

# Asian Journal of Research in Biological and Pharmaceutical Sciences

Journal home page: [www.ajrbps.com](http://www.ajrbps.com)



## FORMULATION AND EVALUATION OF GLICLAZIDE LOADED ETHOSOMES AS TRANSDERMAL DRUG DELIVERY CARRIERS

Vijayakumar K.S<sup>1\*</sup>, S. Parthiban<sup>1</sup>, G.P. Senthilkumar<sup>2</sup>, T. Tamiz mani<sup>3</sup>

<sup>1\*</sup>Department of Pharmaceutics, Bharathi College of Pharmacy, Bharathinagara, Mandya, Karnataka, India.

<sup>2</sup>Department of Pharmaceutical Chemistry, Bharathi College of Pharmacy, Bharathinagara, Mandya, Karnataka, India.

<sup>3</sup>Department of Pharmacognosy, Bharathi College of Pharmacy, Bharathinagara, Mandya, Karnataka, India.

### ABSTRACT

**Aim:** The aim of the present study was to develop and characterized a vesicular drug carrier system (ethosome) for topical delivery of Gliclazide to overcome the problems related with oral route. Ethosomes of Gliclazide were prepared by thin film hydration technique by varying the composition drug, soya lecithin and propylene glycol. ethosome formulations were characterized for compatibility, Vesicle size, % Drug content, % Entrapment efficiency, Surface morphology, Surface charge, *invitro* drug release and stability studies. The ethosomal gel was prepared for optimized ethosomal formulation F3 by incorporated into 1% Carbopol gel. The *in vitro* drug release and *in vivo* skin irritation study and hypoglycemic activity were carried out for the gel F3-G1. **Results:** Drug and physical mixture were characterized by FTIR, the result of IR study showed that no interaction between drug and polymers and other formulation parameters of formulated ethosomes and ethosomal gel are evaluated which showed better results. **Conclusion:** ethosomal gel F3-G1 was proved nonirritant and showed better stability, more hypoglycemic effect as compared to oral formulation because it provide reduction in blood glucose level with controlled manner upto 24 hrs. Hence, ethosomes drug delivery system was better choice for sustained release of drug through topical drug delivery.

### KEYWORDS

Ethosomes, Ethosomal gel, Sustained release and Hypoglycaemic activity.

### Author of correspondence:

Vijayakumar K S, Department of Pharmaceutics,  
Bharathi College of Pharmacy, Bharathinagara,  
Mandya, Karnataka, India.

**Email:** [kshivjaykumar16@gmail.com](mailto:kshivjaykumar16@gmail.com).

### INTRODUCTION

Novel drug delivery system (NDDS) has revolutionized the method of medication. The NDDS should ideally fulfill two prerequisites. Firstly, it should deliver the drug at a rate directed by the needs of the body, over the period of treatment. Secondly, it should channel the active entity to the site of action. Sincere attempts have been made to achieve them through

various novel approaches in drug delivery. Several technological advances have been made over many years. One such technique is vesicular systems which shows a great promise and opens up new market for pharmaceutical and cosmetic industry for drug delivery through skin. Hence, significant enhanced delivery of through transdermal route could be obtained by using vesicular drug carrier systems-Ethosomes<sup>1</sup>.

Ethosomes have been shown to exhibit high encapsulation efficiency for a wide range of molecules including lipophilic drugs. This could be explained by multilamellarity of ethosomal vesicles as well as by the presence of ethanol in ethosomes which allows for better solubility of many drugs. Ethosomes were reported to improve *in vivo* and *in vitro* skin delivery of various drugs. Contrary to deformable liposomes, ethosomes are able to improve skin delivery of drugs both under occlusive and non-occlusive conditions<sup>2</sup>.

Gliclazide is an antidiabetic drug. It is the NIDDM sulfonylureas antidiabetic drug, however, the oral administration of the drug is often associated with number of demerits. The major one is low bioavailability and poor water solubility<sup>3</sup>. Therefore to circumvent drawbacks, administration of drug via transdermal route could be a better option. As transdermal route provides a mean to obtain constant systemic drug levels, high patient compliance because of non-invasive nature. Despite many advantages of the skin as a site of drug delivery, the success of delivery through this route remains limited because the main barrier of the skin is located in the outermost layer of the outermost layer of the skin - the stratum corneum (SC) To overcome the stratum corneum barrier, various mechanisms have been investigated, including use of chemical or physical enhancers such as iontophoresis, sonophoresis, *etc.* liposomes, niosome, transferosomes and ethosomes also have the potential of overcoming the skin barrier and have been reported to enhance permeability of drug through the stratum corneum barrier<sup>4</sup>.

