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# FORMULATION AND EVALUATION OF VORICONAZOLE TRANSFEROSOMAL GEL

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## ABSTRACT

The aim of this research work is to develop voriconazole Transferosomal gel for better transdermal permeation and to produce sustained release of drug for local antifungal activity. Voriconazole is a triazole antifungal drug. It is used orally and intravenously. Formulation of voriconazole as transferosomal gel reduces dose dumping and increases therapeutic efficacy. Transferosomes are appropriate delivery system for skin. They are ultra-deformable vesicles. Voriconazole transferosomes were prepared by Thin Film Hydration method using Phosphatidylcholine and Edge Activators in different ratios. The edge activators used in the formulation are Span 60, Span 80 and Tween 80. The prepared transferosomes were evaluated for entrapment efficiency, drug content and in vitro drug release. Formulation F3 containing phosphatidylcholine (85mg) and Span 60 (15mg) was selected based on entrapment efficiency and drug release. Entrapment efficiency and drug release was 87.62±0.26 and 82.52±0.35. The selected formulation shows Zeta potential of -57.7mV and vesicle size of 597.4nm. The selected formulation F3 was incorporated into gel using Carbopol 934 of different concentrations. Formulated gels were evaluated for visual appearance, pH, drug content and *In vitro* diffusion studies. The selected transferosomal gel of voriconazole shows pH value 6.7, drug content 91.56 and drug release percentage 79.54

**KEYWORDS**: Transferosomes, voriconazole, phosphatidylcholine, Edge Activator, Carbopol 934.

## 1. INTRODUTION

Conventional drug delivery system plays a prominent role among all the other routes of drug delivery system. By conventional route some drugs may show low bioavailability due to incomplete absorption or first pass metabolism. The conventional dosage forms provide drug release immediately and it cause fluctuation of drug level in blood depending upon dosage form. Therefore, to maintain the drug concentration within therapeutically effective range need vesicular drug delivery system. Vesicles are colloidal particles with a concentric bilayer made-up of amphiphilic molecules surrounds an aqueous compartment. They act as very good carriers for delivery of both hydrophilic and hydrophobic drugs. Hydrophobic drugs are encapsulated inside the lipid bilayer whereas the hydrophilic drugs are encapsulated in the interior aqueous compartment. Vesicular drug delivery systems delay drug elimination of rapidly metabolizable drugs and function as sustained release system. It provides a capable technique for delivery to the site of infection, leading to decrease of drug toxicity with no adverse effects. Vesicular drug deliveries reduce the cost of therapy by enhanced bioavailability of medication, mainly in case of poorly soluble drugs (Talegaonkar, S., et al., 2006).

Transdermal drug delivery system can deliver medicines via the skin to systemic circulation at a predetermined rate and controlled rate. Transdermal drug delivery system offers many advantages over conventional dosage forms. It enhances patient compliance and minimizes harmful side effects of a drug caused from temporary overdose. The main disadvantage of transdermal drug delivery is the poor permeation of most compounds across the skin. Several approaches have been developed to weaken this skin barrier. One of the approaches for increasing the skin permeation of drugs is the use of vesicular systems. Transferosomes are specially optimized, ultra-deformable lipid supra molecular aggregate, this gives better penetration of intact vesicles. Due to their flexibility, transferosomes are good candidates for the non-invasive delivery of small, medium, and large sized drugs. Transferosomes mainly composed of phospholipids like phosphatidyl choline, Soya lecithin, Dipalmitoyl phosphatidyl choline which self assembles into lipid bilayer in aqueous environment and closes to form a vesicle. The main components in transferosome are phospholipids and edge activator. Edge activator consists of single chain surfactant that causes destabilization of the lipid bilayer and increases elasticity of the bilayers. Transferosomes are suitable in delivering the low molecular weight and as well as high molecular weight drugs through skin. (Prudvi Kanth 2013).

Due to their more elasticity as comparing to standard liposomes, Transferosomes are well suited for the skin permeation. Transferosomes were developed in order to take the advantage of phospholipids vesicles as transdermal drug carrier. Transferosomes overcome the skin penetration difficulty by squeezing themselves along the intracellular sealing lipid of the stratum corneum (Prasurjya et al, 2013).

Drug voriconazole is an antifungal agent. It is used in the treatment of local and systemic fungal infection. Marketed formulations of voriconazole available are oral tablets, oral suspensions and intravenous injections.

## MATERIALS AND METHODS

Voriconazole was obtained as a gift sample from Chemo pharma Laboratories Pvt.Ltd Hyderabad Telangana. Phosphatidyl Choline was obtained as a gift sample from Aurobindo laboratories, Hyderabad. Span 80, span 60, tween 80 were obtained from SD fine chem.Ltd, India. Carbopol 943 was obtained from NR CHEM, India. Chloroform, methanol were obtained from SD fine chemicals, Mumbai.

**Preparation of transferosomes:** Voriconazole transferosomes were prepared by thin film hydration technique. Phosphatidyl choline, surfactant and drug were dissolved in 15ml of chloroform and methanol in a 100ml round bottom flask. The flask was attached to a rotary evaporator (Superfit, India) immersed in $60^0$C water bath and rotated under vacuum. This process was continued until all the solvent is evaporated and lipid film was deposited on the walls of the flask. The flask was left in vacuum desiccator overnight to ensure complete removal of residual solvent.

