

Development and Evaluation of Novel Ethosomal Vesicular Drug Delivery System of *Sesamum indicum* L. Seed Extract

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Abstract

Aim: The aim of the present research work is to prepare ethosome of *Sesamum indicum* L. seed extract, its incorporation into gel formulations and to characterize the developed ethosomes and gel formulations using various parameters. **Methods:** Different formulations of ethosomes using phospholipids (1–4%) and ethanol (10–40%) were prepared using *S. indicum* L. seed extract by solvent dispersion technique and were characterized. Carbopol 934 was used to prepare ethosomal gel. **Results:** The size of ethosomes was found to be in the range of 139.7 ± 10.55 – 231.8 ± 12.43 nm while polydispersity index ranges from 0.114 to 0.348 and ZP were between –17.0 and 47.7 mV. Morphology studies showed smooth surface under phase contrast microscope showed, transmission electron microscope showed unilamellar nature with near spherical shape. The EE of ethosomes was found to be in the range of $82.12 \pm 1.88\%$ and $97.26 \pm 0.65\%$. Ethosomes were further added to Carbopol 934 for gel formation, and subsequently, evaluated for their physicochemical properties. The pH of the gel formulations was found to be in the range of 5.97 ± 0.01 – 6.22 ± 0.02 . Viscosities of gels were ranging between 6080 and 119200 centipoises at 25 rpm. *In vitro* diffusion study was conducted for ethosomes incorporated in viscous gel. **Conclusions:** The present study revealed that ethosomal vesicular delivery system of seeds extract of *S. indicum* L. is an encouraging novel approach for herbal extract.

Key words: Ethanol, ethosomes, extract, gel, phospholipid

INTRODUCTION

Sesamum indicum L., belongs to the family Pedaliaceae, is a high altitude medicinal plant having an excellent nutritional content along with a huge pharmacological profile. Sesame is used in villages for auspicious occasions, rituals, religious sacrifices, and marriage ceremonies due to its religious and mythological importance. Apart from its religious significance sesame is used as medicine. Sesame is known as the king of oilseeds due to the high oil content (50–60%) of its seed.^[1] The seeds of sesame contain a number of important phytochemicals which includes alkaloids, flavonoids, glycosides, phenols, anthraquinones, tannins, carbohydrates, and proteins. Sesame reveals the truth that it is a more beneficial plant with anti-pyretic, anti-inflammatory, antioxidant, antimicrobial, anti-hypertensive, anticancer, wound healing activity, and other properties.^[2]

According to the World Health Organization, 80% of the population in developed countries

relies on plant-based traditional medicines to maintain their primary health care needs. High treatment cost and side effects along with drug resistance are major problems associated with synthetic drugs.^[3] The medicinal values of plants are due to the presence of chemically active substances that produce a definite physiological action on human and animal health. However, delivery of herbal drugs also requires modifications. Nowadays, novel drug delivery system opens the door toward the development of herbal drug delivery systems. Novel drug delivery system is advantageous in delivering the herbal drug at a predetermined rate, and delivery of drug at the site of action which minimizes the toxic effects with an increase in bioavailability of drugs. Incorporation of novel drug delivery technology to herbals

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reduces the drug degradation or pre-systemic metabolism and serious side effects by accumulation of drugs to the non-targeted areas. Skin is composed of three main layers as subcutaneous tissue, dermis, and epidermis. Stratum corneum decides the rate of permeation of compounds and it is the major obstacle in diffusing the drug across it. Enhanced skin delivery of drugs can be achieved by novel lipid carriers called as ethosomes.^[4]

Ethosomes are soft malleable lipid vesicles composed mainly of phospholipids, alcohol (10–40%), and water. The physicochemical characteristics of ethosomes allow this vesicular carrier to transport active substances more efficaciously through the skin in terms of quantity and depth. Ethosomes play an important role in controlling the release rate of drug over an extended time keeping the drug shielded from immune response or other removal systems. Ethosomes show smaller vesicle size, high entrapment efficiency (EE) as well as improved stability. The size of ethosomes may vary from nanometers to microns. Ethosomes have become an area of research interest in herbal formulation due to its enhanced skin permeation and improved EE. As plant drugs are considered safe due to their natural origin, they exhibit promising therapeutic effect. However, most of the phytoconstituents fail to achieve bioavailability due to poor absorption. The reasons may be the large molecular sizes and low lipid solubility which causes poor absorption of phytoconstituents resulting in reduced bioavailability. Incorporation of these plant actives or extracts into vesicular carriers vastly improves their absorption and consequently bioavailability. In the medical treatment, based on the topical route of administration vesicular systems have been used to improve the safety of the drug and to avoid first-pass hepatic effect of oral administration. They can also permeate intact through the human skin due to its high elasticity properties and can improve the dermal pharmacological action.^[4,5] There are many reports which revealed the pharmacological activity of the extract, but only a few of them were found to convert the extracts into suitable dosage forms.