This route has many advantages from orally dosed Gliclazide<sup>5</sup>

They are,

- It contains non toxic raw materials formulations.
- Potentially reduces cost through fewer side effects.
- Smaller dose is required when Gliclazide in penetrated through skin.
- Improve the bioavailability as well improve the patient compliance.

The main objective of the study is to formulate and evaluate Gliclazide ethosomal gel in order to increase bioavailability and reduce side effects by achieving transdermal drug delivery.

## MATERIALS AND METHOD

### MATERIALS

Gliclazide was gifted from Medreich Limited, Karnataka, India. Soya lecithin was gifted from Pharma Sonic Biochem Extractions Ltd., Indore, India. Carbopol 934, Triethanolamine, Methyl paraben, Alloxan and other solvent like Chloroform and Methanol purchased from SD fine chem limited, Mumbai, India.

### Experimental model

Male Wister albino rats, 150-200 gm weight, were selected for *in vivo* studies. All animals were fed with a standard laboratory diet and water. They were housed in a specific room at a temperature of 20-25 °C and 50 ± 5% relative humidity under a 12 hrs dark/ light cycle and acclimatized for 1 week before the start of experiment. All experimental procedures involving animals were approved by the Institutional of Animal Ethical Committee (IAEC) of Bharathi College of Pharmacy.

### Preformulation studies

#### Determination of Solubility

Gliclazide white, crystalline powder. Solubility was conducted using different solvents.

#### Melting point determination

Capillary method was used for the determination of melting point of Gliclazide. A few quantity of Gliclazide is taken and placed in a thin walled capillary tube about 10-15 cm long and 1mm inside diameter and closed at one end. The capillary which contains the sample and a thermometer are then suspended into an oil bath containing liquid paraffin.

So they can be heated slowly and evenly. The temperature range over which the sample is observed to melt is taken as the melting point.

#### **Drug-Excipient interactions studies by FTIR**

Drug-excipients compatibility studies were carried out using FT-IR. Infrared spectrum of pure drug, soya lecithin, and the physical mixture of drug: soya lecithin in 1:1 ratio were recorded in between 400 to 4000  $\text{cm}^{-1}$  by using liquid sampling technique.

#### **METHODS**

##### **Preparation of Gliclazide ethosome**

Classic mechanical dispersion containing Soya lecithin (1-4%) and ethanol (10 to 50%). The drug concentration was fixed as 0.5 % W/V. Accurately weighed quantity of soya lecithin was dissolved in chloroform: methanol (3:1) mixture and the organic solvents were removed in the rotary flash evaporator above the lipid transition temperature (55 °C) (at 60 rpm) to form a thin lipid film in the flask. The traces of organic solvents mixture were further removed by maintaining the temperature under reduced pressure for additional 30 mins after the thin film was formed. Then the lipid film was hydrated with different concentration of hydro ethanolic mixture containing Gliclazide (0.5% w/v) in the rotary flash evaporator at 60 rpm for 1hour in the room temperature. The preparation was vortexed followed by sonication at 4 °C in an ice bath using probe sonicator. After sonication the ethosomal formulation was stored in refrigerator (4 °C) for further studies (Table No.1).

##### **Preparation of Gliclazide ethosomal gel<sup>6</sup>**

Ethosomal gel was prepared for the optimized formulation, by cold mechanical method as per the composition given in Table No.2. Required quantity of polymer was weighed and it was sprinkled slowly on surface of purified water with continuously stirred by mechanical stirrer and allowed swell for 24 hrs to obtain 1% gel.

Accurately weighed ethosomes was dissolved in 10 ml of methanol and centrifuged at 25000 rpm for 60 min to remove the untrapped drug. The supernant was decanted and sediment was incorporated into the gel vehicle. The incorporation of the ethosomes into gels was achieved by slow mechanical mixing at 25

rpm for 10 min. Triethanolamine was added to bring the pH neutral. The final quantity was made up to 5 gm with distilled water.