Phosphate Buffer pH 6.8 was added to the dried film and rotated under similar conditions of rotary vacuum evaporation for another 30 minutes till the lipid film is completely hydrated. The flask is removed and the transferosomes were transferred to a container and subjected to sonication in a bath sonicator for 15 minutes.

**Table 1: Composition of Transferosomes.**

| Formulation code | Drug (mg) | Edge activator (mg) | Phosphatidylcholine (mg) | Solvent(ml) Chloroform: methanol (2:1) |
|---|---|---|---|---|
| **SPAN 60** | | | | |
| F-1 | 50 | 5 | 95 | 15 |
| F-2 | 50 | 10 | 90 | 15 |
| F-3 | 50 | 15 | 85 | 15 |
| F-4 | 50 | 20 | 80 | 15 |
| F-5 | 50 | 25 | 75 | 15 |
| **SPAN 80** | | | | |
| F-6 | 50 | 5 | 95 | 15 |
| F-7 | 50 | 10 | 90 | 15 |
| F-8 | 50 | 15 | 85 | 15 |
| F-9 | 50 | 20 | 80 | 15 |
| F-10 | 50 | 25 | 75 | 15 |
| **TWEEN 80** | | | | |
| F-11 | 50 | 5 | 95 | 15 |
| F-12 | 50 | 10 | 90 | 15 |
| F-13 | 50 | 15 | 85 | 15 |
| F-14 | 50 | 20 | 80 | 15 |
| F-15 | 50 | 25 | 75 | 15 |

### Evaluation of transferosomes

**Entrapment Efficiency (EE):** Entrapment Efficiency of Voriconazole transferosomal vesicles were determined by centrifugation method. The vesicles were separated in a high-speed centrifuge at 3000rpm for 40 minutes. The sediment and supernatant liquids were separated. Amount of the drug in the supernatant was determined. It was then diluted appropriately and estimated using UV. Visible Spectrophotometer at 253nm. From this,the entrapment efficiency was determined using following formula.

$$\% \text{ Entrapment Efficiency} = \frac{Total\ Drug - free\ drug}{Total\ Drug} \times 100$$

***In-Vitro* drug release studies:** *In-vitro* drug release studies were performed using modified diffusion apparatus using pH 6.8 buffer as a diffusion medium. The cellophane membrane (previously soaked overnight in the buffer) was tied to one end of a specially designed glass cylinder (open at both ends) having inner diameter membrane of 3.4cm. 2ml of formulation was placed into the glass cylinder known as donar chamber. The cylinder was suspended in a beaker (receptor chamber) containing 200ml of diffusion medium so that the membrane just touches the surface of the medium. Receptor chamber was maintained at a temperature of 37 ± $2^0$ C with a stirring rate of 50 rpm using magnetic stirrer. About 3 ml of sample was withdrawn at a time interval of 1 hour and

replaced with an equal volume of fresh diffusion medium. The aliquots were diluted with the diffusion medium and analysed at 253nm using UV spectrophotometer.

**Characterization of transferosomes**

**Surface Morphology:** The surface morphology was determined using Scanning Eletron Microscopy (SEM). SEM gives a three dimensional (3-D) image of globules.One drop of transferosomal suspension was mounted on a clear glass stub. It is then aidried and gold coated using sodium auro thiomalate to visualize under SEM.

**Zeta Potential:** Zeta potential was determined using zetasizer (HORIBA SZ-100). The Zeta potential is a key indicator of stability of colloidal dispersions. The magnitude of Zeta potential indicates the degree of electrostatic repulsion between adjacent, similarly charged particles in dispersion.

**Formulation of Transferosomal gel**

Voriconazole transferosomal gels were prepared by dispersion method using Carbopol 934 in different ratios as shown in the table. Gels were prepared by dispersing the gelling agent in the transfersomal suspension. Then the mixture is allowed to swell overnight.

**Table 2: Composition of Transferosomal Gel.**

| Formulation code | Transferosomal Suspension(ml) | Carbopol concentration (%) | Propylene Glycol (ml) | Triethanolamine (%v/v) |
|---|---|---|---|---|
| TG – 1 | 10 | 0.5 | 5 | 0.5 |
| TG – 2 | 10 | 1 | 5 | 0.5 |
| TG – 3 | 10 | 1.5 | 5 | 0.5 |

**Evaluation of Transferosomal Gel**

**Visual Appearance:** The formulations were tested for its physico-rheological properties like colour, odour, texture and feel upon application.

**pH:** pH was checked using pH meter (Systronics digital pH meter). The electrode was submersed into the formulation at room temperature and the readings were noted.

**Drug content:** 1gm of gel was taken and dissolved in methanol and filtered. The volume was made to 100ml with methanol. The resultant solution was analysed by U.V Spectrophotometer.

***In-Vitro* drug release studies:** *In-vitro* drug release studies were performed using modified diffusion apparatus using pH 6.8 buffer as a diffusion medium. The cellophane membrane (previously soaked overnight in the buffer) was tied to one end of a specially designed glass cylinder (open at both ends) having inner diameter membrane of 3.4cm. 2ml of formulation was placed into the glass cylinder known as donar chamber. The cylinder was suspended in a beaker (receptor chamber) containing 200ml of diffusion medium so that the membrane just touches the surface of the medium. Receptor chamber was maintained at a temperature of 37 ± $2^0$ C with a stirring rate of 50 rpm using magnetic stirrer. About 3 ml of sample was withdrawn at a time interval of 1 hour and replaced with an equal volume of fresh diffusion medium. The aliquots were diluted with the diffusion medium and analysed at 253nm using UV spectrophotometer.