From the above literature, it was decided to develop an ethosomal formulation for *S. indicum* L. seed extract and its incorporation into gel formulations and to characterize and evaluate the formulations.

MATERIALS AND METHODS

Collection of plant material

Authenticated seeds of *S. indicum* L. were procured from Nashik, Maharashtra. All the other solvents and reagents were of analytical grade.

Preparation of extract

Soxhlet extractor was used for sesame oil extraction for 4 h by maintaining solvent to solid ratio (25:1). Ethanol had been used as a solvent for the process, performed in triplicate. The temperature was maintained at 40–50°C. The solvent was removed by distillation under reduced pressure and the resulting semisolid mass was vacuum dried using a rotary flash evaporator to obtain the extract.^[6,7]

Preformulation studies of extract

Identification of extract was carried out by ultraviolet (UV) spectrophotometric methods and Fourier Transform Infrared.

Preparation of ethosomes

Formulation of the ethosomes was followed by solvent dispersion technique. The ethosomal system is comprised 1–4% phospholipids, 20–40% ethanol, and aqueous phase to 100% w/w as shown in Table 1.

Phospholipids were dissolved in ethanol and span 20 in extracted sesame oil this mixture was heated to 30°C ± 1°C in a water bath while the aqueous phase was prepared by dissolving tween 20 in double distilled water then heated to 30°C ± 1°C. The resulting aqueous solution was added slowly in a fine stream to the lipidic solution in the center of the vessel with constant stirring using magnetic stirrer at 700 rpm in a closed vessel. The temperature was kept 30°C throughout the experiment. The mixing was continued for additionally 5 min.^[8] The prepared ethosomes were then sonicated at 4°C using probe sonicator for three cycles of 5 min each with the interval of 5 min and then refrigerated.

Table 1: Composition of ethosomal formulations

Formulation code	Phospholipid (% w/w)	Ethanol (% w/w)	Sesame oil (ml)	Span 20 (ml)	Tween 20 (ml)	Water (ml) q.s. to
F1	1.0	20	7.5	1	0.5	100
F2	2.0	30	7.5	1	0.5	100
F3	2.0	40	7.5	1	0.5	100
F4	3.0	30	7.5	1	0.5	100
F5	4.0	30	7.5	1	0.5	100

Preparation of ethosomal gel

The gels were prepared by dispersion method using Carbopol 934 (2% w/w). Gels were prepared by dispersing gelling agent to the distilled water. Then, the mixture was allowed to swell overnight. The pH was adjusted to 7 pH using triethanolamine. To this gel solution, ethosomal dispersions were added and mixed properly. Mixing was continued until a transparent gel appeared. Methylparaben (0.5%) and Propylparaben (0.2%) were added as preservative. The prepared gels were filled in glass vials and stored.^[9]

CHARACTERIZATION OF ETHOSOMES

In the present study, optical microscopy, phase contrast microscopy, and transmission electron microscopy showed the shape and surface morphology of the ethosome vesicles. Zeta potential, vesicle size, and polydispersity index (PDI) were measured by Zetasizer (Malvern Instruments, Malvern).^[10,11]

Vesicular shape analysis by microscopy method

The prepared ethosomal vesicle formulations were placed on a glass slide and viewed under optical microscopy using motic microscope to observe the shape of vesicles.^[12]

Vesicular shape and surface morphology by transmission electron microscope (TEM) and phase contrast microscope

The ethosomal vesicular formulation was observed under phase contrast microscopy with the magnification power of $\times 100$ (Olympus). Photographs of vesicles were taken using an Olympus camera.

Formulation diluted with water (10 μ l of diluted dispersion) was adsorbed onto a grid with carbon-coated formvar film that was attached to a metal specimen grid. Excess sample was blotted off, and the grid was covered with a small drop of staining solution (2% w/v uranyl acetate). It was left on the grid for few minutes, and excess solution was drained off. The grid was allowed to dry thoroughly in air and sample was examined in the transmission electron microscope with an accelerating voltage of 200 kV for surface appearance and shape.