##### **Evaluation of Gliclazide ethosomes<sup>7</sup>**

Prepared ethosomal formulation was evaluated for the following parameters.

##### **Vesicle size analysis**

Vesicle size analysis was carried out using an optical microscope with a calibrated eyepiece micrometer. About 300 ethosomes were measured individually, average was taken and their size distribution range and mean diameter were calculated. The particle size of the vesicle after hydration of ethosomes was also determined by PALS Zeta potential Analyzer (Brookhaven Instruments Corp.) for the optimized formulation.

##### **Surface morphology by scanning electron microscopy (SEM)**

Surface morphology of the ethosomes will be determined by using a Scanning electron microscope. Ethosomes was coated with Gold-palladium alloy of 120°A Knees on the samples putter coating unit (Model E5100 Polaron, U.K) and their surface morphological was photographed with Jeol JSM-T330A, Japan scanning electron microscope.

##### **Surface charge**

A surface charge of ethosomes was studied by determining the zeta potential of the vesicles. The optimized ethosomes was dissolved in distilled water and made a higher serial dilution 1000 X until a clear solution is obtained. Sample was analyzed for determining the Zeta potential. (PALS Zeta potential Analyzer, Brookhaven Instruments Corp).

##### **Drug content**

100 mg of ethosomes formulation was weighed and vesicles were lysed with 25 ml of solution by sonication for 15 min. The clear solution after suitable dilution was measured by U.V spectrophotometer (Shimadzu UV-1800, Japan) against blank at  $\lambda_{\text{max}}$  226 nm and the drug content was calculated.

##### **Entrapment efficiency**

The entrapment efficiency (EE %) of Gliclazide in the constituted ethosomes was determined after

hydration of ethosomes with distilled water. 10 ml of distilled water was added to the ethosome containing equivalent to 10 mg of drug and the mixture was shaken manually for 2 min. For the separation of untrapped Gliclazide, the ethosomal suspension was subjected to centrifugation on a cooling ultracentrifuge (REMI instrument, Mumbai) at 20000 rpm for 1 hr. The clear supernatant was separated and amount of untrapped drug was determined by UV spectrophotometer at 226 nm.

The % entrapment was determined by following formula:

Percentage entrapment =  $\frac{\text{Total drug content} - \text{Free drug content}}{\text{Total drug content}} \times 100$ .

#### **In vitro drug release studies**

The release of drug was determined by using the treated egg membrane mounted on the one end of open tube, containing ethosomes (equivalent to 10 mg drug). The dialysis tube was suspended in 250 ml beaker, containing 100 ml phosphate buffer pH 7.4. The solution was stirred at 200 rpm with the help of magnetic stirrer at  $37 \pm 0.5$  °C. Perfect sink conditions were maintained during the drug release testing. The samples were withdrawn at suitable time interval (at 1, 2, 4, 6, 8 and 12 hrs). The dissolution medium was replaced with same amount of fresh phosphate buffer pH 7.4 solutions to maintain the volume 100 ml throughout the experiment. The drug content in the withdrawn samples (1 ml) were analyzed by UV spectrophotometer at  $\lambda_{\text{max}}$  226 nm after making the volume up to 10 ml with phosphate buffer pH 7.4 and cumulative % of drug released was calculated and plotted against time (t). The rate and release mechanism of Gliclazide from the prepared ethosomes were analyzed by fitting the release data in to various kinetic models.

#### **Release kinetics**

##### **Zero order kinetics**

Drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly, assuming that the area does not change and no equilibrium conditions are obtained can be represented by the following equation

$$Q_t = Q_0 + K_0 t$$

Where,

$Q_t$  = Amount of drug dissolved in time t,

$Q_0$  = Initial amount of drug in the solution and

$K_0$  = Zero order release constant.

##### **First order kinetics**

To study the first order release rate kinetics the release rate data were fitted to the following equation.

$$\log Q_t = \log Q_0 + K_1 t / 2.303$$

Where,

$Q_t$  = Amount of drug released in time t,

$Q_0$  = Initial amount of drug in the solution and

$K_1$  = First order release constant.

