Comparative Efficiency of Propylene Glycol and Polyethylene Glycol in Enhancing Percutaneous Absorption and Release of a Drug Through Silicone Membrane and Rat Skin

Sadaf Waheed,1,2 Ghulam Murtaza,3,4 Ali Sharit,2 Rao Khurram Ayub1 and Syed Nisar Hussain Shah1
1Faculty of Pharmacy, Bahauddin Zakariya University, Multan
2Department of Pharmacy, University of Lahore, Lahore
3Department of Pharmacy, COMSATS Institute of Information Technology, Abbottabad 22060

Abstract.- The present study describes comparative efficiency of propylene glycol (PG) and polyethylene glycol (PEG) in enhancing percutaneous absorption and release of cetirizine hydrochloride (a model drug) through silicone membrane and rat skin. Various gel formulations of cetirizine HCl were prepared and optimized by using response surface methodology containing different ratios of PG(X1) and PEG(X2) taken as two independent variables whereas cumulative amount of cetirizine HCl was used to calculate dependent (response) variables (Y1 - Y7). The results showed that independent variables had remarkable effects (p < 0.05) on dependant variables. The cetirizine HCl is freely soluble in water and PBS. The value of partition coefficient (Kow) calculated is 1.91±0.03. Formulations G1-G9, G11 and G13 showed good homogeneity while formulations G10 and G12 showed comparatively good homogeneity. Formulations G2-G9 showed spreadability in a range of 3.2-4.6 cm while formulations G1 and G10-G13 showed comparatively less spreadability i.e. 2.0-2.3 cm. The pH values of the prepared gels were measured at 25±1°C which ranged between 5.8-7.2. The viscosity of all prepared gels was determined and they were found within the limits i.e. 130-138 Cps x 105. Primary skin irritation test was performed for optimized gels i.e. G4 and G6 on 11 volunteers and found no irritation or lesions. G4 and G8 possess greater values of flux ER. The values of tlag of these gels were minimum. Therefore G4 and G8 pass across the membrane in less time in comparison with other gels. Values of Kc and IR were also more prominent in G4 and G6. It was concluded that PG and PEG can be successfully used in combination as permeation enhancers for transdermal delivery of cetirizine HCl.

Keywords: Cetirizine, propylene glycol, polyethylene glycol, carbopol-934, Draize’s irritation tests, silicon membrane.

INTRODUCTION

In this experimental study, cetirizine hydrochloride has been observed as suitable drug to prepare its gel for transdermal drug delivery on the basis of its physical, chemical, and biopharmaceutical features (Khan et al., 2011a). Its molecular weight is 461.82 Daltons and value of Log P (octanol/water, pH 7.4) is 3.34. Its metabolism takes place in liver, due to which cetirizine hydrochloride is considered suitable for percutaneous delivery (Khan et al., 2010a). The literature study showed no publication regarding transdermal formulation of cetirizine hydrochloride.

Propylene glycol (PG) and polyethylene glycol (PEG) are non-corrosive compounds having very low volatility and very low toxicity (Baseer et al., 2013). The literature study showed numerous publications regarding the use of PG and PEG as excellent permeation enhancer (Shahzad et al., 2013; Khan et al., 2010b; Murtaza et al., 2009a, 2012; Rasool et al., 2011), due to which, these two enhancers (PEG and PG) were selected to study their combined permeation enhancement efficiency in cetirizine hydrochloride gels prepared in different ratios.

The mechanism of transport through a silicone membrane is comparable to that for the stratum corneum (Shahzad et al., 2013), therefore silicone membrane is selected for this permeation study.

The aim of this study was to develop thirteen batches of cetirizine hydrochloride gels using different ratios in combination of permeation enhancers i.e. PG and PEG using response surface methodology (RSM). To investigate permeation and drug release kinetics from prepared cetirizine hydrochloride gels, permeation experiments were
conducted using silicone membrane in modified Franz diffusion cells. Finally, Fick’s diffusion laws with statistical calculations were used to determine different permeation parameters and then results were compared with that of control.

MATERIALS AND METHODS

Chemicals
The chemicals used in this study viz., cetirizine hydrochloride (99.9 % purity, Hamaz Pharma, Pakistan), propylene glycol (PG) (Merck, Germany), polyethylene glycol (PEG-1000) (Fluka, Germany), methanol-HPLC grade 99% (Merck, Germany), benzyl alcohol (Merck, Germany), carbopol-934 (Merck, Germany), and menthol (Merck, Germany) were of analytical grade.

