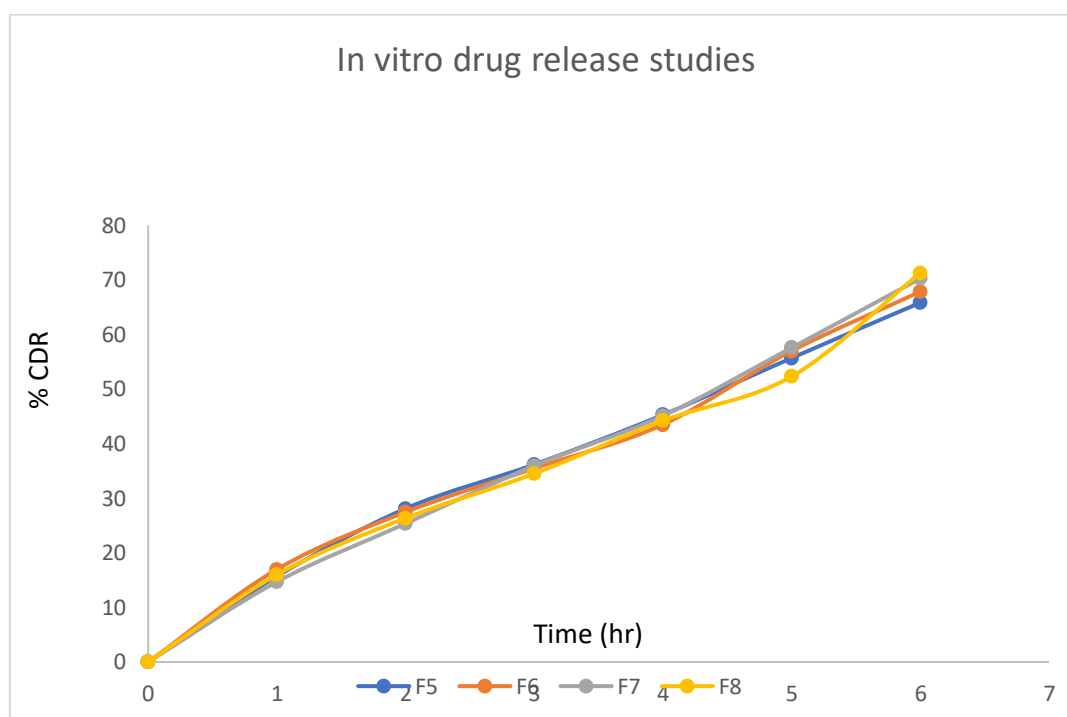


**Fig-7: In vitro drug release studies of F5-F8 formulations**

In vitro drug release studies demonstrated sustained release behavior from all ethosomal formulations over a period of 8 hours. The cumulative percentage drug release ranged from 92.20% to 98.51%. Formulation F4 exhibited the highest drug release (98.51%), followed by F3 (97.48%). The enhanced drug release may be attributed to the nanosized vesicles, improved drug entrapment and increased permeability of the ethosomal system. The results indicate that ethosomes are effective carriers for

enhancing the release of Ganciclovir. Although F3 showed the highest drug release, formulation F4 was considered optimized due to its smaller particle size, higher zeta potential and maximum entrapment efficiency.

#### **Stability studies**

Optimized formulations F4 was selected for accelerated stability studies as per ICH guidelines.

**Table-5: Stability studies of optimized formulations at  $40 \pm 2^\circ\text{C}$  and  $75 \pm 5\%$  RH for 3 months**

| Formulation Code | Initial | 1 <sup>st</sup> Month | 2 <sup>nd</sup> Month | 3 <sup>rd</sup> Month | Limits as per Specifications |
|------------------|---------|-----------------------|-----------------------|-----------------------|------------------------------|
| F-4              | 97.48   | 96.45                 | 95.52                 | 94.69                 | Not less than 85 %           |
| F-4              | 97.48   | 96.40                 | 95.43                 | 94.32                 | Not less than 85 %           |
| F-4              | 97.48   | 96.38                 | 95.20                 | 94.12                 | Not less than 85 %           |

The optimized formulation F4 was subjected to accelerated stability studies for a period of three months at  $40 \pm 2^\circ\text{C}$  and  $75 \pm 5\%$  RH. No significant changes were observed in the physical appearance or drug release profile of the formulation during storage. The cumulative drug release decreased only slightly from 97.48% to 94.69% after three months and remained within the specified limits. These results indicate that the optimized ethosomal formulation possessed good physical and chemical stability during the storage period.

#### SUMMARY AND CONCLUSION:

The present study was successfully carried out to formulate and evaluate Ganciclovir-loaded ethosomes for enhanced drug delivery. Eight different ethosomal formulations (F1–F8) were prepared using varying concentrations of phosphatidylcholine and ethanol by the cold method and evaluated for their physicochemical characteristics, drug entrapment efficiency, in vitro drug release and stability.

Preformulation studies confirmed the identity and purity of Ganciclovir based on its organoleptic properties, melting point, solubility profile and UV spectroscopic analysis. The calibration curve of Ganciclovir in phosphate buffer pH 7.4 exhibited good linearity and obeyed Beer-Lambert's law within the concentration range studied. FTIR studies revealed no significant interaction between Ganciclovir and the selected excipients, indicating the compatibility of the drug with the formulation components.

The prepared ethosomes exhibited particle sizes in the nanometer range (163–238 nm) with good zeta potential values ( $-21$  to  $-32$  mV), indicating satisfactory physical stability. SEM analysis confirmed the spherical morphology and uniform distribution of the ethosomal vesicles. Drug entrapment efficiency ranged from 70.80% to 85.50%, demonstrating effective incorporation of Ganciclovir into the vesicular system. Among all formulations, F4 was identified as the optimized formulation based on its smallest particle size (163

nm), highest zeta potential ( $-32$  mV), highest entrapment efficiency (85.50%) and excellent drug release profile (97.48% within 8 hours). In vitro drug release studies demonstrated sustained release behavior of Ganciclovir from the ethosomal formulations. Stability studies performed under accelerated conditions showed no significant changes in the formulation, confirming its stability during storage.

Therefore, it can be concluded that ethosomal delivery is a promising approach for enhancing the delivery of Ganciclovir. The optimized formulation F4 exhibited desirable physicochemical properties, high drug entrapment, sustained drug release and good stability, making it a potential carrier system for improved therapeutic efficacy and transdermal drug delivery of Ganciclovir.

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