##### **Higuchi model**

Higuchi developed several theoretical models to study the release of water soluble and low-soluble drugs incorporated in semisolids and or solid matrices. Mathematical expressions were obtained for drug particles dispersed in a uniform matrix behaving as the diffusion media. The Higuchi equation is

$$Q_t = K_H \cdot t^{1/2}$$

Where,  $Q_t$  = Amount of drug released in time t and,

$K_H$  = Higuchi dissolution constant.

##### **Kormeyer-peppas release model**

To study this model the release rate data is fitted to the following equation

$$M_t / M_\infty = K \cdot t^n$$

Where,  $M_t / M_\infty$  = Fraction of drug release,

$K$  = Release constant,

$t$  = Drug release time and

$n$  = Diffusional exponent for the drug release that is dependent on the shape of the matrix dosage form.

##### **Stability studies**

To confirm the stability of ethosomal formulation, Intermediate stability testing studies was performed for 6 months as per ICH guidelines. The optimized formulation was kept at  $30 \pm 2$  °C and  $65 \pm 5\%$  RH and  $4 \pm 2$  °C in stability chamber (Thermo lab India). % entrapment, drug particle size and drug release were fixed as physical parameters for stability testing.

## Evaluation of Gliclazide ethosomal gel<sup>8</sup>

### Physical examination

The physical appearance of color, consistency texture and greasiness these all features were done for ethosomal gel formulation.

### Measurement of pH

The pH of various gel formulations was determined by using digital pH meter (Equiptronics EQ-610). The electrode first calibrated with pH 4.0 and pH 7.0 solution then measurement of pH of each formulation was done.

### Viscosity and Rheological properties

Brookfield digital viscometer (DV-I+, Brookfield Engineering Laboratory, INC., USA) was used to measure the viscosity (in cps) of the prepared gel formulation.

### Drug content

2 gm ethosomal gel sample was withdrawn from container and dissolved in 100 ml ethanol. After suitable dilution absorbance was measured by U.V spectrophotometer against blank at  $\lambda_{max}$  226 nm and the drug content was calculated.

### In vitro release studies of proliposomal gel

An *in vitro* drug release study was performed using modified Franz diffusion cell. Egg membrane was placed between receptor and donor compartments. Ethosomal gel equivalent to 1 gm was placed in the donor compartment and the receptor compartment was filled with phosphate buffer pH 7.4. The diffusion cells were maintained at  $37 \pm 0.5^\circ\text{C}$  with stirring at 500 rpm throughout the experiment. At fixed time interval, 5ml of aliquots was withdrawn for every 1, 2, 4, 6, 8, 12 and 24 hrs from receiver compartment through side tube and analyzed by UV spectrophotometer at  $\lambda_{max}$  226 nm.

### In vivo studies

#### Skin irritation test<sup>9</sup>

Four young Wister albino rats were taken for skin irritation studies. Hair on the back area (approximately 6 cm<sup>2</sup> area) of each rat was removed by hair removing cream. Developed formulations were applied to the shaved area, and then rats were secured. The animal were observed and evaluated for any sign of erythema or edema for a period of 7 days.

## Hypoglycemic activity<sup>11,12</sup>

### Induction of diabetes

Rats were fasted for 24 hrs and blood glucose level of each group was assessed to obtain the fasting blood glucose levels. Alloxan at dose of 100 mg/kg body weight in PBS pH 7.4 was administered by intraperitoneal route to each rat and blood glucose level was measured by using digital glucometer (ACCU-CHEK Active) after 24 hrs. Rats showing 200-250% increase in fasting blood glucose levels were selected for study.

### Preparation of animals for studies

Hairs on the backside (interscapular region) of the rats were removed with a depilatory cream and treatment was provided topically on shaved area. Prior to, day of the experiment, animals were divided into 2 groups (n=4) of diabetes rats. The rats as treated as following.

Group I- Gliclazide oral Administration contain 2 mg drug in PBS.

Group II- Ethosomal gel contains Gliclazide.

The blood was be withdrawn by pricking the rat's tail at appropriate time interval for 24 hrs and blood glucose level will be measured immediately by using digital glucometer.

### Stability studies for ethosomal gel

Intermediate stability testing studies was performed for 6 months as per ICH guidelines. The optimized gel formulation was kept at  $30 \pm 2^\circ\text{C}$  and  $65 \pm 5\%$  RH in stability chamber. Drug content, pH and drug release were fixed as physical parameters for stability testing.

