Formulation and Characterization of Atorvastatin Ethosomal Gel

Rekha Bhagya

Department of Pharmaceutics, ASN Pharmacy College, ANU University, Tenali, India.

Abstract

Topical administration of Atorvastatin (ATV) drug is more effective to treat cardiovascular disease than oral administration. Oral therapy requires administration of frequent doses of ATV because of poor intestinal absorption (14%) and thus has side effects like insomnia, myopathy, sinusitis, urinary tract infections. Topical therapy allows administration of small amount of ATV, which is directly applied on the skin such that it penetrates through the skin and reaches the specific site to show its pharmacological action efficiently as in this route of drug delivery first pass metabolism is bypassed and by this route of drug delivery and more than 70% bioavailability was achieved.

Present investigation was focused to enhance transdermal as well as subdermal delivery of ATV using ethosomal system which composed of phospholipid, ethanol and water. Effect of different formulations on characterization and in-vitro drug release was conducted and ethosomes containing 30% w/w ethanol showed better entrapment efficiency, small vesicle size, high transdermal flux and maximum skin penetration. Further sonication reduced the size of the vesicles and vesicles were more uniform in size and shape and showed better characterization. Release kinetic of ATV from ethosomes was found to be zero order while other formulations showed far away from ethosomes. Ethosomes were found stable in refrigeration and room temperature during storage of 8 weeks. It is concluded from the present investigation that ethosomes increase the transdermal flux and gives predictable release rate of atorvastatin and hence ethosomal system is a promising candidate for delivery of atorvastatin into and through the skin.

Keywords: Atorvastatin (ATV), Ethosome, phospholipid, ethanol, transdermal flux.

Introduction

Optimization of drug delivery through human skin is important in modern therapy. Recently, the transdermal route viewed with oral treatment as the most successful innovative research area in drug delivery [1].

Transdermal delivery is an important delivery route that delivers precise amount of drug through the skin for systemic action. Improved methods of drug delivery for biopharmaceuticals are important for two reasons; these drugs represent rapidly growing portion of new therapeutics and are most often given by injection. Discovery of new medicinal agents and related innovation in drug delivery system have not been only enabled the successful implementation of novel pharmaceutical, but also permitted the development of new medical treatment with existing drugs. Throughout the past two decades, the transdermal patches have become a proven technology holding the promise that new compound could be delivered in a safe and convenient way through the skin.
Transdermal route offers several potential advantages over conventional routes like avoidance of first pass metabolism, predictable and extended duration of activity, minimizing undesirable side effects, utility of short half-life drugs, improving physiological and pharmacological response, avoiding the fluctuation in drug levels, and most importantly, it provides patient convenience. But one of the major problems in transdermal drug delivery is the low penetration rate through the outer most layer of skin [3].

The non-invasive approaches for providing transdermal drug delivery of various therapeutic substances are:

**Drug and vehicle interactions**
- Selection of correct drug or prodrug
- Chemical potential adjustment
- Ion pairs and complex coacervates
- Eutectic systems

**Stratum corneum modification**
- Hydration
- Chemical penetration enhancers

**Stratum corneum bypassed or removed**
- Micro needle array
- Stratum corneum ablated
- Follicular delivery

**Electrically assisted methods**
- Ultrasound (Phonophoresis, Sonophoresis)
- Iontophoresis
- Electroporation
- Magnetophoresis
- Photomechanical waves

**Vesicles and particles**
- Liposomes and Niosomes
- Transferosomes and Ethosomes

**Ethosomes**
Ethosomes are slight modification of well established drug carrier liposome. Ethosomes are lipid vesicles containing phospholipids, alcohol in relatively high concentration and water. The size range of ethosomes may vary from tens of nanometers to few microns. Ethosomes permeate through the skin layers more rapidly and possess significantly higher transdermal flux.

Vesicles would also allow to control the release rate of drug over an extended time, keeping the drug shielded from immune response or other removal systems and would be able to release just the right amount of drug and keep that concentration constant for longer periods of time [7].

Ethosomal carriers are systems containing soft vesicles and are composed mainly of phospholipid (Phosphotidyl choline; PC), ethanol at relatively high concentration and water. It was found that ethosomes penetrate the skin and allow enhanced delivery of various compound to the deep strata of the skin or to the systemic circulation Figure 1.