Preparation of hydro-alcoholic gels of cetirizine HCl

Hydro-alcoholic gels (20 g each) of cetirizine HCl with various concentrations of PG and PEG were formulated (Khan et al., 2011).

For the preparation of hydro-alcoholic gels of cetirizine HCl, dilution solution (water) was taken in conical flask. Then 0.2 g of cetirizine HCl was dissolved in 4.1-5.2g of distilled water and 1.3-1.7g PEG-1000 was added with continuous stirring using magnetic stirrer till completely dissolved. PG (3-7g) was taken in another conical flask and 0.5g of carbopol-934 was added to it. The stirring was continued with drop-wise addition of methanol (1.5-3.5g) till carbopol-934 became lump free, then triethanolamine (0.5 g) was added to neutralize carbopol-934. Then contents of 1st conical flask were added into 2nd conical flask under continuous magnetic stirring followed by addition of 3.5-6.5 g benzyl alcohol and ethylene glycol (0.1 g) in portions with continuous stirring. Finally, menthol (0.05g) was added for fragrance and then stored in collapsible tubes for further use (Murtaza et al., 2009b).

Preparation of calibration curve of cetirizine HCl

A carefully weighed quantity of cetirizine HCl was dissolved in distilled water in 100 ml of volumetric flask. Further dilutions (i.e. 1, 2, 3, 4, 5, 6, 7 and 8 µg/ml) were made from this stock solution (Rasool et al., 2010). The UV absorbance of resultant dilutions was measured by using UV spectrophotometer. Cetirizine HCl shows a maximum absorbance at 231 \( \lambda_{max} \). Then UV absorbance of each sample was analyzed by using UV spectrophotometer (Ermeko, Germany).

In \( Y = 0.023x + 0.155, R^2 = 0.998 \), \( x \) is concentration (µg/ml) of cetirizine HCl, \( y \) is absorbance at 231 nm and \( R^2 \) correlation coefficient.

In vitro diffusion studies through silicone membrane

For diffusion studies, Franz-type diffusion cells having diffusion area of \(~0.788cm^2\) with receptor phase volume of \(~5 ml\) were used. Silicone membrane was cut to appropriate sizes in round-shape and allowed to soak for overnight in receptor solution (distilled water). Between donor and receptor compartments, a membrane was placed. Vacuum grease was applied on the inner surfaces (collar) of two compartments to made leak proof before placing membrane. After placing donor over receptor compartment, both compartments were clamped. To remove air bubble, receptor compartment was filled with receptor fluid (distilled water) through cell arm and was degassed in an ultrasonic bath. For uniform mixing, a magnetic stirrer was placed in the receptor compartment. In order to maintain a temperature of \(~35°C\) at the membrane surface, diffusion cells were placed on a stirring bed immersed in a water bath. The receptor phase was completely removed after 1 h and pre-thermostated receptor fluid was filled again. About 1 mg of formulated gel was placed on the donor compartment. At time intervals of 15, 30, 45, 60, 90, 120, 150 and 180 min, about 0.2 ml of sample was drawn through micropipette from the receptor solution. In order to maintain sink conditions, 0.2 ml of pre-thermostated receptor fluid was added to receptor arm. At 231 nm wavelength, samples were analyzed using spectrophotometer for obtaining permeated amount through silicone membrane (Murtaza et al., 2010; Aamir et al., 2010; Ansari et al., 2010). To obtain a significant statistical data, experiments were conducted in triplicate.

In vivo diffusion studies through rat skin

Franz-type diffusion cells were used to perform diffusion studies of the different prepared
gels across rat skin. It has a receptor phase volume of ~5 ml, with diffusion area of ~0.788 cm².

Preparation of rat skin
The rat skin was carefully excised after sacrificing it. Subcutaneous fats and other extraneous tissues adhering to the dermis were completely removed and trimmed with forceps and scissor. Phosphate buffer saline at pH 7.4 was used for cleaning of skin and stored in 500 ml of normal saline in refrigerator (18-20°C) and the skin was then used within one week. Sheets of rat skin were cut to suitable sizes (~ 1 cm²) in round-shape and soaked overnight in distilled water (Murtaza et al., 2009c; Kopcha et al., 1991).

