ABSTRACT
The objective of present study is to determine the permeation of Lamotrigine from transdermal patch into microcirculation of skin. Matrix type transdermal drug delivery system (TDDS) of Lamotrigine was prepared by the solvent evaporation technique. Several batches were prepared by using combination of HPMC (400, 425 and 450mg) and ethyl cellulose, Eudragit RSPO (50, 75 and 100 mg) in different ratios. Propylene glycol was used as plasticizer and as a permeation enhancer. Formulated transdermal patches were characterized for their physicochemical parameters like thickness, tensile strength, folding endurance, moisture content, moisture uptake and drug content uniformity. Patches were evaluated for their in-vitro drug release profile and ex-vivo skin permeation studies. Patches were also subjected to stability studies and skin irritation studies to determine their compatibility with skin. Result of evaluation studies revealed that Lamotrigine can be administered as a controlled drug delivery system to reduce frequency of drug administration. But this hypothesis requires further confirmation via in-vivo pharmacodynamic and pharmacokinetic studies in animal and human models.

KEYWORDS: Lamotrigine, Transdermal, HPMC, EC, Eudragit, Eudragit, etc.

INTRODUCTION
Lamotrigine is an antiepileptic drug belonging in the phenyltriazine class used in the treatment of epilepsy and bipolar disorder. For epilepsy it is used to treat partial seizures, primary and secondary tonic-clonic seizures, and seizures associated with Lennox-Gastaut syndrome. Lamotrigine also acts as a mood stabilizer. It is the first medication since lithium granted Food and Drug Administration (FDA) approval for the maintenance treatment of bipolar type I. In the US, lamotrigine is available as oral tablets under the market name World Journal of Pharmaceutical Research

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FORMULATION DEVELOPMENT AND EVALUATION OF TRANSDERMAL PATCHS OF ANTIEPILEPTIC DRUG

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Lamictal.\textsuperscript{[1,2,3]} Chemically unrelated to other anticonvulsants, lamotrigine has relatively few side-effects and does not require blood monitoring. While lamotrigine is primarily indicated for epilepsy and bipolar disorders, there is evidence that it could have some clinical efficacy in some neuropathic pain states. Lamotrigine is also used as an off-label drug in treating other neurologic and psychiatric pathologies like borderline personality disorder. The exact mechanism of action of lamotrigine is not fully elucidated, as it may have multiple cellular actions that contribute to its broad clinical efficacy.\textsuperscript{[4,5]}

![Figure 1: Structure of Lamotrigine.\textsuperscript{[6]}](image)

Lamotrigine resembles the actions of phenytoin and carbamazepine in inhibiting voltage-sensitive sodium channels thereby stabilizing neuronal membranes and consequently modulating presynaptic transmitter release of excitatory amino acids such as glutamate and aspartate. Studies on lamotrigine show binding to sodium channels similar to local anesthetics, which is explain potential clinical benefit of lamotrigine in some neuropathic pain states. Lamotrigine displays binding properties to several different receptors. It mediates a weak inhibitory effect on serotonin 5-HT\textsubscript{3} receptor with IC\textsubscript{50} of 18 \textmu M. It also weakly binds to Adenosine A\textsubscript{1}/A\textsubscript{2} receptors, \(\alpha_1/\alpha_2/\beta\) adrenergic receptors, dopamine D\textsubscript{1}/D\textsubscript{2} receptors, GABA A/B receptors, histamine H\textsubscript{1} receptors, k-opioid receptor (KOR), mACh receptors and serotonin 5-HT\textsubscript{2} receptors with an IC\textsubscript{50}>100 \textmu M. Lamotrigine had weak effects at sigma opioid receptors (IC\textsubscript{50} = 145 \textmu M). A study demonstrated an evidence \textit{in vivo} that lamotrigine inhibits Cav2.3 (R-type) calcium currents that could also contribute to its anticonvulsant activity. This inhibition of calcium currents is also observed in topiramate.\textsuperscript{[8,9,10]}

Lamotrigine is used alone or with other medications to prevent and control seizures. It may also be used to help prevent the extreme mood swings of bipolar disorder in adults.
Lamotrigine is known as an anticonvulsant or antiepileptic drug. It is thought to work by restoring the balance of certain natural substances in the brain.\textsuperscript{6,8,11,12}