Vesicular size analysis

The mean size was analyzed by dynamic light scattering technique with a Zetasizer 3000 HSA (Malvern Instruments, Malvern, UK). The sample was placed in a quartz cuvette, and size measurements were carried out at a scattering angle of 90°. All observations were recorded in triplicate for each formulation.

EE

The EE was determined by ultracentrifugation, 10 ml of ethosomal formulation were mixed with 1 ml of 1% Triton $\times 100$ solution. Each sample was vortexed for 2 cycles of 5 min with 2 min time interval between the cycles. Specified quantity 1.5 ml of vortexed sample and fresh untreated ethosomal formulations were taken into different centrifugal tubes. These samples were centrifuged at 20,000 rpm for 3 h. The supernatant layer was separated, diluted with water suitably and drug concentration was determined at 290 nm in both vortexed and unvortexed samples. The EE was calculated as follows:

$$\text{Entrapment Efficiency} = \frac{T-C}{T} \times 100$$

Where, "T" = total amount of drug that detected from supernatant of vortexed sample

"C" = the amount of drug untrapped and detected from supernatant of unvortexed sample.

CHARACTERIZATION OF ETHOSOMAL GEL

The herbal ethosomes incorporated gels were evaluated for physical characteristics, pH, viscosity and rheological studies, gel strength, extrudability, spreadability, and washability based on the methods in literature.^[13,14]

Physical characteristics

The prepared herbal ethosomal gel formulations were examined visually for their color, appearance, consistency, homogeneity, and phase separation manually.

Consistency

The measurement of consistency of the prepared gels was done by dropping a cone attached to a holding rod from a fix distance of 10 cm in such way that it should fall on the center of the glass cup filled with the gel. The penetration by the cone was measured from the surface of the gel to the tip of the cone inside the gel. The distance traveled by the cone was noted after 10 s.

Homogeneity

All the developed gels were tested for homogeneity by visual inspection after setting the gels in the container. They were observed for their appearance and presence of any aggregates.

pH measurement

The pH of the prepared ethosomal gel formulations was determined using a digital pH meter. Ethosomal gel formulations (1 g) were stirred in distilled water, to get uniform dispersion

then was kept aside for 2 h. The volume was then made up to 100 mL (1% solution) than pH measured in triplicate.

Viscosity and rheological studies

Brookfield digital viscometer (Model DV2TRVTJ0) was used for the determination of viscosity of ethosomal gel using spindle No. 7. Ethosomal gel (100 g) was taken in a beaker, and the spindle was dipped in it.

Gel strength

The apparatus for measuring gel strength consisted of a plunger having a pan to hold weights at one end whereas the other end was immersed into the gel. Formulated gels were placed in a glass bottle where marking was done at 1 cm below the filling mark. The weight required for the plunger to sink to a depth of 1 cm through the prepared gel was measured for each formulation.

Extrudability

A closed collapsible tube containing about 20 g of gel was pressed firmly at the crimped end, and a clamp was applied to prevent any rollback. The cap was removed, and the gel was extruded. The amount of the extruded gel was collected and weighed. The percentage of the extruded gel was calculated.^[15]

Spreadability

The spreadability was measured by taking an excess of the sample then applied between the two glass slides and was compressed to a uniform thickness by placing (1 gm) weight for 5 min. The time required to separates these slides (i.e., the time during which the upper glass slide shifts over the lower glass slide) measures the spreadability (g.cm/s). A shorter interval indicates better spreadability.

$$S = \frac{M \times L}{T}$$

Spreadability was calculated using the formula given below: Where, S= Spreadability, M = weight tied to upper slide, L = length moved on the glass slide, T = time (in s) taken to separate the slide completely each other.

Washability

On to the skin, a small amount of gel was applied and then it was washed with water and checked whether the gel was able to be totally washed or not.

In vitro diffusion studies

The release of ethosomal gel containing sesame oil was determined using Franz diffusion by cell diffusion technique.

The formulated ethosomal gel was taken in a donor compartment, between donor and acceptor compartment soaked osmosis cellophane membrane was placed the acceptor compartment was filled with phosphate buffer of pH 7.4. The temperature of the acceptor medium maintained at $37 \pm 1^\circ\text{C}$. The acceptor medium was stirred by a magnetic bead fitted to a magnetic stirrer at a speed of 500 rpm. At defined time intervals, sample aliquots of 1mL sample were withdrawn periodically, and the same volume of medium was replaced for maintenance of sink condition. The collected samples were analyzed at 290 nm in UV spectrophotometer using a phosphate buffer of pH 7.4 as a blank.