## RESULTS AND DISCUSSION

Gliclazide is a white, crystalline, freely soluble in methanol and soluble in chloroform and poor soluble in water. Melting point was determined by capillary method and it was found to be  $181^\circ\text{C}$ , which complied with IP standards, thus indicating the purity of drug. FTIR spectra of pure Gliclazide showed sharp characteristic peaks at 1710, 1162, 1089, 997, 920,  $667\text{cm}^{-1}$ . FTIR characteristic peaks of pure drug are also observed in the spectra of physical mixture indicating no modification for interaction between the drug and excipients. This

proves that there is no potential incompatibility with the drug and the excipients used in the ethosomal formulation. Comparative study of FTIR graphs are showed in Figure No.1 and 2.

Ethosomes were prepared using film deposition on carrier method using vacuum rotary evaporator. The result showed in Table No.4, we observed that, increase in the concentration of soya lecithin vesicle size, % Drug content and % Entrapment efficiency was found to be increased. The surface morphology was studied by Scanning electron microscopy (SEM). The SEM photographs of optimized ethosomes formulation F3 as shown in Figure No.3. The spherical structure in the images confirmed the formation ethosomes that is confirmed the incorporation of lipids and drug. Zeta potential of optimized formulation F3 was found to be - 58.87 mV, which indicates that the formulation is good to be stable.

The release of drug from ethosomes formulation was varied according to concentration of soya lecithin and ethanol. The progressive increase in the amount of drug diffused through a dialysis membrane from formulations F1 to F4 attributed to gradual increase in soya lecithin. It has been concluded that, if we increase the concentration of soya lecithin, the diffusion of drug also decreases. The amount of drug diffused from formulation F3 was showed 86.12 % which was higher among the formulations F1 to F4 and showed in Figure No.4. Stability studies were carried out for the most satisfactory formulation F3 at  $30\pm 2$  °C and  $65\pm 5$ % RH for 6 months. At the end of 1, 3, 6 months intervals, samples were evaluated for different parameters includes vesicle size, entrapment efficiency and % CDR and results indicates that stability studies of selected formulation F3 showed negligible changes in evaluated parameters that revealed that the formulations are stable on storage (Figure No.4).

The optimized formulation F3 was incorporated in 1% carbopol 934 polymers and gel was prepared. The prepared ethosomal gel formulation was evaluated for the following parameters.

### **Physical appearance**

The Physical appearance of the Gliclazide ethosomal gel formulations was checked and showed Translucent, yellowish glossy, smooth and non-greasy on application.

### **pH measurement**

The prepared Gliclazide ethosomal gel was checked for their pH and the formulation was found to be 6.09. Therefore there is no need for adjusting pH of the formulation.

### **Viscosity**

The viscosity of gels formulation was determined and formulation F3-G1 showed 12160 cps.

### **Drug content**

The prepared Gliclazide ethosomal gel was subjected to drug content uniformity and it was found to 4.23mg/gm which indicated the drug uniformly dispersed throughout the formulation.

### **In vitro drug release**

The releases of drug from these gels were characterized by an initial phase of high release (burst effect). However, as gelation proceeds, the remaining drug was released at a slower rate followed by a second phase of moderate release.

The result of *In vitro* release of Gliclazide from the gel formulation is given in Figure No.5. However, the results clearly show that the gels have ability to retain the drug for prolonged periods. The % CDR of ethosomal gel formulation F3-G1 was found to be 80.37 % and which follows Higuchi model. The 'n' values for all the formulation were found to be more than 0.5. This indicates that the release approximates non-Fickian diffusion mechanism and this formulation was selected for next *invivo* and stability studies.

### **Skin irritation studies**

The skin irritation study of ethosomal gel formulations F3-G1 was performed and tabulated in Table No.5. The Average primary irritation index of formulations F3-G1 was found to be 0.16, and it shows that the ethosomal gel formulation did not show any irritation and erythema after 7 days.

### Hypoglycemic activity

The reduction in blood glucose level in sustained manner after topical administration of Gliclazide ethosomal gel formulation F3-G1 as showed in Table No.6. The pure Gliclazide suspension was administered orally. A maximum reduction in blood glucose level was observed within 2 hrs. The Gliclazide ethosomal gel formulation F3-G1 both are showed significant reduction in blood glucose level but in sustained manner as compared to oral Gliclazide in PBS pH 7.4. From the reported literature, it was well defined that a 25 % reduction

in blood glucose levels is considered hypoglycemic effect. Results of present study revealed that topical Gliclazide ethosomal gel formulation F3-G1 was more effective as compared to conventional formulation because it provide reduction in glucose level with controlled manner up 24 hrs.