**Mechanism of penetration**

Although the exact process of drug delivery by ethosomes remains a matter of speculation, high concentration of ethanol makes the ethosomes unique, as ethanol is known for it’s disturbance of skin lipid bilayer organization; therefore, when integrated into a vesicle membrane, it gives that vesicles have the ability to penetrate the stratum corneum.

Ethanol interacts with lipid molecules in the polar hard group region, resulting in a reducing the rigidity of the stratum corneum lipids, increasing their fluidity. The intercalation of ethanol into the polar head group environment can result in an increase in the membrane permeability. In addition to the effect of ethanol on stratum corneum structure, the ethosome itself may interact with the stratum corneum barrier.

**Methods of preparation of ethosomes**
Ethosomes can be prepared by two very simple and convenient methods that is:

**Cold method:** This is the most common method utilized for the preparation of ethosomal formulation. In this method phospholipid, drug and other lipid materials are dissolved in ethanol in a covered vessel at room temperature by vigorous stirring with the use of mixer. Propylene glycol or other polyol is added during stirring. This mixture is heated to 30°C in a water bath and added to the mixture, which is then stirred for 5 min in a covered vessel. The vesicle size of ethosomal formulation can be decreased to desire extent using sonication or extrusion method. Finally, the formulation is stored under refrigeration [8].

**Hot method:** In this method phospholipid is dispersed in water by heating in a water bath at 40°C until a colloidal solution is obtained. In separate vessel ethanol and propylene glycol are mixed and heated to 40°C. Then the organic phase is added to the aqueous one. The drug is dissolved in water or ethanol depending on its hydrophilic/hydrophobic properties. The vesicle size of ethosomal formulation can be decreased to the desire extent using sonicaton or extrusion method [9].

![Figure 1: Structure of ethosomes.](image-url)
**Advantages of ethosomes:** Enhanced permeation through the skin. Ethosomes are safe; they have various applications in pharmaceutical, veterinary and cosmetic field. Better patient compliance. Better stability and solubility of many drugs as compared to conventional vesicles. Relatively smaller size as compared to conventional vesicles.

**Limitations of ethosomes:** Poor yield. In case if shell locking is ineffective then the ethosomes may coalescence and fall apart on transfer into water. Loss of product during transfer from organic to water media.

**Materials and Methods**

**Materials**

Atorvastatin, Soya Lecithin, Propylene glycol, Alcohol, Cholesterol, Carbopol 934, Triethanol amine, ultrapure water.

**Equipment:**

Electronic weighing balance, UV spectrophotometer (Schimadzu 1800), Magnetic stirrer (REM elektro), Sonicator, pH meter, SEM, FTIR, Humidity chamber.

**Preparation of Atorvastatin Drug Ethosomes - Cold Method [8,9].**

Preparation of Atorvastatin drug ethosomes was followed by method suggested by Touitou et al., with little modification. The ethosomal system of Atorvastatin drug comprised of 2-5 % phospholipids, 20-50 % ethanol, 10 % of propylene glycol, 0.005g of cholesterol and aqueous phase to 100 % w/w. Atorvastatin 0.025 g was dissolved in ethanol in a covered vessel at room temperature by vigorous stirring. Propylene glycol was added during stirring. This mixture was heated to 30°C in a separate vessel and was added to the mixture drop wise in the center of the vessel, which was stirred for 5 minutes at 700 rpm in a covered vessel. The vesicle size of ethosomal formulation can be decreased to desire extend using sonication or extrusion method. Finally, the formulation is stored under refrigeration. Ethosomes were formed spontaneously by this process Table 1.

**Preparation of Atorvastatin Ethosomal Gel**

The best achieved ethosomal vesicles suspension, formula EF-6 was incorporated into carbopol gel (1%, 1.5%, 2% w/w). The specified amount of carbopol 934 powder was slowly added to ultrapure water and kept at 100°C for 20min. Tri ethanolamine (TEA) was added to it drop wise. Appropriate amount of formula EF-6 containing atorvastatin drug (1.5% w/w was then incorporated into gel-base. Water q.s was added with other formulation ingredients with continuous stirring until homogenous formulation were achieved (G-1,G-2,G-3and G-4). Gel containing free Atorvastatin drug was prepared by similar method using 1.5% Carbopol Table 2.