Mounting the rat skin
The rat skin was placed between two compartments of diffusion cells in such a way that its epidermis faced the donor compartment while the dermal side was bathed in distilled water (receptor fluid). The magnetic stirrer was used to mix the receptor fluid. Bubbles were removed between the underside of the skin and the solution in the receiver compartment. The membrane and the two compartments were made leak proof by the use of vacuum grease (Dow, USA) (Murtaza et al., 2011; Khan et al., 2011b,c).

Charging the Franz cell diffusion
Distilled water was filled in the receptor and donor compartments. Distilled water was degassed to remove air bubbles in an ultrasonic bath. The cell arm and the donor compartment were covered with a parafilm to avoid evaporation from compartments. A magnetic stirrer was placed in receptor compartment for constant mixing. The diffusion cells were placed on a stirring-bed immersed in a water bath at 37±2°C to maintain a temperature of ~35°C at the membrane surface. After 24 h, distilled water had been withdrawn from chambers and then pre-thermostated distilled water was again filled into the receptor compartment. During whole treatment, skin remained in contact with donor compartment. About 1 g of the gel (test solution) was placed on the donor compartment. About 0.2 ml of sample was withdrawn from receptor solution after time intervals of 15, 30, 45, 60, 90, 120, 150 and 180 min using micropipette. In order to maintain sink conditions, same volume of pre-thermostated receptor solution was added into the receptor chamber. The withdrawn samples were analyzed spectrophotometrically at 231 nm to obtain the amount permeated through rat skin (Aamir et al., 2011a,b). Experiments were conducted in triplicate to obtain a statistically significant data.

Solubility studies
An excess amount of pure cetirizine hydrochloride was added in 3 separate volumetric flasks of 25 ml containing 5 ml of solvents i.e. methanol, distilled water and phosphate buffer saline (PBS) at pH 7.4. At a constant temperature of 37±1°C for 48 h, above mixtures were stirred in a thermodynamically controlled stirrer at 4000 rpm for a time period of 30 min. After specified time, supernatant layer was taken out by a pipette and analyzed spectrophotometrically at 231 nm to determine the concentration in µg/ml (Shah et al., 2012).

Partition co-efficient (K_{o/w}) studies
A small amount of cetirizine HCl was dissolved in 10 ml of distilled water in separating funnel, shaked it for 10 min, added 10 ml of octanol and shaked vigorously for 10 min. Then the solution was allowed to stand for 24 h resulting in two layers which were separately collected in two different test tubes and analyzed by UV spectrophotometer at 231 nm and octanol to water ratio were calculated (Shah et al., 2012). Each experiment was carried out in triplicate (n=3).

Physical properties
The appearance and other physical properties, including clarity, homogeneity consistency and spreadibility of the prepared Cetirizine HCl gel were inspected (Shah et al., 2012).

Homogeneity
Through visual appearance the homogeneity of prepared gels was checked after setting in the container. In order to check the presence of aggregates the prepared gels were carefully tested (Shah et al., 2012).
Spreadability test
In order to determine the spreadibility of the prepared cetirizine HCl gels about 0.1g of the gel sample was put on the surface of the two glass slides which were of 5mm sides and made to press between them. A weight of about 1 kg was placed on the slides. The apparatus was allowed to stand for about 5 minutes. The diameters of the spreaded circles were measured in cm. Three readings were taken and take the average of three readings (Shah et al., 2012).

pH values
In order to determine the pH of cetirizine HCl gels about 1 gm of prepared gel was dissolved in 100 ml of distilled water and shaked it well and then determine the pH by using digital pH meter (WTW, pH 526, Germany). Three readings were taken and used their average values (Shah et al., 2012).

Viscosity
In order to determine viscosity, Brookfield viscometer (Model RVTDV II, Brookfield Engineering Laboratories, Inc, Stoughton, MA) was used (Shah et al., 2012).

Determination of drug content of cetirizine HCl gels
Standard solutions was prepared by dissolving and diluting 200mg of Cetirizine HCl working standard in 100 ml of 0.1M HCl in a 100 ml volumetric flask. Filter the above solution by using Whatman 42 filter paper. Discard the first part of filtrate. Add about 60-70 ml of 0.1 M HCl. Filter through the filter paper and discard the first part of filtrate. About 50 ml of 0.1M HCl was added. The absorbance of the sample and standard solution was measured at 231 nm using 0.1M HCl as a blank (Shah et al., 2012).

Ex-vivo studies (Primary skin irritation test/Draize’s skin irritation test)
In present study, 11 human volunteers were selected to perform primary test for irritation for optimized gels and a small amount of optimized gel formulation was applied on an area of 2 squares into the back of hand. The volunteers were then observed for lesions or irritation (Shah et al., 2012).