In vitro release kinetics

The models selected were zero-order, first-order, Higuchi, and Korsmeyer–Peppas model. The parameters such as “K” the release rate constant and “R²” the regression coefficient were determined to know the release mechanism.

Stability study of the optimized formulation as per the ICH guidelines

Stability study was carried out for the optimized formulation of ethosomal gel formulation at two different temperatures, i.e., refrigeration temperature ($4 \pm 2^\circ\text{C}$) and at room temperature ($27 \pm 2^\circ\text{C}$) for 3 months. The ethosomal formulations were analyzed for any physical changes such as color and appearance. Other studies carried out were changes in pH, viscosity, drug content, and *in vitro* diffusion study.^[16]

RESULTS AND DISCUSSION

In the present study, sesame oil extract has been prepared from seeds of *S. indicum* L. Extracted sesame oil was scanned in phosphate buffer saline (PBS) pH 7.4 and 10% methanol between 200 nm and 400 nm using UV-visible

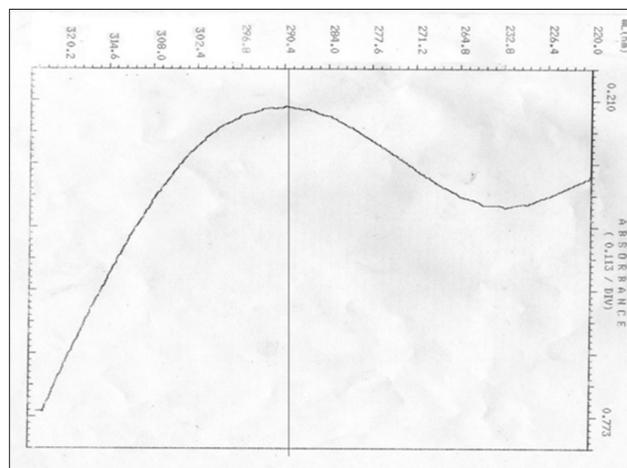


Figure 1: Ultraviolet spectrophotometric graph of sesame oil extract

spectrophotometer. Sesame oil was identified by its light absorption pattern which follows the absorption of light in the range 225–375 nm, shown in Figure 1.

From the UV scan of extracted sesame oil, maximum absorbance was observed at 290.2 nm in media PBS pH 7.4 at different concentration. The reported λ max is 290 nm; hence, it can be taken as a working wavelength for UV spectroscopic analysis of sesame oil.

The Fourier transform-infrared spectroscopy for sesame oil extract [Figure 2] showed that extract was pure and authentic as the characteristic peaks obtained at 3401 –OH OH of phenolic O–H; 3007 –CH Unsaturated–CH; 2896 –CH Saturated–CH; 2777 –CH₂ Symmetric stretching; 1637 Phenyl skeletal frequency; 1504 Phenyl Out-of-plane CH bending; 1471 –CH₂ CH₂ bending (1480 cm⁻¹) 1397 Methyl Methyl symmetric bending; and 1274 C–O C–O of phenolic OH; 1185 C–H In-plane bending of aromatic C–H.

Ethosomes of *S. indicum* extract have been prepared and evaluated. The microscopic evaluation showed the surface morphology of ethosomes. The shapes of most of the ethosome vesicles were observed spherical in shape. Its smooth surface was further confirmed by phase contrast microscopy [Figure 3].

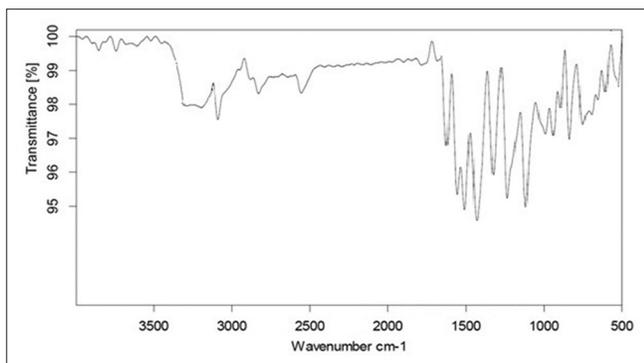


Figure 2: Fourier transform-infrared spectroscopy spectroscopic graph of sesame oil (Frequency region 4000–500 cm⁻¹)