**Stability Studies:** The stability studies of the developed transferosomal formulations were performed according to the ICH guidelines. The best selected formulations were carried out for 3 months at two different temperature i.e., refrigerator condition (4-8$^0$C) and room temperature (25 ± $2^0$C). Samples were observed and checked for the percentage drug content.

## RESULTS AND DISCUSSION

**Melting point determination**

The melting point of Voriconazole was determined by capillary tube method. The result obtained indicated the melting point to be **128°c.**

Certificate of analysis indicated the melting point of voriconazole as **127 - 130 °C.** Hence the drug is pure.

**Determination of absorption maxima of voriconazole in Phosphate Buffer pH 6.8**

10µg/ml of voriconazole was scanned in UV range of 200 – 400nm using UV Visible double beam Spectrophotometer. The spectrum obtained is indicated in fig.1.

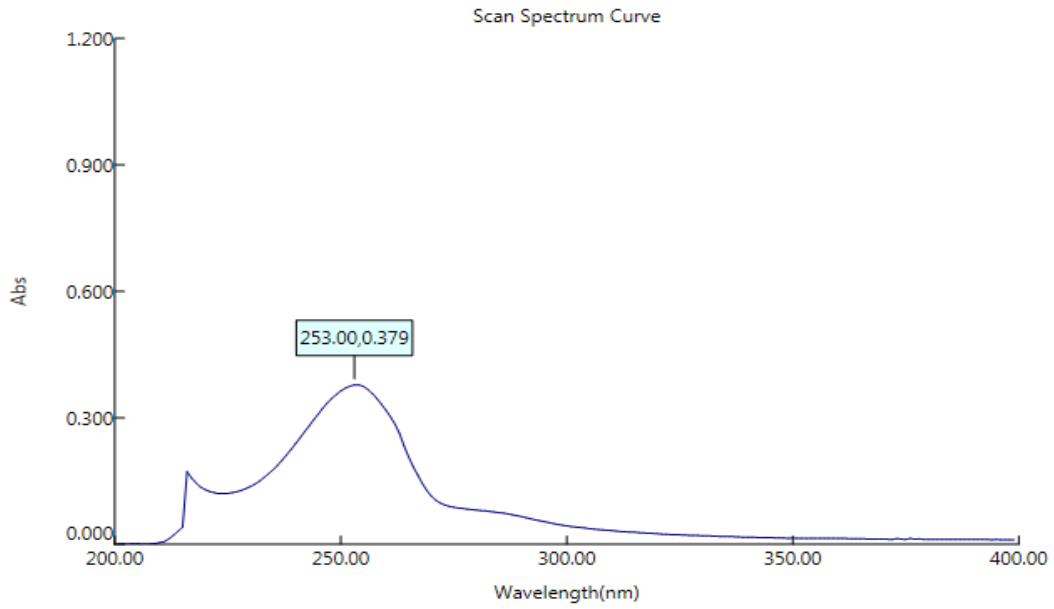


**Figure 1: UV Absorption spectrum of 10 µg/ml voriconazole in PH 6.8 buffer.**

The absorption maxima of voriconazole was found to be 253nm with an absorbance of 0.379.

**Preparation of standard graph of voriconazole in Phosphate Buffer pH 6.8**

Dilute solutions of 5,10,15,20 and 25 µg/ml were scanned for absorbance in a UV Visible Spectrophotometer at wavelength 253nm using 6.8 pH Phosphate buffer as a blank. A standard graph was plotted taking concentration on x-axis and absorbance on y-axis. The absorbance data obtained is indicated in Table 3 and the graph in fig 2.

**Table 3: Absorbances of Voriconazole at various concentrations in 6.8 pH Phosphate buffer.**

| S. NO | Concentration (µg/ml) | Absorbance (mean± S.D, n=3) |
|---|---|---|
| 1 | 5 | 0.197±0.03 |
| 2 | 10 | 0.366±0.04 |
| 3 | 15 | 0.541±0.02 |
| 4 | 20 | 0.731±0.03 |
| 5 | 25 | 0.963±0.02 |