**Size and Shape Analysis**

A sample of ethosomes were suitably diluted with distilled water in order to observe individual vesicle and a drop of diluted suspension was put on a glass slide covered with cover slip and examined under microscope (magnification 15 × 45 X). The diameters of 150 vesicles were determined randomly using calibrated eyepiece micrometer with stage micrometer. The average diameter was calculated using the formula.

\[
\text{Average diameter} = \frac{nd}{n}
\]

n = number of vesicles

\(d\) = diameter of vesicles

Sonication reduced the vesicular size. Since vesicular size of these vesicles could not be analysed using microscopic method at magnification 15 × 45 X. Hence analysis of sonicated vesicles was done under a special microscope which is connected with a software and photomicrographs were taken under 400 and 800 magnification. Further selected photomicrographs were analysed for size analysis by using special software “particle size analysis” developed by BIOVIS. This special software works on images of photomicrographs with standard dimension.

**Scanning Electron Microscopy:** Determination of surface morphology (roundness, smoothness and formation of

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**Table 1:** Ethosomes formulation table.

<table>
<thead>
<tr>
<th>Ethosomal formulation</th>
<th>Lecithin (Soya lecithin%)</th>
<th>Ethanol (%)</th>
<th>Propylene glycol (%)</th>
<th>Drug (mg)</th>
<th>Cholesterol(mg)</th>
<th>Water</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF1</td>
<td>1</td>
<td>20</td>
<td>10</td>
<td>20</td>
<td>0.005</td>
<td>q.s.</td>
</tr>
<tr>
<td>EF2</td>
<td>2</td>
<td>20</td>
<td>10</td>
<td>20</td>
<td>0.005</td>
<td>q.s.</td>
</tr>
<tr>
<td>EF3</td>
<td>3</td>
<td>20</td>
<td>10</td>
<td>20</td>
<td>0.005</td>
<td>q.s.</td>
</tr>
<tr>
<td>EF4</td>
<td>4</td>
<td>20</td>
<td>10</td>
<td>20</td>
<td>0.005</td>
<td>q.s.</td>
</tr>
<tr>
<td>EF5</td>
<td>5</td>
<td>20</td>
<td>10</td>
<td>20</td>
<td>0.005</td>
<td>q.s.</td>
</tr>
<tr>
<td>EF6</td>
<td>2</td>
<td>30</td>
<td>10</td>
<td>20</td>
<td>0.005</td>
<td>q.s.</td>
</tr>
<tr>
<td>EF7</td>
<td>2</td>
<td>40</td>
<td>10</td>
<td>20</td>
<td>0.005</td>
<td>q.s.</td>
</tr>
<tr>
<td>EF8</td>
<td>2</td>
<td>50</td>
<td>10</td>
<td>20</td>
<td>0.005</td>
<td>q.s.</td>
</tr>
</tbody>
</table>

**Table 2:** Ethosomal gel formulations table.

<table>
<thead>
<tr>
<th>Gel formulation</th>
<th>Atorvastatin ethosomal suspension(ml)</th>
<th>Carbopol (%)</th>
<th>Triethanolamine (ml)</th>
<th>Phosphate buffer (pH 7.4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G-1</td>
<td>20</td>
<td>1</td>
<td>0.5</td>
<td>q.s.</td>
</tr>
<tr>
<td>G-2</td>
<td>20</td>
<td>1.5</td>
<td>0.5</td>
<td>q.s.</td>
</tr>
<tr>
<td>G-3</td>
<td>20</td>
<td>2</td>
<td>0.5</td>
<td>q.s.</td>
</tr>
<tr>
<td>G-4</td>
<td>0.025g</td>
<td>1.5</td>
<td>0.5</td>
<td>q.s.</td>
</tr>
</tbody>
</table>

*G4 drug free gel*
aggregates) of model drug ethosomal gel with polymer was carried out by scanning electron microscopy (SEM).

**ZETA POTENTIAL:** The charge of the ethosomal vesicle is an important parameter than can influence both vesicular properties such as stability as well as skin-vesicle interactions and it’s zeta potential was determined using a computerized inspection system \([4-7]\).