### Stability studies of ethosomal gel

Stability studies of ethosomal gel formulation F3-G1 shows negligible changes in pH, drug content and % CDR revealed that the formulations are stable on storage.

**Table No.1: Formulation design for the preparation Gliclazide ethosomes**

S.No	Formulation code	Drug(mg)	Soya lecithin (%w/v)	Ethanol (%w/v)	Propylene glycol (%w/v)
1	F1	0.5	1	30	10
2	F2	0.5	2	30	10
3	F3	0.5	3	30	10
4	F4	0.5	4	30	10

**Table No.2: Formulation design for the preparation Gliclazide ethosomal gel**

S.No	Ingredients	F3-G1
1	Gliclazide ethosomes (containing pure drug in mg)	20
2	Carbopol 934(mg)	50
4	Dimethyl sulfoxide(mg)	0.11
5	Methyl paraben(mg)	0.75
6	Distilled water	Up to 5gm

**Table No.3: Standards for skin irritation study<sup>10</sup>**

S.No	Skin Responses	Score
<b>Erythema and scar Formation</b>		
1	No Erythema	0
2	Very slight erythema (barely perceptible )	1
3	Well-defined erythema	2
4	Moderate to severe erythema	3
5	Severe erythema (beet-redness) to slight scar formation (injuries in depth)	4
<b>Edema formation</b>		
1	No edema	0
2	Very slight edema (barely perceptible)	1
3	Slight edema (edges of area well-defined by definite raising)	2
4	Moderate edema (raised approximately 1.0 mm)	3
5	Severe edema (raised more than 1.0 mm and extending beyond exposure area)	4
6	Total possible score for irritation	8

**Table No.4: Vesicle size, % Drug content and % Entrapment efficiency of ethosomes formulations**

S.No	Formulation code	Average vesicle size in $\mu\text{m}$	% Drug content	% Entrapment efficiency
1	F1	4.62	90.59	79.53
2	F2	6.13	92.42	81.65
3	F3	6.98	98.95	87.89
4	F4	6.18	95.02	85.43

**Table No.5: Reading after Skin irritation study of ethosomal gel formulation F3-G1**

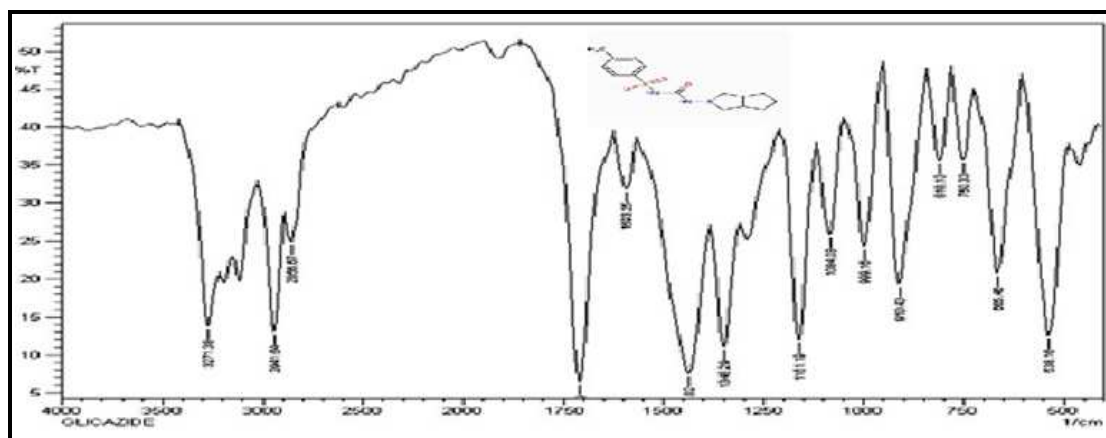
S.No	Skin responses	Days	Score	
			Rat 1	Rat 2
1	Erythma and Scar formation	1	0	0
		3	0	1
		7	1	0
2	Edema Formation	1	0	0
		3	0	0
		7	0	0
3	Primary irritation index (PII)		0.16	0.16