*n=3 results are mean of triplicate reading

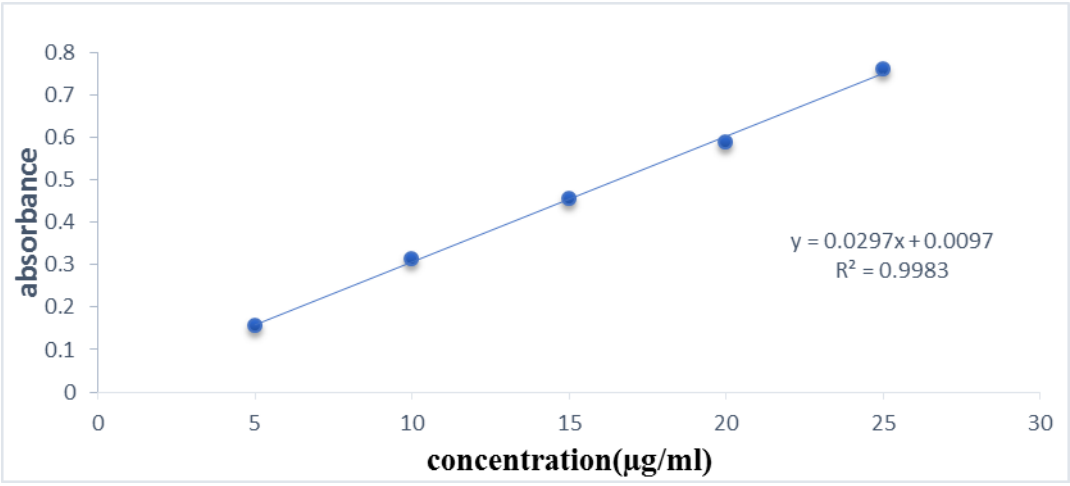


**Figure 2: Standard graph of Voriconazole in 6.8 pH phosphate Buffer.**

**Table 4: Regression analysis of Standard graph of voriconazole in 6.8 pH phosphate Buffer.**

| S. No | Parameters | Result |
|---|---|---|
| 1 | Regression equation | y = 0.0297x + 0.0097 |
| 2 | Correlation coefficient | $R^2$ = 0.9983 |
| 3 | Calibration range | 5 to 25 µg/ml |

$R^2$ value of 0.9983 indicates that the relationship between concentration and absorbance is fairly linear.

**Entrapment efficiency:** Entrapment efficiency was determined by centrifugation method. The entrapment efficiency was found to be higher for the formulations F2 and F3 containing phosphatidylcholine: span60 in the ratios 90:10 and 85:15 respectively. At this concentration phosphatidyl choline increases hydrophobicity of the bilayer and improves stability. The length of the alkyl chain influences the hydrophilic lipophilic balance (HLB value) of the surfactant. Higher the HLB value of the surfactant, the entrapment efficiency of the formulation increases. (HLB-span60-4.7, span80-4.3, tween80-15.0).

**Table 5: Entrapment efficiency of voriconazole transferosomes.**

| Formulation code | Entrapment efficiency (%) | Formulation code | Entrapment efficiency | Formulation code | Entrapment efficiency (%) |
|---|---|---|---|---|---|
| F-1 | 76.38 ± 0.22 | F-6 | 66.28 ± 0.33 | F-11 | 71.53±0.39 |
| **F-2** | **81.14 ± 0.47** | F-7 | 69.35 ±0.67 | F-12 | 74.31±0.52 |
| **F-3** | **87.62 ± 0.26** | F-8 | 73.61 ±0.46 | F-13 | 79.46±0.31 |
| F-4 | 79.48 ± 0.32 | F-9 | 80.57 ±0.67 | F-14 | 76.18±0.27 |
| F-5 | 73.61 ± 0.19 | F-10 | 71.72 ± 0.29 | F-15 | 71.26±0.54 |

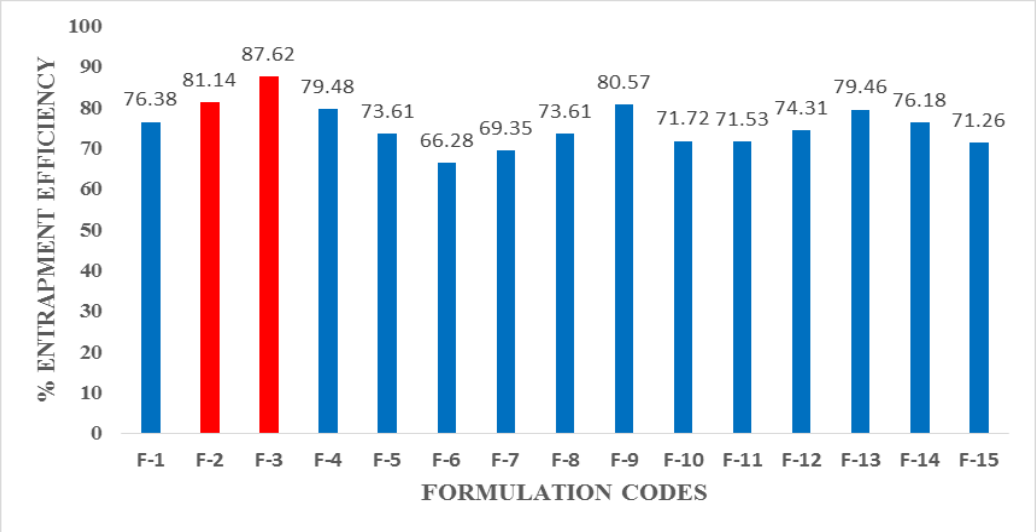


**Figure 3: Entrapment efficiency of voriconazole transferosomes.**

***In-Vitro* Drug release studies**

Percentage drug release from F-1 to F- 15 are shown in the tables 6 to 9 and the release profiles of the formulations are represented in the Figures 4 to 6.

**Table 6: Percentage drug release of the formulations F – 1 to F – 5.**

| Time (Hrs) | DR of F-1±SD (n=3) | % DR of F-2±SD (n=3) | % DR of F -3 ± SD (n=3) | % DR of F - 4 ± SD (n=3) | % DR of F -5± SD (n=3) |
|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 11.48± 0.17 | 10.49 ± 0.25 | 12.36 ± 0.18 | 10.23 ± 0.32 | 9.67 ± 0.42 |
| 2 | 19.63± 0.54 | 18.49± 0.12 | 21.76 ± 0.29 | 17.96 ± 0.25 | 17.13 ± 0.23 |
| 3 | 27.38± 0.26 | 26.74 ± 0.31 | 29.78 ± 0.23 | 26.53 ± 0.11 | 26.97 ± 0.16 |
| 4 | 39.86 ± 0.24 | 38.43 ± 0.26 | 41.31 ± 0.51 | 38.97 ± 0.53 | 37.36 ± 0.51 |
| 5 | 47.79 ± 0.32 | 46.89 ± 0.21 | 48.94 ± 0.43 | 46.35 ± 0. 47 | 44.76 ± 0.43 |
| 6 | 56.37 ± 0.42 | 54.42 ± 0.47 | 57.98 ± 0.31 | 55.87 ± 0.62 | 53.42 ± 0.38 |
| 7 | 68.38 ± 0.36 | 66.84 ± 0.54 | 69.85 ± 0.64 | 65.78 ± 0.45 | 64.13 ± 0.68 |
| 8 | 74.84± 0.43 | 72.73 ± 0.19 | 82.52 ± 0.35 | 71.56 ± 0.73 | 68.75 ±0.78 |