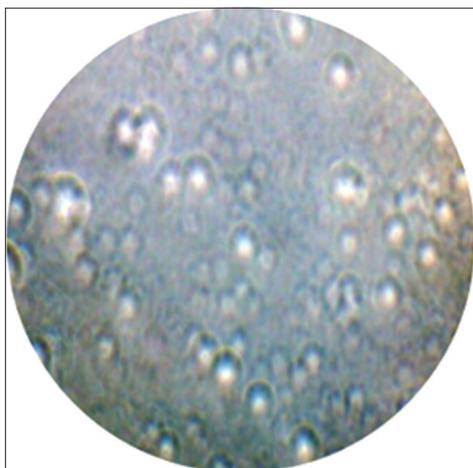


Figure 3: Visualization of ethosomes by phase contrast microscopy

It was seen from TEM photomicrograph that ethosomal vesicles were unilamellar in nature with near spherical shape [Figure 4]. All the images depict smooth surface. It is evident from the results that the size of the vesicles increased with increasing concentrations of phospholipids from 1% to 4%, whereas the concentration of ethanol affected the vesicle size inversely, i.e., higher concentrations of ethanol produced lower vesicle size. This observation supports the findings^[17] of which state that higher concentration of ethanol is responsible for the decrease in the size of vesicle as it furnishes a surface negative net charge to the vesicular systems by altering some surface characteristics.

Ethosomal dispersions were produced with increasing amounts of ethanol (20%, 30%, and 40%) and phospholipid concentration (1%, 2%, 3%, and 4%) [Figure 5]. In the study, although keeping the concentration of phospholipid at 2%, it was found that by increasing concentration of ethanol from 20% to 40%, the size of the vesicles decreased which was observed vesicle size in between 389.65 and 33.65 nm. Transmission electron photomicrograph of ethosomes confirmed the above findings. In the similar manner, the phospholipid concentration was taken at 3% and 4% while keeping the concentration of ethanol was 30%. It was found that vesicle size increased from 187.3 nm to 231.8 nm.

PDI was considered for evaluation of homogeneity of prepared ethosomes on the basis of their vesicle size distribution. The values obtained for PDI lies in between 0.114 and 0.348 as shown in Table 2, interpret that the formulated batches showing narrow to broad size distribution.

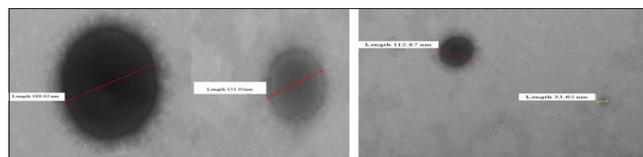


Figure 4: Visualization of ethosomes by transmission electron microscopy

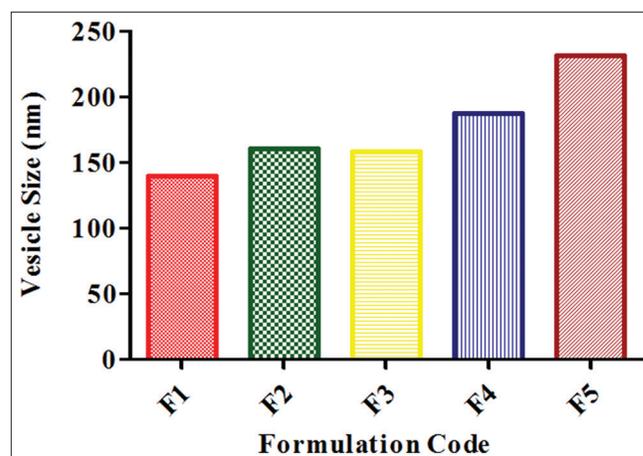


Figure 5: Vesicle size of the ethosomal formulations of F1 to F5

Table 2: EE, vesicle size, polydispersity index and zeta potential of ethosomal batches

Formulation code	EE * (%)	Vesicle Size* (nm)	PDI	Zeta potential (mV)
F1	87.61±1.53	139.7±10.55	0.114	-23.9
F2	93.28±1.16	160.6±11.20	0.259	-17.5
F3	82.12±1.88	158.1±19.40	0.194	47.7
F4	94.77±0.72	187.3±08.80	0.209	-31.1
F5	97.26±0.65	231.8±12.43	0.348	-25.5

*Data represented as mean±SD, n=3. PDI: Polydispersity index, EE: Entrapment efficiency