Average Primary irritation index of formulation F3-G1 =0.16

**Table No.6: Hypoglycemic activity of Gliclazide ethosomal gel formulation F3-G1**

**Group-I = Oral, Group-II = F3G1 (Topical)**

S.No	Time in hrs	% Reduction in blood glucose level (mean $\pm$ SEM n=4)	
		Group-I	Group-II
1	1	50 $\pm$ 1.12	21 $\pm$ 2.31
2	2	56 $\pm$ 1.27	27 $\pm$ 2.14
3	3	41 $\pm$ 1.92	38 $\pm$ 2.59
4	4	38 $\pm$ 2.42	45 $\pm$ 2.97
5	6	22 $\pm$ 1.29	38 $\pm$ 2.38
6	8	-	36 $\pm$ 1.42
7	12	-	23 $\pm$ 1.64
8	24	-	08 $\pm$ 1.96



**Figure No.1: FT-IR Spectroscopy of Gliclazide**



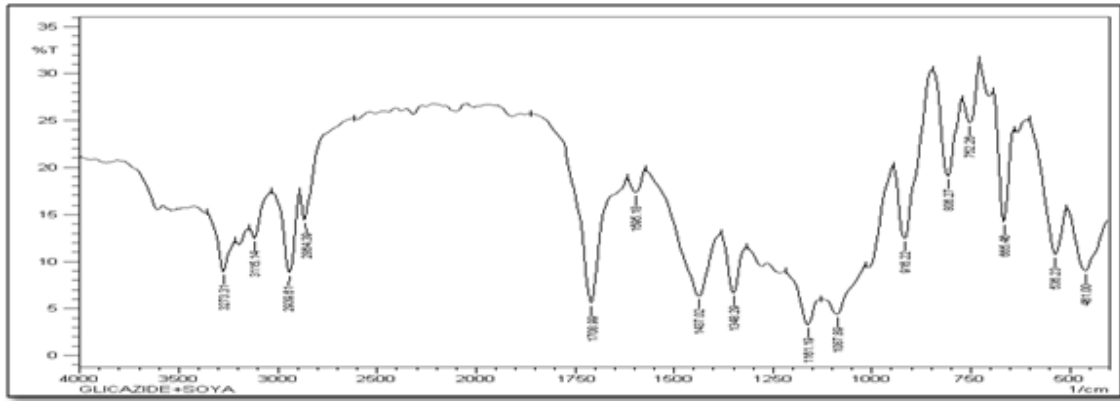


Figure No.2: FT-IR Spectroscopy of Gliclazide +Soya lecithin

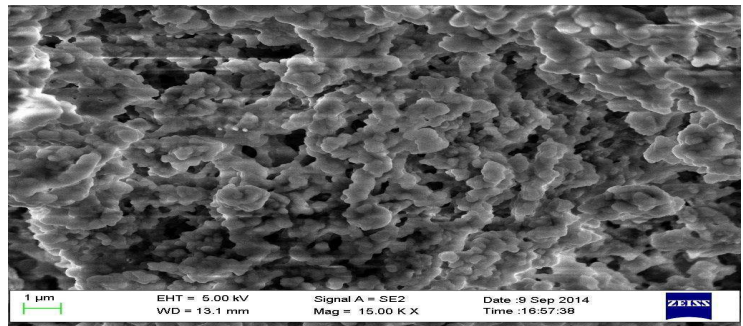


Figure No.3: Scanning electron micrograph of ethosomes formulation F3

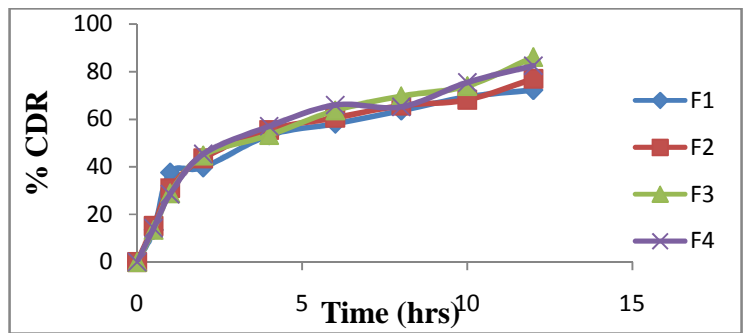


Figure No.4: % CDR of ethosomes formulations

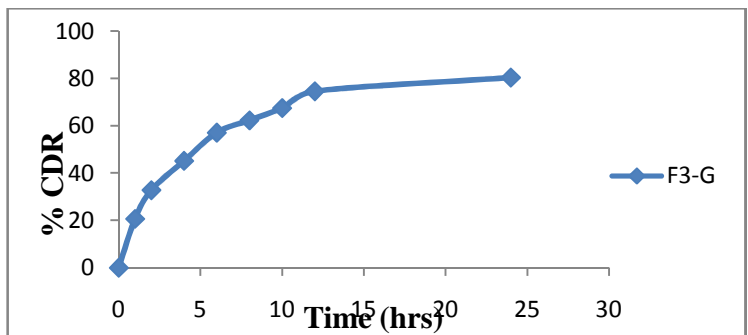


Figure No.5: % CDR of ethosomal gel formulation F3-G1

## CONCLUSION

Ethosomes exhibited superior stability. Ethosomal gel shows no skin irritation and delivered the Gliclazide in sustained or controlled manner as compared to conventional dosage form, as evidenced by a significant sustained decrease in blood glucose level in diabetes rats. Hence, ethosomes drug delivery system was better choice for sustained release of drug through topical drug delivery and topical delivery of Gliclazide is viable and could improve patient compliance and it may be the most convenient topical formulation for the patient unable to take drug orally.

## ACKNOWLEDGEMENT

All authors would like to thank Bharathi College of Pharmacy, Bharathinagara, Mandya, and Karnataka, India for supporting for the fulfillment of this work.

## BIBLIOGRAPHY

1. Gupta N B, Loona S, and Khan M U. Ethosomes as elastic vesicles in transdermal drug delivery: An overview, *IJPSR*, 3(3), 2012, 682-687.