*n=3 results are mean of triplicate reading

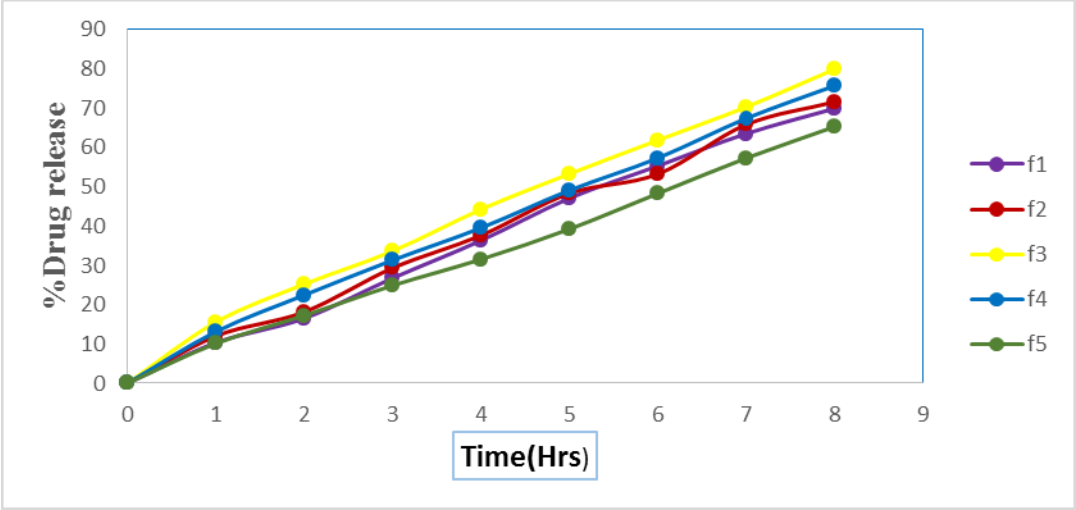


**Figure 4: Drug release profiles of formulations F-1 to F-5.**

The experimental data indicated that formulation F-3 showed higher percentage drug release of 78.52±0.35 in 8 hours respectively.

**Table 7: Percentage drug release of the formulations F – 6 to F – 10.**

| Time (Hrs) | % DR of F -6± SD | % DR of F -7 ± SD | % DR of F -8± SD | % DR of F - 9± SD | % DR of F -10± SD |
|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 9.73±0.30 | 10.23±0.14 | 11.56±0.26 | 12.78±0.22 | 10.12±0.18 |
| 2 | 16.64±0.11 | 17.56±0.32 | 20.87±0.15 | 22.39±0.30 | 16.98±0.31 |
| 3 | 25.85±0.47 | 26.74±0.25 | 29.78±0.30 | 32.52±0.15 | 26.14±0.29 |
| 4 | 36.86±0.23 | 38.43±0.30 | 41.31±0.26 | 42.31±0.12 | 36.78±0.14 |
| 5 | 47.79±0.52 | 46.89±0.62 | 48.97±0.49 | 51.13±0.25 | 44.76±0.42 |
| 6 | 56.37±0.18 | 54.43±0.44 | 57.98±0.32 | 58.63±0.37 | 53.42±0.61 |
| 7 | 68.38±0.26 | 66.84±0.56 | 69.85±0.55 | 69.85±0.49 | 64.13±0.17 |
| 8 | 74.84±0.19 | 72.73±0.23 | 74.36±0.31 | 76.23±0.34 | 68.75±0.54 |