**Entrapment Efficacy:** The entrapment efficiency of atorvastatin drug by ethosomal vesicle was determined by ultracentrifugation 10 ml of (ethosomal suspension) each sample was vortexed for 2 cycles of 5 min with 2 minutes rest between the cycles. 1.5ml of each vortexed sample and fresh untreated ethosomal formulations were taken into different centrifugal tubes. These samples were centrifuged at 20,000 rpm for 3 hours. The supernatant of unvortexed sample. The entrapment efficiency was calculated as follows

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

\(T\) is total amount of drug that detected from supernatant of vortexed sample.

\(C\) is the amount of drug unentraped and detected from supernatant of unvortexed sample.

**Organoleptic Characteristics:** The formulations were tested for its physiological rheological properties like colour, odour, texture, phase separation and feel upon application (grittiness, greasiness).

**Washability:** A small quantity of gel was applied on the skin. After washing with water, checked for whether the gel was completely washable or not.

**Spreadability:** It was determined by modified wooden block and glass slide apparatus. A measured amount of gel was placed on fixed glass slide, the movable pan with a glass slide attached to it and was placed over the fixed glass slide, such that the gel was sandwiched between the two glass slides for 5 min. The weight was continuously removed. Spreadability was determined using the formula

\[
S = \frac{M}{T}
\]

Where,

\(S\) is the Spreadability in g/s,

\(M\) is the mass in grams & 

\(T\) is the time in seconds.

**pH:** Solution of 1gm of gel dissolved in 30ml of distilled water (pH 7) was prepared. The pH of the ethosomal gel was determined by using digital pH meter, measured by bringing the probe of the pH meter in contact with the samples.

**Drug content:** 1g of gel was dissolved in a 100ml of phosphate buffer pH 7.4 for 48 hrs with constant stirring using magnetic stirrer. Solution was filtered and observed with u.v spectrophotometer at \(\lambda_{\text{max}} 242\text{nm}\) the measurements were made in triplicate.

**Skin irritation test:** Rat (male wristar rat) were taken, the abdominal skin of the rat was clipped free of hair 24 h prior to the formulation application. Formulation, 0.5 g of each was applied on the hair-free skin of rat by uniform spreading over an area of 4 cm². The skin surface was observed for any visible change such as erythema (redness) after 24, 48 and 72 h of the formulation application. The mean erythemal scores were recorded depending on the degree of erythema: no erythema = 0, slight erythema (barely perceptible- light pink) = 1, moderate erythema (dark pink) = 2, moderate to severe erythema (light red) = 3, and severe erythema (extreme redness) = 4.

**Drug Release Study from Rat Skin** [3-6]: The skin permeation of atorvastatin drug from ethosomal formulation was studied using Franz diffusion cell specially designed in our laboratory according to the literates. The effective permeation area of the diffusion cell and receptor cell volume was 2.4 cm and 20 ml respectively. The temperature was maintained at 37 ± 0.5°C. The receptor compartment contained 20 ml of pH 7.4 buffer and was constantly stirred by magnetic stirrer at 100 rpm. The rat skin was mounted between the donor and the receptor compartments. Ethosomal formulation 1g was applied to the epidermal surface of rat skin and the content of diffusion cell was kept under constant stirring then 1 ml of samples were withdrawn from receptor compartment of diffusion cell at predetermined time intervals and analysed by spectrometric method at 242 nm after suitable dilution. The receptor phase was immediately replenished with equal volume of fresh pH 7.4 buffer. TriPLICATE experiments were conducted for skin permeation study.

**In-Vitro Release Studies**

**Drug Release Study from Dialysis Membrane**

The skin permeation of atorvastatin drug from ethosomal formulation was studied using open ended diffusion cell specially designed in our laboratory according to the literates. The effective permeation area of the diffusion cell and receptor cell volume was 2.4 cm and 200 ml respectively. The temperature was maintained at 37 ± 0.5°C.

The receptor compartment contained 200 ml of pH 7.4 buffer and was constantly stirred by magnetic stirrer at 100 rpm. Prepared dialysis membrane was mounted between the donor and the receptor compartments. Ethosomal formulation \{EF₁,EF₂,(20ml), and also for optimized ethosomal gel (30ml)\} was applied to the dialysis membrane and the content of diffusion cell was kept under constant stirring then 5 ml of samples were withdrawn from receptor compartment of diffusion cell at predetermined time intervals and analysed by spectrometric method at 242 nm after suitable dilution. The receptor phase was immediately replenished with equal volume of fresh pH 7.4 buffer. TriPLICATE experiments were conducted for drug release studies.