So, the objective of present work is to develop a controlled release dosage form of Lamotrigine other than oral route and injectables. Hence, a non-invasive system in the form of transdermal patch of Lamotrigine was thought to be developed and evaluated with the aim of achieving controlled release of Lamotrigine over a prolong time period so that frequency of drug administration will be minimised.\textsuperscript{13,14}

Transdermal drug delivery has certain advantages over other systems of drug administration which in turn leads to increase patient compliance. Its non-invasive nature, ease of application and removal, predetermined rate of drug permeation, increased bioavailability of drug and decreased hepatic metabolism; all these factors make this system most suitable for systemic delivery of drug over long time periods of 24hrs.

Therefore, market of transdermal patches has made tremendous growth in recent years.

**MATERIALS**
Lamotrigine was obtained from Aurobindo pharmaceutical company. Propylene glycol 400, HPMC and RSPO purchased from Himedia Laboratory, Mumbai. Eudragit RS-100 and Ethyl Cellulose was provided by the institute. All other ingredients used were of analytical grade.

**METHOD**
Technology Employed\textsuperscript{15,16}: Transdermal patch of Lamotrigine was prepared by solvent evaporation technology. In this technology, The casting solution was prepared by dissolving weighed quantities of HPMC (350, 400 and 450mg) and ethyl cellulose, Eudragit RSPO (50, 100 and 150mg) in 10 mL of methanol and chloroform mixture in ratio 1:1. To the resulting solution, 0.5% w/w of propylene glycol as plastisizer and 10% w/w penetration enhancer was added in this solution. Then drug (25 mg) was added and mixed thoroughly to form a homogeneous mixture. The casting solution was then poured into glass mould/Petri dish specially designed to seize the contents. The glass mould containing the casting solution was dried at room temperature for 24 hours in vacuum oven. The patch was removed by peeling and cut into round shape of 1 cm\textsuperscript{2}. These patches were kept in desiccators for 2 days for further drying and enclose in aluminum foil and then packed in self-sealing cover.
Table 1: Different Formulation used for Optimization TDDS.

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>Drug (mg)</th>
<th>HPMC (mg)</th>
<th>Eudragit RSPO (mg)</th>
<th>Ethyl cellulose (mg)</th>
<th>Total polymer weight (mg)</th>
<th>Propylene glycol (Plasticizer) % w/w</th>
<th>Permeation Enhancer % w/w</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>300</td>
<td>450</td>
<td>-</td>
<td>50</td>
<td>500</td>
<td>0.5</td>
<td>10</td>
</tr>
<tr>
<td>F2</td>
<td>300</td>
<td>425</td>
<td>-</td>
<td>75</td>
<td>500</td>
<td>0.5</td>
<td>10</td>
</tr>
<tr>
<td>F3</td>
<td>300</td>
<td>400</td>
<td>-</td>
<td>100</td>
<td>500</td>
<td>0.5</td>
<td>10</td>
</tr>
<tr>
<td>F4</td>
<td>300</td>
<td>450</td>
<td>50</td>
<td>-</td>
<td>500</td>
<td>0.5</td>
<td>10</td>
</tr>
<tr>
<td>F5</td>
<td>300</td>
<td>425</td>
<td>75</td>
<td>-</td>
<td>500</td>
<td>0.5</td>
<td>10</td>
</tr>
<tr>
<td>F6</td>
<td>300</td>
<td>400</td>
<td>100</td>
<td>-</td>
<td>500</td>
<td>0.5</td>
<td>10</td>
</tr>
</tbody>
</table>

Dose calculations

- Width of the plate (mould) = 5 cm
- Length of the plate (mould) = 12 cm
- No. of 2.5 x 2.5 cm patch present whole(mould) = 12
- Each film contains 25 mg of drug.
- 12 no. of films contains mg of drug? = 25×12 = 300mg
- The amount of drug added in each plate was approximately equal to 300 mg.

Characterization of transdermal patches

- The prepared transdermal patches were evaluated for the following parameters:

1) Thickness\(^{[17]}\)

Patch thickness was measured using digital micrometer screw gauge at three different places, and the mean value was calculated.