*n=3 results are mean of triplicate reading

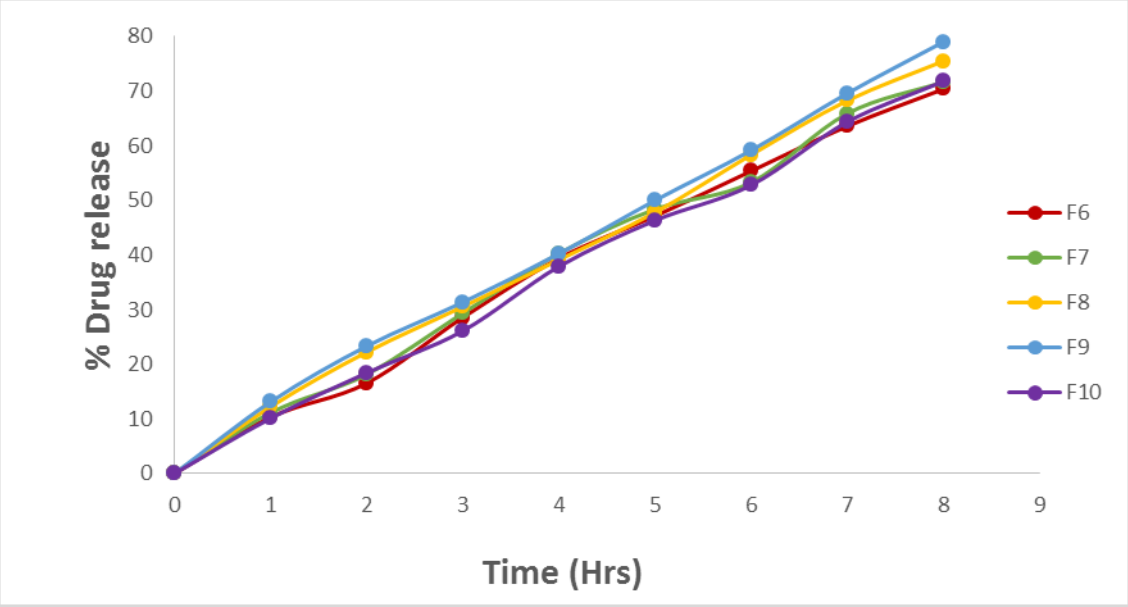


**Figure 5: Drug release profiles of formulations F-6 to F-10.**

The experimental data indicated that formulation F-9 showed higher percentage drug release of 76.29±0.35 in 8 hours respectively.

**Table 8: Percentage drug release of the formulations F – 11 to F – 15.**

| Time (Hrs) | % DR of F -11± SD | % DR of F -12 ± SD | % DR of F -13 ± SD | % DR of F - 14 ± SD | % DR of F -15± SD |
|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 9.45±0.22 | 11.341±0.31 | 12.65±0.31 | 11,12±0.26 | 10.43±0.20 |
| 2 | 18.45±0.50 | 20.23±0.24 | 21.12±0.18 | 19.56±0.35 | 18.34±0.33 |
| 3 | 26.56±0.36 | 28.12±0.19 | 29.34±0.46 | 25.87±0.37 | 25.33±0.19 |
| 4 | 36.23±0.26 | 38.34±0.44 | 39.54±0.35 | 36.14±0.15 | 35.34±0.41 |
| 5 | 46.23±0.47 | 48.12±0.15 | 49.32±0.61 | 46.23±0.48 | 45.89±0.28 |
| 6 | 54.12±0.21 | 55.17±0.27 | 56.43±0.39 | 54.65±0.31 | 54.12±0.53 |
| 7 | 64.23±0.36 | 66.45±0.59 | 68.65±0.25 | 64.12±0.75 | 63.34±0.36 |
| 8 | 68.23±0.40 | 70.89±0.43 | 72.54±0.58 | 69.34±0.46 | 69.14±0.24 |

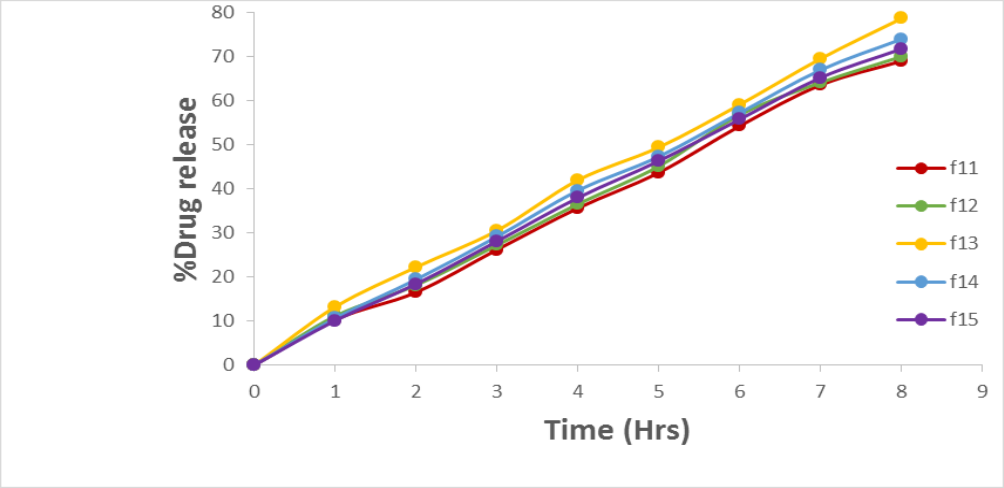


**Figure 6: Drug release profiles of formulations F-11 to F-15.**

The experimental data indicated that formulation F-13 showed higher percentage drug release of 72.54±0.58 in 8 hours respectively. Out of all the formulations, formulation F-3 exhibited more drug release than the other formulations.

**Visual microscopy**

A drop of voriconazole transferosomal suspension was placed on the glass slide and observed under optical microscope**.**

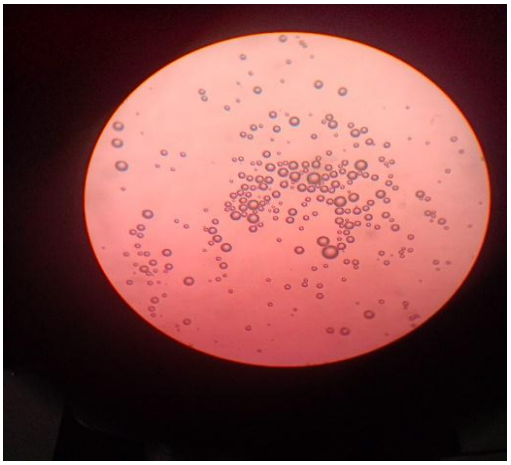

**Figure 7: Microscopic Image of voriconazole transferosomes(F3).**

**Scanning electron microscopy**

Determination of vesicle shape and surface morphology was done using scanning electron microscope. The SEM image is shown in figure 8.

