RESEARCH ARTICLE

Formulation and *Ex-vivo* Permeation Study of Tamoxifen Citrate Loaded Transfersomal Gel

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ABSTRACT

Objective: The current study's objective is to assess the transfersomal gel, administration of tamoxifen citrate transdermally for Design of Experiments (DoE) Approach.

Materials and Methods: Supramolecular clusters with extreme flexibility, known as transferosomes can penetrate untouched animal skin. The formulations were designed by Box-Behnken design (BBD). The *ex-vivo* skin permeation study of tamoxifen citrate-loaded transferosomal gel was compared with commercial gel and blank drug solution. A total of 100 mg of the maximal drug release (94.32%) from the tamoxifen citrate optimized transferosome formulation demonstrated excellent results.

Conclusion: According to this study, the comparatively stable transferosomes represent a promising long-term administration strategy for tamoxifen citrate. According to this study, transdermal drug delivery of skin cancer could be treated by employing transferosomes containing the tamoxifen citrate.

Keywords: Edge Activator, Flexibility, Penetration, Transferosome, Tamoxifen citrate

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INTRODUCTION

Over twenty years ago, it was predicted that skin cancer would make up more than one-third of all cancers. This prediction has already started to materialize. Based on the cells tangled, keratinocytes and melanocytes, there are two categories of skin malignancies. They are non-melanoma skin cancer (NMSC) and melanoma skin cancer (MSC).

Due to its unique advantages, transdermal drug delivery is proving to be more effective than traditional oral drug delivery. However, it also has its own drawbacks, like the inability to move large molecules and the incapacity to get past the stratum corneum's barriers. These issues might be resolved by combining this medication delivery pathway with cutting-edge methods. One such strategy involves creating a transfersome from the medication.[1,2]

Box-Behnken Design

"Box-Behnkenn design (BBD) expert version 12" was used to create the formulations. Factorial experimental design for drug-loaded transferosome optimization. Using a design expert, a 3^3 factorial design was used to examine the quadratic response surfaces and create second-order polynomial models. An experimental design matrix with 27 runs is created, and the non-linear computer-generated quadratic model. We selected ethanol: chloroform mixture (X1), sodium deoxycholate (X2), and phosphatidylcholine as independent variables (X3). The dependent variables were particle size (Y1), entrapment effectiveness (Y2), and poly dispersive index (PDI) (Y3) to prepare transfersomes as shown in Table 1.[3-6]

MATERIALS AND METHOD

A small sample of the pure drug tamoxifen was received from Pfizer Inc. We bought methanol, chloroform, and soya lecithin from Delpha Drugs and Pharmaceuticals in India. Soya phosphatidylcholine, carbopol-940 and potassium dihydrogen orthophosphate were bought from S.D. Fine Chemicals Ltd. in India. The experiments only employed analytical-grade substances. It was utilized in freshly made purified water. The Table 2 expresses the formulation table of transferosomal gel loaded with tamoxifen citrate.[7-9]

My previous research covered factors, including pre-formulation studies, entrapment effectiveness, drug content, particle size, zeta potential, invitro drug release, and release kinetics.[10-12]

Ex-vivo Skin Penetration Study

A Franz diffusion cell, with a 15.0 mL receptor compartment capacity and a 2.54 cm^2 diffusion area was used for the

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Table 1: Formulation table of transferosome

Factors	*Levels*	
Independent variable	Low	High
X_1=Phosphatydyl choline(mg)	30	90
X_2= Sodium deoxycholate(mg)	20	60
X_3=Solvent mixture (Choloform:methanol=3:1) mL	1	3

experiment, which was carried out at 37°C. The modified method was used to prepare the abdomen goat skin. Throughout the experiment, the receptor medium containing 50% phosphate buffer (pH : 5.7) was continuously stirred. The experiment was started by directly putting the commercial gel, plain drug solution, and transferosomal gel loaded with encapsulated tamoxifen citrate, each of which contained trusted computing group (TCG) entering the donor compartment, corresponding to 0.1 mg, to the mounted skin. A new receptor medium was used in place of the 200 l of the receptor fluid at 2, 4, 6, 8, 12, 16, and 24 hours.[13-15]

Ex-vivo Skin Deposition Study

The goat skin, mounted on the Franz-diffusion cell was removed following the accomplishment of the *ex-vivo* skin penetration study for 24 hours. The goat skin tissue was then thoroughly cleansed, rinsed three times with water, and dried with a cotton swab free of lint. Heat treatment was used to separate the epidermis from the dermis. Small portions of the divided skin samples were cut up and placed in a flask with sufficient methanol. The trials were blended for 120 seconds using a vortex mixer, and then homogenized for 45 minutes using a Ultra-Turrax® homogenizer . The collected amount of TCG in the epidermis and dermis was then removed by centrifuging the samples for 15 minutes at 8000 rpm. The samples were then run through a syringe filter, (0.45 m) before the sample was assessed using the approved (HPLC) method.[16-17]

RESULTS AND DISCUSSION

No liposomal formulation employed in this investigation facilitated tamoxifen citrate skin penetration throughout the course of 8 hours, according to *ex-vivo* skin permeation experiments. However, tamoxifen citrate skin deposition was promoted by all varieties of transferosomal gel formulations. Depending on the amount of tamoxifen citrate present, tamoxifen citrate-loaded transferosomal gel showed 41% penetration and 2% deposition over the course of 7 hours, whereas commercial gel showed 8–20% permeation and 2–3% deposition over the same time period. Our observations of the penetration effect in both produced formulation and

Table 3: *Ex-vivo* permeation study of tamoxifen citrate loaded transferosomal gel