Table 2: Results of Thickness.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Formulation Code</th>
<th>Thickness (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>F1</td>
<td>85.5</td>
</tr>
<tr>
<td>2.</td>
<td>F2</td>
<td>89.5</td>
</tr>
<tr>
<td>3.</td>
<td>F3</td>
<td>93.3</td>
</tr>
<tr>
<td>4.</td>
<td>F4</td>
<td>80.1</td>
</tr>
<tr>
<td>5.</td>
<td>F5</td>
<td>83.3</td>
</tr>
<tr>
<td>6.</td>
<td>F6</td>
<td>86.4</td>
</tr>
</tbody>
</table>
Percent moisture content\(^{[18]}\)

Weighed individually the films (1cm\(^2\)) and kept them in desiccators containing calcium chloride at room temperature for at least 24 hrs. Film was weighed again; the difference in weight (initial and final weight) gives moisture content.

\[
\text{% Moisture content} = \frac{\text{Initial weight} - \text{final weight}}{\text{Initial weight}} \times 100
\]

Percent moisture uptake\(^{[18,19]}\)

Weighed individually the films and kept them in desiccator containing calcium chloride at room temperature for at least 24 hrs. remove the films from desiccators and exposed to 4% relative humidity (Rh) using saturated solution of potassium chloride in a another desiccator until a constant weight is achieved.

\[
\text{% Moisture uptake} = \frac{\text{final weight} - \text{Initial weight}}{\text{final weight}} \times 100
\]

All the formulation show lowest moisture content i.e. less than 2%. Moisture in this value is required to provide strength and flexibility to the patches. Formulations F1, F2, F3, F4, F5 and F6 were found to be contains 2.25±0.45, 2.12±0.62, 1.98±0.32, 1.36±0.45, 2.05±0.63 and 1.99±0.48\% of moisture content respectively (fig. 3-4). In all formulations formulation F4 contain minimum moisture contain 1.36±0.45.
Table 3: Results of % Moisture Content & % Moisture Uptake.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Formulation Code</th>
<th>% Moisture Content</th>
<th>% Moisture Uptake</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>F1</td>
<td>2.25±0.45</td>
<td>14.56±0.36</td>
</tr>
<tr>
<td>2.</td>
<td>F2</td>
<td>2.12±0.62</td>
<td>15.23±0.45</td>
</tr>
<tr>
<td>3.</td>
<td>F3</td>
<td>1.98±0.32</td>
<td>15.32±0.25</td>
</tr>
<tr>
<td>4.</td>
<td>F4</td>
<td>1.36±0.45</td>
<td>13.56±0.36</td>
</tr>
<tr>
<td>5.</td>
<td>F5</td>
<td>2.05±0.63</td>
<td>14.65±0.78</td>
</tr>
<tr>
<td>6.</td>
<td>F6</td>
<td>1.99±0.48</td>
<td>14.98±0.45</td>
</tr>
</tbody>
</table>

Figure 3: % Moisture content in transdermal patches.

Figure 4: % Moisture uptake in transdermal patches.

Folding endurance[^20]

This was determined by repeatedly folding one film at the same place until it broken. The number of times the film could be folded at the same place without breaking / cracking gave
the value of folding endurance. The maximum folding endurance was found 209.7±6.7 in formulation F3.

Table 4: Results of folding endurance.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Formulation Code</th>
<th>Folding Endurance (Number of fold)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>F1</td>
<td>250</td>
</tr>
<tr>
<td>2.</td>
<td>F2</td>
<td>265</td>
</tr>
<tr>
<td>3.</td>
<td>F3</td>
<td>241</td>
</tr>
<tr>
<td>4.</td>
<td>F4</td>
<td>312</td>
</tr>
<tr>
<td>5.</td>
<td>F5</td>
<td>295</td>
</tr>
<tr>
<td>6.</td>
<td>F6</td>
<td>210</td>
</tr>
</tbody>
</table>

Figure 5: Folding endurance of transdermal patches.