**In-vitro release kinetics** [10]: (Harris shoai et al., 2006)

The results of in vitro release profile obtained for all the formulations were plotted in modes of data treatment
as zero order model, first order model, higuchi model and korsmeyer / peppa’s model:

**In-vitro stability release study:** Stability of drug and stability of vesicles are the major determinant for the stability of formulation, studies were carried to evaluate total drug content at room temperature (27±2° C) and refrigeration temperature (4±2° C). Samples was collected for every 2 weeks and absorbance was seen at 242nm in U.V spectrophotometer Figure 2.

**Results**

**FTIR:** IR spectra was compared and checked for any shifting in functional peaks and non-involvement of functional group. From the spectra it is clear that there is no interaction between the selected carriers, drug and mixtures. Hence the selected carrier was found to be compatible in entrapping the selected atorvastatin drug with carriers without any mutual interactions Figure 2, 3.

**Size Distribution of Atorvastatin Ethosomal Formulations**

The results obtained by vesicular size analysis showed concentration of ethanol affect vesicular size. The size of ethosomes decreased as the concentration of ethanol increased with the largest vesicles size 6.012 µm containing 20% ethanol and smallest 4.32 µm containing 50% ethanol Figure 5.

Microphotograph (figure 10-12) showed that size of the ethosomes. The results of size and shape are consistent with the observations made by Jain NK et al [2].

Since the size of vesicles is reduced by sonication, microscopic analysis followed previously to find the size distribution may not be satisfactory. Hence special software developed by “BIOVIS” was used to find the proper vesicular size distribution of the sonicated product.

Result obtained here showed the maximum vesicular size is 6.012 µm for formulation containing 20% ethanol (EF4) and minimum is 4.32 µm for formulation containing 50% ethanol (EF8), (figure 17, 20). Results obtained here are in same relation with concentration of ethanol.

When the results of size distribution were compared, sonication found to reduce the size of vesicles from 3.904...
µm, 5.00 µm, 5.25 µm, 6.012 µm, 4.472 µm, 6.00 µm, 3.52 µm, and 4.32 µm for ethosomes containing 20%, 20%, 20%, 20%, 30%, 40%, and 50% w/w ethanol respectively.

In average sonication found to reduce the size to three or more times of initial. **ZETA POTENTIAL.**

It is an important parameter that affects the aggregation of vesicles and depicts the physical stability of vesicular system. Zeta potential of optimized formulation EF6 was found to be high (-36.5). High zeta potential prevents the aggregation between vesicles and hence enhances physical stability. It has been investigated that high zeta potential in ethosomes increase the inter bilayer distance owing to electrostatic repulsion Figure 6, Table 3.

The maximum entrapment efficiency of ethosomal vesicles as determined by ultracentrifugation was 73.02% for ethosomal formulation containing 20% ethanol (EF3) which was almost double to the formulation containing 50% ethanol (EF8). As the ethanol concentration increased from 20% to 50% w/w, there was increase in the entrapment efficiency and with further increase in the ethanol concentration (>30% w/w) the vesicle membrane becomes more permeable that lead to decrease in the entrapment efficiency. Results of entrapment efficiency also suggest that 2% phospholipid is optimal concentration for entrapment efficiency and hence increased or decreased in concentration of phospholipid reduces the entrapment efficiency of vesicles. These results further supported by observation made by Jain NK et al. [8].

Increase in entrapment efficiency may be due to the possible reduction in vesicle size. The detrimental effect on the vesicle during ultra-centrifugation which are larger

![Figure 5: Size distribution a) EF1 b) EF2 c) EF3 d) EF4 e) EF5 f) EF6 g) EF7 h) EF8.](image)

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Entrapment efficiency (%)</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF1</td>
<td>52.90</td>
<td>52.95 ± 0.024</td>
</tr>
<tr>
<td>EF2</td>
<td>71.45</td>
<td>71.47 ± 0.020</td>
</tr>
<tr>
<td>EF3</td>
<td>73.05</td>
<td>73.02 ± 0.044</td>
</tr>
<tr>
<td>EF4</td>
<td>65.0</td>
<td>65.04 ± 0.024</td>
</tr>
<tr>
<td>EF5</td>
<td>55.27</td>
<td>55.25 ± 0.016</td>
</tr>
<tr>
<td>EF6</td>
<td>72.52</td>
<td>72.50 ± 0.068</td>
</tr>
<tr>
<td>EF7</td>
<td>64.38</td>
<td>64.42 ± 0.034</td>
</tr>
<tr>
<td>EF8</td>
<td>59.47</td>
<td>59.52 ± 0.036</td>
</tr>
</tbody>
</table>

N=3

![Figure 6: Zetapotential.](image)
in size. Sonication gives the more uniform lamellae, smaller vesicle and uniform size and hence it may be the reason for higher vesicular stability and lesser vesicular disruption during ultra-centrifugation.