Stability studies
Stability studies were performed on the optimized gels. The formulations were packed in collapsible aluminum tubes (5g) and subjected to stability studies at 25°C / 60% RH and 300°C/65% RH for a period of three months. Samples were withdrawn after specified time was evaluated for physical appearance, rheological properties and chemical assay. Both the gels were found stable under stated storage conditions (Shah et al., 2012).

Optimization data analysis
In present study Design Expert® software version 8.0.1 having numerous RSM calculations was used in order to optimize the study. Multiple linear regression analysis (MLRA) approach was used for all the response variables in various polynomial models consisting of interaction and quadratic terms. MLRA model contains the following general equation.

\[ Y = b_0 + b_1X_1 + b_2X_2 + b_{12}X_1X_2 + b_{11}X_1^2 + b_{22}X_2^2 \]

Where, \( b_0 \) = intercept representing the arithmetic average of all quantitative results of 13 runs, \( b_0, b_2, b_{12}, b_{11}, \) and \( b_{22} \) are the coefficients calculated from the observed experimental response values of \( Y \), while \( X_1 \) and \( X_2 \) are called the coded levels of the independent variables. Two-dimensional contour plots were also plotted based on the model polynomial functions in order to see interaction effects of the factors on responses.

The effect of enhancers on various responses i.e. \( t_{lag} (Y_1) \), flux \( (Y_2) \), \( D \) \( (Y_3) \), permeability coefficient \( (K_p, Y_4) \), \( K \) \( (Y_5) \), enhancement ratio \( (ER, Y_6) \), and Input Rate \( (IR, Y_7) \) is presented in below mentioned polynomial equations:

\[ t_{lag} = 33.49 - 0.69X_1 + 0.17X_2 - 3.175X_1X_2 + 0.712X_1^2 - 2.125X_2^2 \]
\[ J = 11.49 + 0.15X_1 + 0.25X_2 + 0.30X_1X_2 + 0.05X_1^2 + 0.15X_2^2 \]
\[ D = 4.31 \times 10^{-4} + 8.667 \times 10^{-5}X_1 + 6.33 \times 10^{-5}X_2 + 1.0 \times 10^{-5}X_1X_2 + 1.98 \times 10^{-7}X_1^2 + 2.69 \times 10^{-7}X_2^2 \]
The viscosity of all prepared gels was within the limits \( i.e. \) 130-138 Cps \( \times 10^{3} \).

In vitro diffusion studies through silicone membrane

Table I illustrates the cumulative amount of cetirizine HCl permeated via silicone membrane using various formulations. In the presence of PG and PEG, there was significant difference (\( P<0.05 \)) between the cumulative amount of cetirizine HCl permeated through silicone membrane. The synergism was observed in the permeation enhancement effect of PG and PEG across this artificial membrane possibly due to occupation of hydrogen bonding sites of membrane and their solublization effect (Shah et al., 2013b). Moreover, there was a direct effect of PG and PEG concentration on the permeation of cetirizine HCl. Similar results have already been presented in previous publication (Shah et al., 2013a). Table II describes various permeation kinetic parameters of cetirizine HCl Gel. Table II shows that G4 and G8 possess greater values of flux (12.10±0.02 \( \mu g/cm^2/min \)) and 12.12±0.01 \( \mu g/cm^2/min \), respectively) and ER (1.52 of both formulations). The values of \( t_{lag} \) (22.71±0.13min and 21.74±0.19min, respectively) of these gels were minimum. Therefore G4 and G8 pass across the membrane in less time in comparison with other gels. Values of \( K_p \) and I/R were also more prominent in G4 and G8. By considering these features both the gels G4 and G8 are selected for further analysis for in vitro rat skin permeation studies to validate our results.