Tensile Strength\[24\]

The tensile strength of the patch was evaluated by using the tensiometer. It consists of two load cell grips. The lower one was fixed and upper one was movable. Film strips with dimensions of 2×2cm were fixed between these cell grips, and force was gradually applied till the film broke. The tensile strength was taken directly from the dial reading in kg.

\[
Tensile \, Strength \, (s) = \frac{Applied \, force \, (m \times g)}{Cross \, sectional \, area \,(b \times t)}
\]

Where, 
S = tensile stress
m = mass in grams
\(g\) = acceleration due to gravity
b = breadth of strip in centimeters
t = thickness of strip in centimeters

**Table 5: Results of tensile strength.**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Formulation Code</th>
<th>Tensile Strength (kg/cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>F1</td>
<td>0.989</td>
</tr>
<tr>
<td>2.</td>
<td>F2</td>
<td>0.856</td>
</tr>
<tr>
<td>3.</td>
<td>F3</td>
<td>1.145</td>
</tr>
<tr>
<td>4.</td>
<td>F4</td>
<td>1.256</td>
</tr>
<tr>
<td>5.</td>
<td>F5</td>
<td>0.852</td>
</tr>
<tr>
<td>6.</td>
<td>F6</td>
<td>0.458</td>
</tr>
</tbody>
</table>

**Figure 6: Tensile strength of transdermal patches.**

**Drug Content**\(^{25,26}\)

The patches (2.5*2.5 cm (Equivalent to 25 mg of drug) were taken into a three separate 10 ml volumetric flask and dissolved in methanol (10ml) with the help of shaker. The solution was centrifuged to separate out any particulate matter. 1mL of sample was withdrawn and transferred in volumetric flask (10 mL of capacity). The sample was dilute upto the mark with methanol and dilute suitably and analyzed by UV spectrophotometer at 222.0 nm.

The drug content was found more than 90% in all the formulations with slight fluctuation (fig. 7.6). The drug content analysis of different formulations was done according to the procedure given in section. The drug content ranged between 92.56±0.23 and 98.89±0.85. The percentage drug content of all formulations the maximum drug content was found in formulation F4, 98.89±0.85%.
Table 6: Percentage drug content of all the formulations.

<table>
<thead>
<tr>
<th>S. No</th>
<th>Formulation Code</th>
<th>% Drug Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F1</td>
<td>92.56±0.23</td>
</tr>
<tr>
<td>2</td>
<td>F2</td>
<td>94.68±0.45</td>
</tr>
<tr>
<td>3</td>
<td>F3</td>
<td>95.65±0.64</td>
</tr>
<tr>
<td>4</td>
<td>F4</td>
<td>98.89±0.85</td>
</tr>
<tr>
<td>5</td>
<td>F5</td>
<td>96.41±0.41</td>
</tr>
<tr>
<td>6</td>
<td>F6</td>
<td>97.56±0.23</td>
</tr>
</tbody>
</table>

Values are represented as mean ±SD (n=3)

Figure 7: Percent drug content of transdermal patches.

In Vitro skin permeation study[27,28,29]

The in vitro skin permeation study was carried out by using a Franz diffusion cell (receptor compartment capacity: 80 ml; area: 2.5*2.5 cm (Equivalent to 25 mg of drug). The egg membrane was separated and used for in vitro study. The receiver compartment was filled with 40 ml of phosphate buffer, pH 7.4. The Transdermal patch was firmly pressed onto the centre of the egg membrane and then the membrane was mounted on the donor compartment. The donor compartment was then placed in position such that the surface of membrane just touches the receptor fluid surface. Heat is provided using a thermostatic hot plate with a magnetic stirrer. The receptor fluid is stirred by Teflon coated magnetic bead which is placed in the diffusion cell. The temperature of receptor compartment was maintained at 37±0.5ºC.

The samples were withdrawn at different time intervals and analyzed for drug content. At the same time receptor phase was replaced with an equal volume of buffer solution at each time interval.
Release Kinetics Studies\(^{[30]}\)

- **Zero order kinetics** - Drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly (assuming that area does not change and no equilibrium conditions are obtained) can be represented by the following equation:

\[
Q_t = Q_o + k_o t
\]

Where, \(Q_t\) = amount of drug released in time ‘t’, \(Q_o\) = initial amount of drug in the solution, \(k_o\) = zero order release constant.