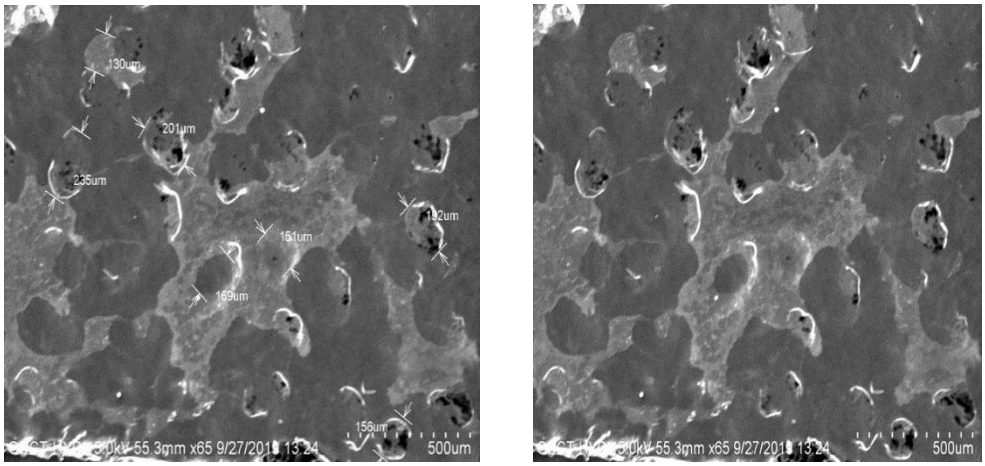


**Figure 8: Scanning Electron Microscopic images of voriconazole transferosomes.**

The microscopic view of the voriconazole transferosomes(F-3) indicated the presence of sphereshaped vesicles.

**Vesicle size**

Vesicle size of voriconazole transferosomal suspension was analyzed by Horiba particle analyzer. Figure 9 Shows the vesicle sizes of selected voriconazole transferosomes(F3).

**Table 9: vesicle size of voriconazole transferosomes.**

**Calculation Results**

| Peak No. | S.P.Area Ratio | Mean | S. D. | Mode |
|---|---|---|---|---|
| 1 | 0.46 | 91.7 nm | 21.9 nm | 88.0 nm |
| 2 | 0.54 | 1339.1 nm | 416.0 nm | 1277.4 nm |
| 3 | --- | --- nm | --- nm | --- nm |
| Total | 1.00 | 767.4 nm | 693.0 nm | 88.0 nm |

**Cumulant Operations**

Z-Average : 594.7 nm

PI : 0.546

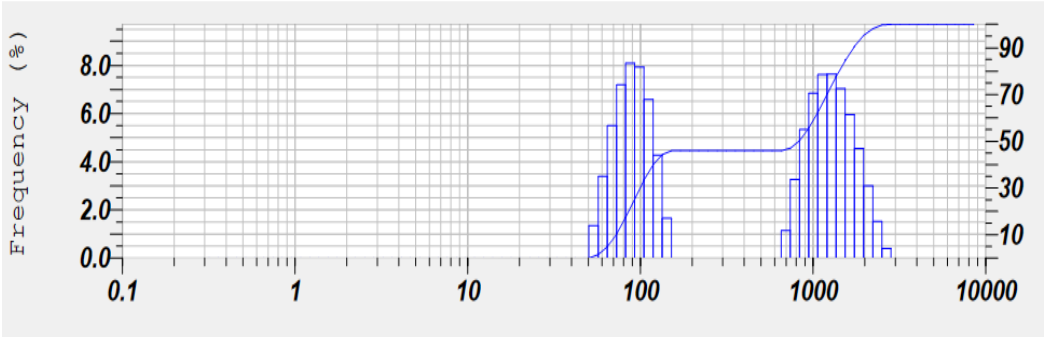


**Figure 9: Particle size analysis of voriconazole Transferosomes.**

The diameter(nm) of the vesicle of voriconazole transferosomal suspension was found to be in range of 100 to 1000 nm. The average size is found to be 594.7 nm with polydispersity index 0.546. The results indicated that the voriconazole transferosomes are present in polydispersive range and vesicle size is in narrow range.

**Zeta potential**

The zeta potential of transferosomal suspension of voriconazole is determined using Zetasizer. The data was shown in table 10.

**Table 10: Zeta potential of voriconazole transferosomes.**

**Calculation Results**

| Peak No. | Zeta Potential | Electrophoretic Mobility |
|---|---|---|
| 1 | -57.7 mV | -0.000447 cm2/Vs |
| 2 | --- mV | --- cm2/Vs |
| 3 | --- mV | --- cm2/Vs |

Zeta Potential (Mean) : -57.7 mV

Electrophoretic Mobility mean : -0.000447 $cm^2/Vs$

It was observed that the zeta potential value of selected voriconazole formulation(F3) was -57.7mV indicating good stability of the formulation. The formulations have sufficient negative charge on the surface of the vesicle to prevent the collision and aggregation of vesicles.

**Evaluation of transferosomal gel**

**Visual Appearance**

Transferosomal gel was examined in light against the white and black background. All formulations were opaque, yellow, smooth to touch and free from grittiness.

**pH:** pH value of transferosomal gels was determined using systronic pH meter. The data obtained was shown in the table 4.11. pH of all formulations was found to be in the range of 6.8 which is close to skin pH and ideal for skin application.