In vitro permeation studies across rat skin

In order to conduct in-vitro permeation studies of optimized formulated gels of cetirizine HCl across rat skin, G8 was used which has maximum flux values in silicone membrane studies (Table II). Flux values and all other permeation parameters through rat skin were also calculated by method explained earlier. Factor of difference (FoD) of permeation studies of cetirizine HCl across rat skin vs. silicone membrane shows that the flux values determined by using silicone membrane (SM) were in the same order of magnitude as that of flux values calculated with rat skin or/and human epidermis for permeation up to 3 h study.

\[
\begin{align*}
K_p &= 1.156 \times 10^{-3} + 1.91 \times 10^{-3} X_1 + 1.75 \times 10^{-3} X_1 \times X_2 + 1.75 \times 10^{-3} X_2 + 5.99 \times 10^{-4} X_3 + 9.89 \times 10^{-3} X_1^2 + 3.82 \times 10^{-3} X_2^2 + 2.24 \times 10^{-3} X_3^2 \\
K &= 0.024 + 8.5 \times 10^{-4} X_1^3 + 2.033 \times 10^{-3} X_1^2 + 1.20 \times 10^{-3} X_1 + 3.58 \times 10^{-3} X_2^3 + 2.244 \times 10^{-3} X_2^2 + 1.44 \times 10^{-3} X_3^2 \\
\text{ER} &= 1.46 + 6.91 \times 10^{-3} X_1 + 0.022 X_1 \times X_2 - 4.84 \times 10^{-3} X_1^2 + 9.91 \times 10^{-3} X_2^2 + 1.91 \times 10^{-2} X_3^2 \\
\text{IR} &= 9.20 - 0.29 X_1 + 0.14 X_2 - 0.20 X_1 \times X_2 - 0.26 X_1^2 + 5.93 \times 10^{-3} X_2^2
\end{align*}
\]

**RESULTS AND DISCUSSION**

Physical properties of cetirizine HCl

The solubility (\( \mu g/ml \)) of cetirizine HCl was 24347, 19913 and 0.12 in water, PBS and methanol, respectively. The cetirizine HCl is freely soluble in water and PBS whereas sparingly soluble in methanol.

The partition coefficient (\( K_{o/w} \)) is 1.91±0.03.

The formulations G1-G11 were transparent, while G12 and G13 were comparatively less transparent. Formulations G1-G9, G11 and G13 showed good homogeneity, while formulations G10 and G12 showed comparatively less homogeneity. Formulations G2-G9 showed spreadability in a range of 3.2-4.6 cm while formulations G1 and G10-G13 showed comparatively less spreadability \( i.e. \) 2.0-2.3 cm.

The pH values of the prepared gels at 25±1°C ranged between 5.8-7.2.

Statistical data analysis

In present study, SPSS version 17.0 was used to analyze statistical data. Regression analysis and analysis of variance (ANOVA) with \( p<0.05 \) as a minimal level of significance were used to determine statistically significant difference between 13 different formulations.

Response surface methodology (RSM) having polynomial equation was used to optimize results and to check the effects of response variables on drug permeation. As per standard protocol, a central composite design (CCD) with \( \alpha=2 \) was used. PG and PEG were used as permeation enhancers and their effect on the response variables were observed. The central point (0, 0) was studied in quintuplicate. All other formulation and process variables were kept unchanged throughout the study.
testing for three months as per

strong effect. Thus this animal model and silicone

c is no direct relation between the permeation of

From the abo

values and physiochemical properties in this study.

Table II.