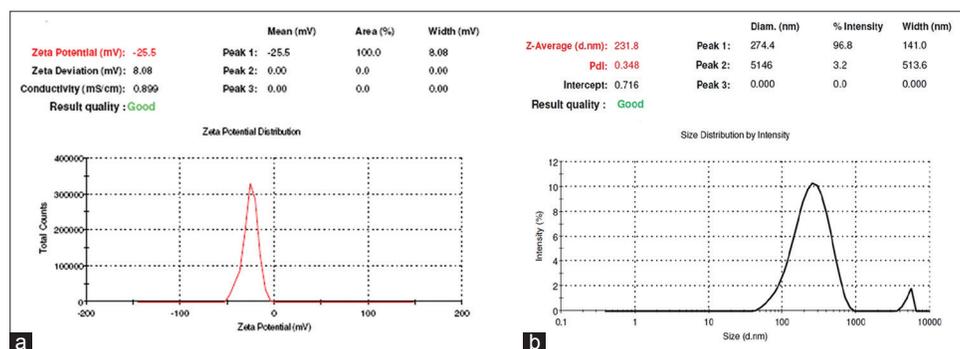


Figure 6: (a) The zeta potential of optimized F5 ethosomal formulation (b) The size and size distribution optimized F5 ethosomal formulation

The zeta potential is an important parameter that affects stability and was determined using zeta sizer. In general, particles with zeta potentials values more than +30 mV or -30 mV are normally considered stable^[18] as it prevents aggregation between vesicles due to electrostatic repulsion and depicts the physical stability of vesicular systems. High zeta potential prevents the aggregation between vesicles and hence, enhances its physical stability. Formulated ethosomal formulation showed negative ZP (-17.0–47.7 mV) caused by the net charge of the lipid composition in the formulation. The negative ZP is responsible for enhanced percutaneous permeation of drug. From Figure 6a and b, the value of the optimized ethosomal formulation was found to be -25.5 mV which indicated that ethosomes were stable.

The delivery potential of ethosomal system is directly affected by its drug carrying capacity which is determined in terms of EE. The EE of ethosomes was determined for all the formulations. The ranges of EE of ethosomes were between 82.12 ± 1.88% and 97.26 ± 0.65%. The ethanol concentration in the ethosome system should not be too high, and generally, should be kept below 45%. As increasing concentration of ethanol results in leaking of the drug from the lipid bilayer due to which EE decreases;^[19,20] therefore, ethanol concentration only up to 40% was considered. The maximum EE of ethosomal vesicle containing sesame oil extract as determined by ultracentrifugation was 97.26 ± 0.65% for F5 formulation containing 30% ethanol concentration. This was much higher than ethosomal formulation F3 with 40% ethanol. The EE was 82.12 ± 1.88% for F3. As the ethanol concentration increased from 20% to 30%, there was an improvement in EE [Figure 7]. The formulation F1 with

20% ethanol concentration was having EE of 87.61 ± 1.53%, beyond 30% ethanol concentration the EE was found to be declining. Higher EE with an increased amount of ethanol is possibly due to increased solubility of *S. indicum* extract in ethanol present in the ethosomal core. This is in accordance with the previous finding by Paolino *et al.*, 2012.^[21] The result suggested that 4% phospholipid is optimal concentration along with 30% ethanol concentration for better EE and any increase or decrease in concentration of phospholipids or ethanol reduces the EE of ethosomes.

In the evaluation of ethosomal topical gel, all the ethosomal gel formulations were pale yellowish to white viscous, creamy preparations with a smooth, homogeneous texture and glossy appearance. From the results, it is concluded that all the formulated gels showed good to excellent homogeneity and gel strength. The texture of the formulations was smooth with the absence of lumps and no phase separation. Formulations were easily washable without leaving any residue on the surface of the skin. The consistency and spreadability of the formulated ethosomal gels were seen significantly same, as Carbopol 934 used in all the formulations is in identical concentration (2%) as shown in Table 3.

Among the ethosomal gel formulations F2, F4, and F5, >90% of the contents were extrudable indicating they have excellent extrudability except for F1 and F3 as 80% of the contents were extrudable [Table 4].

The pH for all the formulations exhibited in the range of 5.97 ± 0.01–6.22 ± 0.02 at 25°C. The viscosity of all the gel formulations ranged from 6080 to 119200 cps at 25 rpm.

It is clearly observed from Figure 8 that as the shear stress increased, the viscosity decreased in all the formulations.