The pharmaceutical dosage forms following this profile, release the same amount of drug by unit of time and it is the ideal method of drug release in order to achieve a pharmacological prolonged action. This relation can be used to describe the drug dissolution of several types of modified release pharmaceutical dosage form, as in the case of some transdermal systems, as well as matrix tablets with low soluble drugs coated form, osmotic systems, etc.

- **First order kinetics** - The application of this model to drug dissolution studies was first proposed by Gibaldi and Feldman (1967). The following relation can express this model:

\[
\log Q_t = \log Q_o + k_t t/2.303
\]

Where, \(Q_t\) = amount of drug released in time ‘t’, \(Q_o\) = initial amount of drug in the solution, \(k_t\) = first order release constant. The pharmaceutical dosage forms following this dissolution profile, such as those containing water soluble drugs in porous matrices release the drug in a way that is proportional to the amount of drug remaining in its interior, in such way, that the amount of drug released by unit of time diminishes.

- **Higuchi model** - Higuchi (1961, 1963) developed several theoretical models to study the release of water soluble drugs incorporated in semisolid and/or solid matrixes. Simplified Higuchi model can be expressed by following equation:

\[
f_t = k_H t^{1/2}
\]

Where, \(k_H\) = Higuchi diffusion constant, \(f_t\) = fraction of drug dissolved in time ‘t’.

Higuchi describes drug release as a diffusion process based in the Fick’s law, square root time dependent. This relation can be used to describe the drug dissolution from several types modified release pharmaceutical dosage forms, as in the case of some transdermal systems and matrix tablets with water soluble drugs.
- **Korsmeyer-Peppas model** - Korsmeyer et al., (1983) developed a simple, semi empirical model, relating exponentially the drug release to the elapsed time (t);

\[ f_t = a t^n \]

Where, \( a \) = constant incorporating structural and geometric characteristics of the drug dosage form, \( n \) = release exponent, \( f_t = M_t/M_\infty \) = fraction release of drug.

The objectives in the developments of in-vitro diffusion study are to show the release rates and extent of drug release from dosage form. The study was carried out for 12 hr duration which was represented graphically.

**Table 7: In Vitro cumulative % drug release from optimized batch of transdermal patches F4.**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Time (Hrs.)</th>
<th>Square Root of Time</th>
<th>Log Time</th>
<th>Cumulative* Percentage Drug Release ± SD</th>
<th>Log Cumulative Percentage Drug Release</th>
<th>Cumulative Percent Drug Remaining</th>
<th>Log cumulative Percent Drug Remaining</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.5</td>
<td>0.707</td>
<td>-0.301</td>
<td>14.56±0.36</td>
<td>1.163</td>
<td>85.44</td>
<td>1.932</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>20.23±0.25</td>
<td>1.306</td>
<td>79.77</td>
<td>1.902</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>1.414</td>
<td>0.301</td>
<td>33.45±0.45</td>
<td>1.524</td>
<td>66.55</td>
<td>1.823</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>2</td>
<td>0.602</td>
<td>48.95±0.32</td>
<td>1.690</td>
<td>51.05</td>
<td>1.708</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>2.449</td>
<td>0.778</td>
<td>63.65±0.45</td>
<td>1.804</td>
<td>36.35</td>
<td>1.561</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
<td>2.828</td>
<td>0.903</td>
<td>78.98±0.28</td>
<td>1.898</td>
<td>21.02</td>
<td>1.323</td>
</tr>
<tr>
<td>7</td>
<td>10</td>
<td>3.162</td>
<td>1</td>
<td>84.85±0.69</td>
<td>1.929</td>
<td>15.15</td>
<td>1.180</td>
</tr>
<tr>
<td>8</td>
<td>12</td>
<td>3.464</td>
<td>1.079</td>
<td>93.23±0.51</td>
<td>1.970</td>
<td>6.77</td>
<td>0.831</td>
</tr>
</tbody>
</table>

*Values are represented as mean ±SD (n=3)

**Figure 8: Cumulative Percent Drug Released Vs Time (Zero Order Plots).**
7.4 Stability Studies\cite{31}

Stability studies were carried out with optimized formulation which was stored for a period of one, two and three months at 40±2°C temperature and 75±5% relative humidity for a period 3
months. The % Assay of formulation was determined by U.V. spectrophotometer using calibration curve method. The % assay was found to slightly decrease at higher temperature. Minor difference was found between evaluated parameters before and after ageing/storage and all was in acceptable limits. Therefore formulation remains stable for sufficient time.