**In-Vitro Skin Permeation Study**

In-vitro skin permeation study or in-vitro diffusion study have been extensively studied, developed and used as an indirect measurement of drug solubility, especially in preliminary assessments of formulation factors and manufacturing methods that are likely to influence bioavailability. The objectives in the development of in-vitro diffusion tests are to show the release rate and extent of drug from the dosage form. The in-vitro skin permeation study of atorvastatin drug from ethosomal formulation was studied using franz diffusion cell. The release data was obtained for all the ethosomal formulations. Spectrophotometric results were obtained and given consideration to sampling loss, to calculate actual cumulative drug diffused was calculated since the volume of receptor cell was only 20 ml. The obtained diffused amount of drug was extrapolated to diffusion by unit surface area of rat skin. This cumulative values were plotted as a function of time and steady state transdermal flux was calculated from the slope of linear portion (Figure 20). Figure 7-11, Table 4,5.

**Organoleptic properties**

| Organoleptic Characteristics: | Color: golden yellow | Greasiness: Non-greasy | Grittiness: Free from grittiness | Ease of application: Easily/smoothly applied | Skin irritation: No skin irritation |
| Washability: | Easily washable without leaving any residue on the surface of the skin. |
| Spreadability: | 6.4g.cm/sec |

**Release kinetics**

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Zero order(R²)</th>
<th>First order(R²)</th>
<th>Higuchi(R²)</th>
<th>Korsmeyer-peppas(R²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF6</td>
<td>0.5913</td>
<td>0.4683</td>
<td>0.8998</td>
<td>0.3951</td>
</tr>
</tbody>
</table>

The release kinetics of atorvastatin drug optimized formulation EF6, 30% ethanol followed higuchi’s order of diffusion. This is an encouraging observation.

**Stability studies**

<table>
<thead>
<tr>
<th>Formulation code (EF)</th>
<th>Percentage of drug release</th>
<th>Loss in percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial 4±2 ° C, 27±2 ° C</td>
<td>76.42, 76.42</td>
<td>0, 0</td>
</tr>
<tr>
<td>After 2 weeks 4±2 ° C</td>
<td>76.42</td>
<td>0</td>
</tr>
<tr>
<td>After 4 weeks 4±2 ° C</td>
<td>76.31</td>
<td>0.11</td>
</tr>
<tr>
<td>After 6 weeks 4±2 ° C</td>
<td>76.12</td>
<td>0.3</td>
</tr>
<tr>
<td>After 8 weeks 4±2 ° C</td>
<td>75.95</td>
<td>0.47</td>
</tr>
</tbody>
</table>

**Conclusion**

1. The method described by Touitou et al., (2000) was employed with little modification for the preparation
method showed highest value respect to all other formulation; so it is concluded ethosomal prepared by sonication and containing 30 % w/w ethanol as the best formulation considering all other aspects.

4. Bioavailability is enhanced through transdermal route and more than 70% bioavailability can be achieved when compared to oral route of administration which is having only 14% due to first pass metabolism. The ethosomal formulation containing 30% w/w ethanol is the indication of complete and rapid penetration through the skin may be because of tiny vesicular size. This is an encouraging observation for drugs which are poorly absorbed from skin.

5. Optimized formulation showed higuchi’s order of drug diffusion.

An extensive further investigation is needed with reference to depth of penetration into the skin, determination of zeta potential and confirmation of configuration of phospholipid in lipid bilayer.

There is a need to develop suitable transdermal formulation by prepared ethosomes for transdermal application and also for commercial exploitation.

Thus, the specific objectives were achieved namely design, characterization and release studies of atorvastatin ethosomes. Further these findings may help the industry for development and scaling up a new formulation.

References