The cumulative amount of drug release from *in vitro* diffusion studies was estimated for F1-F5. Percent cumulative amount of drug release in 6 h was found to 49.53%, 59.25%, 67.51%, 73.21%, and 69.52%, respectively, for formulation F1–F5 which showed a significant ($P < 0.001$) (Two-way ANOVA) increase in drug release [Figure 9]. F5 was adjudged the best based on *in vitro* percentage drug release parameter which

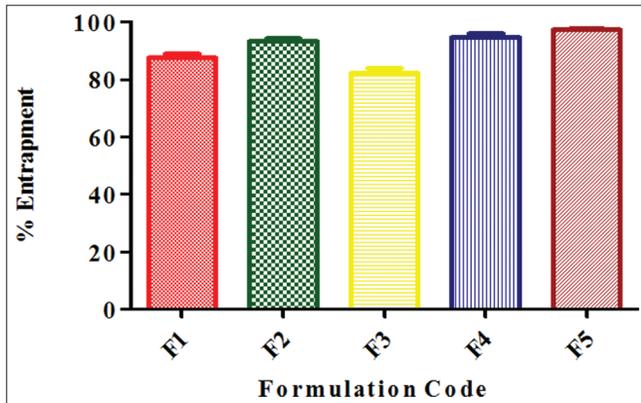


Figure 7: Entrapment efficiency of ethosomal vesicle of formulations F1 to F5

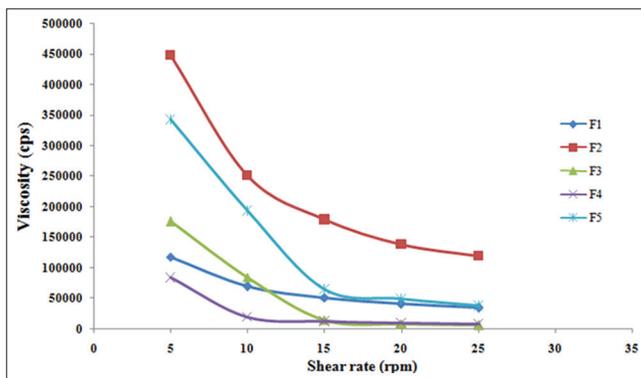


Figure 8: Rheological studies of the ethosomal gel formulations of F1 to F5

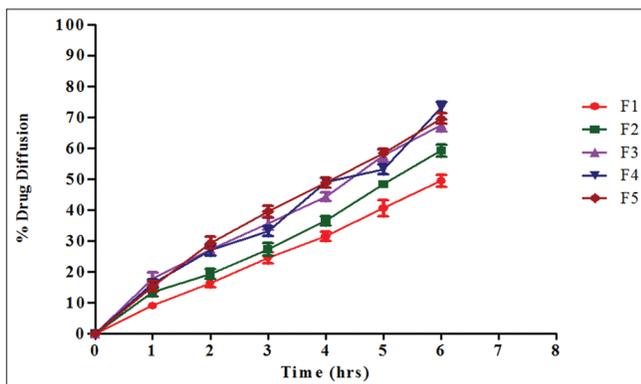


Figure 9: *In vitro* diffusion studies of ethosomal gel formulations of F1 to F5

showed significantly ($F_5 = 69.52\%$, $P < 0.001$) enhanced the drug release. This may be due to the presence of ethanol in ethosomal formulations as compared to conventional gel which is devoid of any ethanol concentration. Ethanol tenders the vesicles pliable elastic distinctiveness which permits them to pervade more readily into deeper layers of skin.

From above observations, it was observed that ethosomes loaded with sesame oil extract incorporated in gel formulations were almost significant values as the concentration of Carbopol used in all the formulations is same (2% w/w) with respect to the gel characteristics and ease of applications.

On the basis of small vesicle size, uniform size distribution, higher EE of ethosomal vesicles, and *in vitro* diffusion studies of ethosomal gel containing sesame oil extract, Formulation F5 was selected for further studies as transdermal flux, release kinetics, and stability studies.