2. Jain N, Talegonkar S, Jain N K. New ways to enter the blood stream: Emerging strategies in transdermal drug delivery, *Pharm Rev*, 4(2), 2004, 41-60.
3. Wadkar K A, Magdum C S, Patil S S, Naikwade N S. Anti-diabetic potential and Indian medicinal plants, *Journal Herbal Medicinal and Toxicology*, 2(1), 2008, 45-50.
4. Verma D D, Fahr A. Synergistic penetrations effect of ethanol and phospholipids on the topical delivery of Cyclosporin, *J Control Release*, 97(1), 2004, 55-66.
5. Kumar R, Aslam M D, Tripathi A, Prasad D, Chaudhary V, Jain V, Mishra S K and Singh R et al. Ethosomes: novel vesicular carriers in transdermal drug delivery, *J Global Pharma Tech*, 2(6), 2010, 1-7.
6. Anilkumar J Shinde, Amit L Shinde, Harinath N More. Design and evaluation of transdermal drug delivery system, *Asian J Pharm*, 4(1-2), 2010, 121-129.
7. Touitou E, Dayan N, Bergelson L, Godin B, Eliaz M. Ethosomes-novel vesicular carriers for enhanced delivery: characterization and skin penetration properties, *J Control Release*, 65, 2000, 403-418.
8. Atul Kumar Garg, Lalit Mohan Negi, Meenakshi Cuauhan. Gel containing ethosomal vesicles for transdermal delivery of Aceclofenac, *Int J Pharm Sci*, 2(2), 2010, 102-108.
9. Suresh Jain, Manish Goswami, Anil Bhandari and Vimal Arora. Skin irritation study of intradermal patch of chitosan containing trazodone-HCl on rat skin, *Int J Res Pharm BioSci*, 2(3), 2011, 1082-1084.
10. Draize J H, Woodard G and Calvery H O. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes, *J Pharmacolo Exp Ther*, 82, 1994, 377-390.
11. Rakesh Kumar Sharma, Navneet Sharma, Sudha Rana, Hosakote G. Shivkumar. Solid lipid nanoparticles as a carrier of metformin for transdermal delivery, *Int J of Drug Deliv*, 5, 2013, 137-145.
12. Manish K Singh, Vikas Chandel, Vandana Gupta and Suman Ramteke. Formulation development and characterization of microemulsion for topical delivery of Glipizide, *Der Pharmacia Lettre*, 2(3), 2013, 33-42.