**Table 11: pH of voriconazole transferosomal topical gel.**

| S. No | Formulation | pH |
|---|---|---|
| 1 | TG-1 | 6.6 |
| 2 | TG-2 | 6.7 |
| 3 | TG-3 | 6.6 |

pH of all formulations was found to be in the range of 6.7 which is close to skin pH and ideal for skin application.

***In-Vitro* Drug release studies:** *In-Vitro* drug release studies were performed using cellophane membrane.

**Table 12: Percentage Drug release of the Transferosomal Gels.**

| Time (Hrs) | %DR of TG - 1 ± SD | %DR of TG - 2 ± SD | %DR of TG - 3 ± SD |
|---|---|---|---|
| 0 | 0 | 0 | 0 |
| 1 | 17.96±0.20 | 18.63±0.14 | 16.49±0.31 |
| 2 | 25.79±0.11 | 26.62±0.23 | 24.89±0.21 |
| 3 | 33.95±0.47 | 37.75±0.31 | 31.76±0.43 |
| 4 | 40.85±0.31 | 43.98±0.25 | 39.87±0.32 |
| 5 | 47.65±0.28 | 48.38±0.31 | 44.13±0.26 |
| 6 | 54.38±0.52 | 59.23±0.23 | 51.79±0.21 |
| 7 | 66.98±0.25 | 68.36±0.17 | 63.49±0.34 |
| 8 | 74.45±0.19 | 79.54±0.35 | 72.12±0.41 |

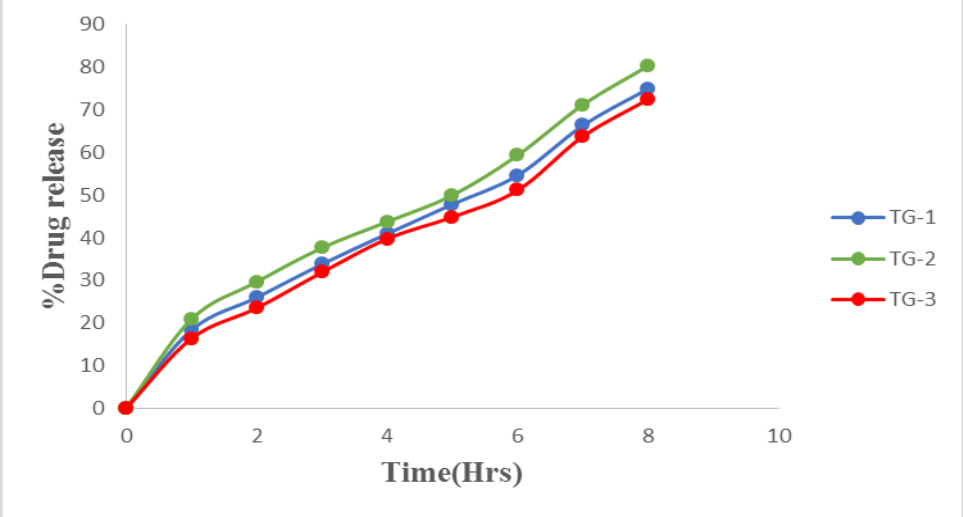


**Figure 1: Drug release profile of Transferosomal gel.**

Out of all these three formulations, formulation TG -2 exhibited a better drug release. From this result, the formulation TG -2 was selected.

**Stability Studies**

Stability studies were performed as per ICH guidelines at two different temperatures for 3 months. Refrigerator conditions (2-8$^0$C ± 2$^0$C) and Room temperature (25$^0$C ±2$^0$C). The drug content of the optimized formulations was monitored for a period of 90 days.

**Table 4.13: Stability study data.**

| Time Period (Days) | % Drug content at Refrigerator conditions (2-8$^0$C ± 2$^0$C) | % Drug content at Room temperature conditions (25$^0$C ±2$^0$C) |
|---|---|---|
| 0 | 90.54 | 90.54 |
| 30 | 89.43 | 89.21 |
| 60 | 89.12 | 89.04 |
| 90 | 87.23 | 86.98 |

The formulations were analyzed for the drug content and from the obtained results it can be observed that the transferosomal formulations were found to be stable at different temperature conditions.

## CONCLUSION

Voriconazole is an antifungal drug. It is used in the treatment of local and systemic fungal infection. Transferosomes are a novel approach for transdermal drug delivery. Transferosomes permeate through skin easily due to their flexibility of the membrane. In this study, transferosomes of voriconazole was prepared by Thin film hydration method using different phospholipid-surfactant ratios. Transferosomes of voriconazole were evaluated for entrapment efficiency, drug content and *In-Vitro* drug release. Formulation F3 containing phosphotidylcholine (85mg) and Span 60 (15mg) were selected as best formulation based on entrapment efficiency and drug release. Entrapment efficiency and drug release of 87.62±0.26 and 82.52±0.35. The selected formulation F3 was further evaluated for visual microscopy, SEM, Zeta potential. Vesicle size of 597. 4nm, zeta potential of -57.7mV. The selected formulation F3 was formulated into transferosomal gel by dispersion method. Formulated gels were evaluated for visual appearance, pH, drug content and *In vitro* diffusion studies. The selected transferosomal gel of voriconazole shows pH value 6.7,drug content 91.56 and drug release % is 79.54.

Finally, it was concluded that transferosomal gel improve the transdermal delivery and sustained release. Transferosomes provides a new opportunity for the well-controlled transdermal delivery of a number of drugs that have a problem of administration by other routes.

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