Permeation kinetic parameters of different gels of cetirizine HCl

<table>
<thead>
<tr>
<th>Trial no.</th>
<th>$t_{lag}$ (min)</th>
<th>J($µg/cm^2/min$)±SD</th>
<th>$D_2$($10^{-4}$) (cm/$min$)</th>
<th>$K$ ($Y_4$)±SD</th>
<th>$K_p$($10^{-5}$) (cm/$min$)</th>
<th>IR($µg/min$) ($Y_7$)±SD</th>
<th>ER ($Y_8$)±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>23.6±1.0</td>
<td>11.32±0.27</td>
<td>3.04±0.00</td>
<td>0.03±0.00</td>
<td>1.13±0.21</td>
<td>8.91±0.21</td>
<td>1.42</td>
</tr>
<tr>
<td>G2</td>
<td>22.7±1.89</td>
<td>11.62±0.07</td>
<td>3.00±0.00</td>
<td>0.03±0.00</td>
<td>1.16±0.00</td>
<td>8.95±0.05</td>
<td>1.45</td>
</tr>
<tr>
<td>G3</td>
<td>28.41±4.50</td>
<td>11.10±0.19</td>
<td>3.60±0.00</td>
<td>0.03±0.00</td>
<td>1.11±0.00</td>
<td>8.75±0.15</td>
<td>1.39</td>
</tr>
<tr>
<td>G4</td>
<td>22.71±0.13</td>
<td>12.10±0.02</td>
<td>3.00±0.00</td>
<td>0.03±0.00</td>
<td>1.21±0.00</td>
<td>9.54±0.01</td>
<td>1.52</td>
</tr>
<tr>
<td>G5</td>
<td>35.5±0.96</td>
<td>11.62±0.10</td>
<td>3.04±0.00</td>
<td>0.02±0.00</td>
<td>1.16±0.00</td>
<td>9.16±0.08</td>
<td>1.46</td>
</tr>
<tr>
<td>G6</td>
<td>38.8±0.05</td>
<td>11.30±0.03</td>
<td>6.02±0.00</td>
<td>0.01±0.00</td>
<td>1.21±0.00</td>
<td>7.02±0.02</td>
<td>1.42</td>
</tr>
<tr>
<td>G7</td>
<td>30.71±0.18</td>
<td>11.22±0.01</td>
<td>4.02±0.00</td>
<td>0.02±0.00</td>
<td>1.12±0.00</td>
<td>8.85±0.009</td>
<td>1.41</td>
</tr>
<tr>
<td>G8</td>
<td>21.74±0.19</td>
<td>12.12±0.01</td>
<td>3.02±0.00</td>
<td>0.03±0.00</td>
<td>1.21±0.00</td>
<td>9.50±0.01</td>
<td>1.52</td>
</tr>
<tr>
<td>G9</td>
<td>32.9±0.34</td>
<td>11.71±0.01</td>
<td>4.24±0.00</td>
<td>0.02±0.00</td>
<td>1.17±0.00</td>
<td>9.24±0.01</td>
<td>1.47</td>
</tr>
<tr>
<td>G10</td>
<td>40.68±9.3</td>
<td>11.22±0.91</td>
<td>5.00±0.00</td>
<td>0.02±0.00</td>
<td>1.12±0.00</td>
<td>8.85±0.72</td>
<td>1.41</td>
</tr>
<tr>
<td>G11</td>
<td>35.51±0.16</td>
<td>11.61±0.005</td>
<td>5.10±0.00</td>
<td>0.02±0.00</td>
<td>1.16±0.00</td>
<td>9.15±0.004</td>
<td>1.46</td>
</tr>
<tr>
<td>G12</td>
<td>30.9±0.85</td>
<td>11.80±0.03</td>
<td>4.01±0.00</td>
<td>0.03±0.00</td>
<td>1.18±0.00</td>
<td>9.34±0.02</td>
<td>1.48</td>
</tr>
<tr>
<td>G13</td>
<td>33.5±0.48</td>
<td>11.71±0.02</td>
<td>4.32±0.00</td>
<td>0.02±0.00</td>
<td>1.17±0.00</td>
<td>9.22±0.01</td>
<td>1.47</td>
</tr>
</tbody>
</table>

using optimized G8 having high flux values in silicone membrane studies. The factor of difference value (FoD) of G8 across rat skin and silicone membrane at 37°C±1 was 0.03 with $J_{RS}$ ($µg/cm^2$) and $J_{SM}$ ($µg/cm^2$) as 11.97 and 12.0, respectively.

There is no relationship between the FoD values and physiochemical properties in this study. From the above results it can be suggested that there is no direct relation between the permeation of cetirizine HCl across both the rat skin and silicone membrane, rather it confirms that it possesses a strong effect. Thus this animal model and silicone membrane gives us a prediction that cetirizine HCl may permeate through human membrane.

Draize skin irritation test

Primary skin irritation test for optimized gels i.e. G4 and G8 did not produce any irritation or lesions on 11 volunteers.

Stability studies

The optimized gels G4 and G8 were allowed to stand for stability testing for three months as per ICH norms at a temperature of 25 ± 1°C. The
optimized selected cetirizine HCl gels were analyzed for the change in their appearance (C & T), pH and drug content. No change in appearance and pH was observed for both formulations. There was non-significant (P>0.05) reduction (from 98.57% to 97.52% for G4 and from 98.92% to 97.65% for G8) in drug contents (%) of both formulations during this period of study.

**CONCLUSION**

It was concluded that PG and PEG can be successfully used in combination as permeation enhancers for transdermal delivery of cetirizine HCl.

**REFERENCES**


RASOOL, R., AHMAD, M., MURTAZA, G., KHAN, H.M.S. AND KHAN, S.A., 2011. Comparative dissolution study of metoprolol tartrate loaded PLGA (50:50) and...


(Received 22 October 2013, revised 13 November 2013)