On the analysis of transdermal flux of the F5 formulation, it was found that results followed the similar pattern as that of

Table 3: Consistency of the formulations of ethosomal gel

Formulation code	Consistency (mm)	Spreadability (g.cm/s)
F1	5.2±0.17	6.83
F2	5.5±0.16	7.41
F3	5.6±0.17	7.00
F4	5.1±0.30	7.22
F5	5.07±0.29	6.72

Data represented as mean±SD, $n=3$

Table 4: Extrudability values of the formulations of ethosomal gel

Formulation code	Extrudability (%)	Remarks
F1	81.25±5.6	Good
F2	93.88±3.1	Excellent
F3	83.27±5.3	Good
F4	90.11±4.6	Excellent
F5	95.56±4.3	Excellent

Data represented as mean±SD, $n=3$

Table 5: Release kinetic data of different model for optimized formulation F5

Model	R^2 value	K value
Zero-order	0.9913	12.0707
First-order	0.9921	-0.1824
Matrix	0.9687	24.9767
Peppas	0.9987	15.7934
Hix.Crow.	0.9977	-0.0525

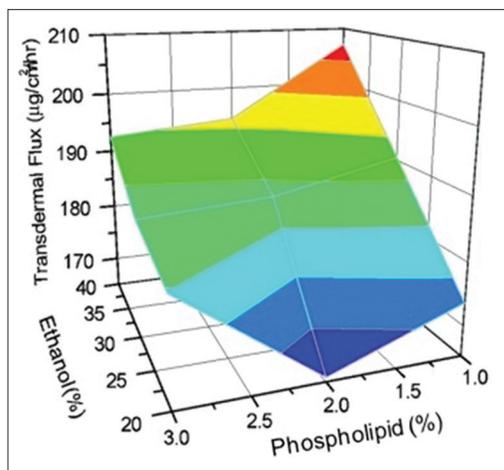


Figure 10: Transdermal flux for the optimized formulation F5

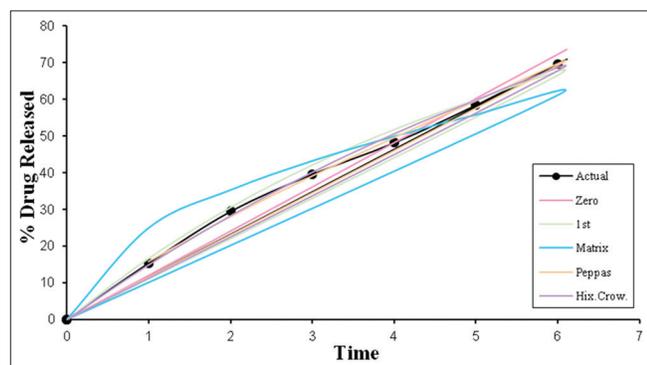


Figure 11: Percentage drug release from optimized formulations F5

cumulative percent drug release. It is evident from the results that flux of formulated ethosomal gel of sesame oil extract F5 showing good permeation [Figure 10].

The release kinetic mechanism of sesame oil in ethosomal gel was diffusion controlled. It was verified with different kinetic model [Table 5 and Figure 11]. The optimized formulation of ethosomal gel F5 follows Korsmeyer's plot having an R^2 value of 0.9987 which indicate that there is anomalous diffusion or diffusion coupled with erosion.

Stability studies revealed that the physical appearance, rheological properties, EE, and drug release in the prepared ethosomal gel remained unchanged on storage at refrigeration temperature ($4 \pm 2^\circ\text{C}$) and room temperature ($27 \pm 2^\circ\text{C}$) for 3 months. The initial diffusion profile of F5 formulation was 69.52 ± 0.74 , after 3 months of evaluation it was calculated as $73.02 \pm 0.55\%$ and 63.86 ± 0.31 , respectively, under refrigeration and room temperature. The result showed that in refrigeration temperature there was some increase in dissolution profile by 3.2% and decrease at room temperature by 5.66%. The stability of ethosomal formulation containing sesame oil extract was found to be intact under different temperature conditions.

CONCLUSIONS

The *S. indicum* L. seed extract loaded ethosomal formulation was successfully prepared by loading phospholipids and ethanol and ethosomal gel based formulations were prepared with hydrophilic polymer Carbopol 934. The study confirmed that ethosomes are very promising carrier for the transdermal delivery of *S. indicum* L. seed extract revealed from higher EE and better stability profile. The *in vitro* release efficiency of ethosomal gel was found up to $69.52\% \pm 0.74$, at 6 h which support the potential of these carriers in penetrating the lipid-rich biological membrane. The stability of ethosomal formulation containing sesame oil extract was also found to be intact under different temperature conditions. The study revealed that this ethosomal formulation containing *S. indicum* L. seed extract has been considered as a possible novel vesicular carrier for the herbal extract.

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