Transdermal patch preparations were observed for any change in appearance or color for the period of 3 weeks. There was no change in appearance in formulation throughout the period of study. The stability of drug was further confirmed by spectral data and there was no change observed.

RESULTS

Preformulation of drug and excipient was performed in which physiochemical properties and other parameters of drug were studied. Physiochemical parameters such determination of solubility, melting point, $\lambda_{\text{max}}$ scan using UV-spectrophotometry, FT-IR spectrophotometry were performed in this study. The obtained data from these studies were matched with the data given in standard monographs to confirm the authenticity of procured drug.

Procured drug was odorless and white to off white in nature. In solubility study it was found that drug was freely soluble in 0.1 N HCl and 0.1 N NaOH and soluble in ethanol, methanol and phosphate buffer pH 6.8 and sparingly soluble in chloroform and water. Melting point of drug was found 216-218°C while it was 216 ºC reported in standard monograph. The pH of drug solution was found to be 7.09. The obtained FT-IR characteristic peaks of drug was matched with the peaks of drug given in standard monograph was revealed similar. Moisture content of lamotrigine was found 0.038.

The drug solution was scan on UV-spectrophotometer at 200-400 nm in wave length range to determine the maximum absorbance ($\lambda_{\text{max}}$) and it was found at 222 nm. The calibration curve was prepared in phosphate buffer pH 6.8. The regression coefficient ($R^2$) was 0.998 which was shows the linearity of curve. The line of equation for the standard curve was $y = 0.026x + 0.014$.

All the data of preformulation study was found similar as given in standard monograph which confirmed that the drug was authenticate and pure in form and it could be used for formulation development of lamotrigine loaded transdermal patches.
The lamotrigine containing transdermal drug delivery patches were formulated by casting method and were characterize on the basis of uniformity in thickness, sufficient folding endurance, tensile strength, % moisture content and uptake, drug content and drug release. The values obtained for all the formulations are given in the table. The thickness was approximately close to every formulation. It depends on polymer ratio.

Folding endurance values of all formulation more than 100 indicating good elasticity and strength. Folding endurance and tensile strength was found increase with the formulation which contains Eudragit RSPO in comparison of formulation containing the EC.

It is dependent on the polymer and humectants and plasticizer ratio. Small amount of moisture in transdermal patch is good to prevent the brittleness and also maintain the stability of formulation. If formulation content higher moisture it can lead the microbial contamination during the storage of patches. As seen in the formulation moisture content was increase with increasing the HPMC concentration.

This slight fluctuation in drug content was due to the increase or decreases the concentration of polymers. Every polymer having limit (upto saturation level) entrapped drug molecule in their matrix. After saturation it will leach out from the matrix.

The \textit{in vitro} skin permeation study was done by using a Franz diffusion cell. The temperature of receptor compartment was maintained at 37±0.5°C. The samples were withdrawn at different time intervals up to 12 hr and analyzed for drug content. Receptor phase was replaced with an equal volume of buffer solution at each time interval.

The \textit{in-vitro} permeation study was done to see the effect of polymers through the Franz diffusion cell from patch having Eudragit RSPO, HPMC and EC in different conc. to optimized formulation for in-vitro study. All the formulation was studied and all data fitted on Zero Order, First Order to explain the diffusion mechanism and pattern. The % cumulative drug release was calculated over the study time range in 0-12 hr and it was found that, all the formulation shows the matrix diffusion Pappas release kinetic.

Transdermal patch preparations were observed for any change in appearance or color for the period of 3 weeks. There was no change in appearance in formulation throughout the period of study. The stability of drug was further confirmed by spectral data and there was no change observed.
CONCLUSION
From the present work it can be concluded that Lamotrigine can be administered via matrix type transdermal drug delivery system, which provides controlled release which ultimately reduces the frequency of administration of drug in patients suffering from epilepsy and fibromyalgia. Hence this non-invasive, compatible patch with ease of application and removal may find increase patient compliance but present work required to be supported by further studies involving in-vivo pharmacodynamic and pharmacokinetic studies in animal and human models.

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