Formulation	*"Transdermal flux" (µg/ ch-2/h)*	*"Permeability coefficient" (Ch/h)*	*"Lag time" (min)*	*"Diffusion coefficient" (Ch2/h)*
Pure drug gel	6.39 ± 0.46	0.722 ± 0.47	2.5	6.4
Marketed gel formulation	6.57 ± 0.18	0.634 ± 0.27	2.1	7.1
Tamoxifen citrate transferosomal gel	7.32 ± 0.22	0.822 ± 0.35	1.8	8.5

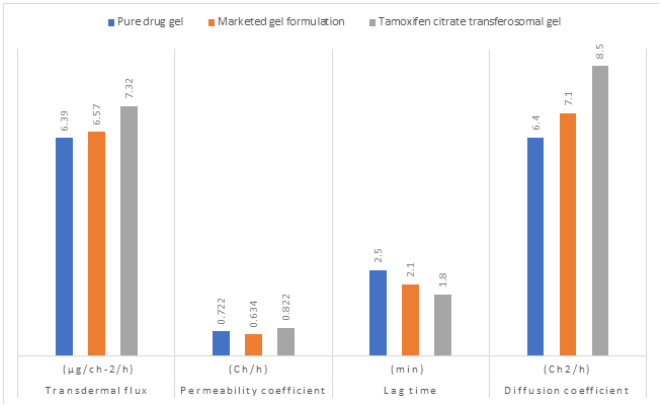


Figure 1: *Ex-vivo* permeation study of tamoxifen-loaded transferosomal gel

commercial gel are explained by the fact that transferosomes interact with the skin more favorably than other molecules because of their hydrophobic nature. Additionally, the transferosomes appear to have good tamoxifen citrate penetration and deposition. The fact that the permeability coefficient through the $CaCo_2$ cell monolayers in transwells exhibited a range of 4 to 6 times higher permeability than the permeability coefficient through goat skin[18] is also highly intriguing and supports the findings of this investigation Table 3 (Figure 1). As a result, the amount of sodium deoxycholate and phosphatidylcholine in a transferosomal gel loaded with tamoxifen citrate determines how well it is delivered to the skin. Edge activators and skin-penetration enhancers are chemicals that promote the transport of transferosomal bioactive compounds to the skin, including skin deposition, especially when included in transferosomes as shown in Table 4 and graphical representation shown in Figure 2.

Table 2: Formulation table of transferosomal gel loaded with tamoxifen citrate

S.no	*Transfersome (mg)*	*Carbopol-940 (mg)*	*Triethanolamine (mL)*	*Propylene glycol (mL)*	*Isopropyl alcohol (mL)*	*Water (mL)*
TG1	100	250	10	5	5	q.s
TG2	100	500	10	5	5	q.s
TG3	100	1000	10	5	5	q.s

Table 4: Comparison of drug retention time of tamoxifen transferosomal gel with marketed formulations

Formulation	*Drug retention in 24 hours*
Raw drug gel	0.63 ± 0.24
Commercial gel formulation	0.68 ± 0.82
Tamoxifen citrate transferosome gel	0.84 ± 0.26

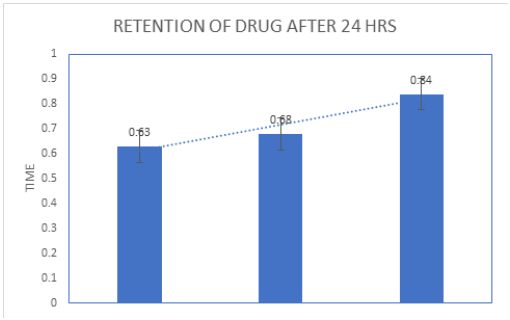
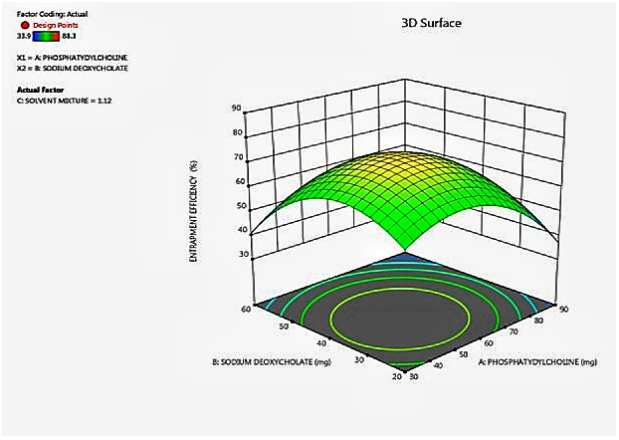
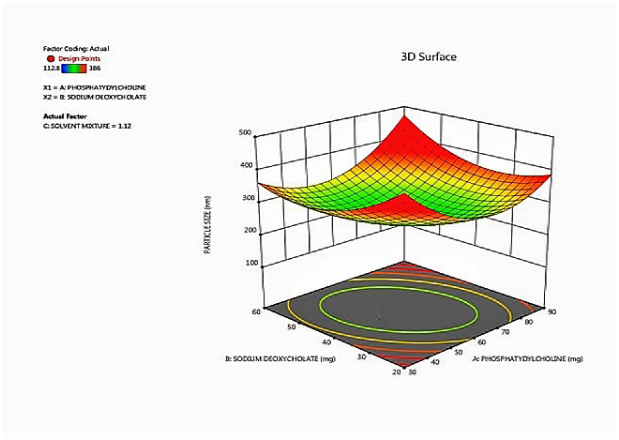


Figure 2: Drug retention time of Tamoxifen citrate transferosomal gel with marketed formulations

The transferosomal gel exhibits optimal penetration and skin deposition when compared to commercial gel and drug solution, according to the skin deposition results of this study.[19]

Effect of independent variable on formulation of tamoxifen-loaded transferosomal gel is shown in a 3D Response plot.





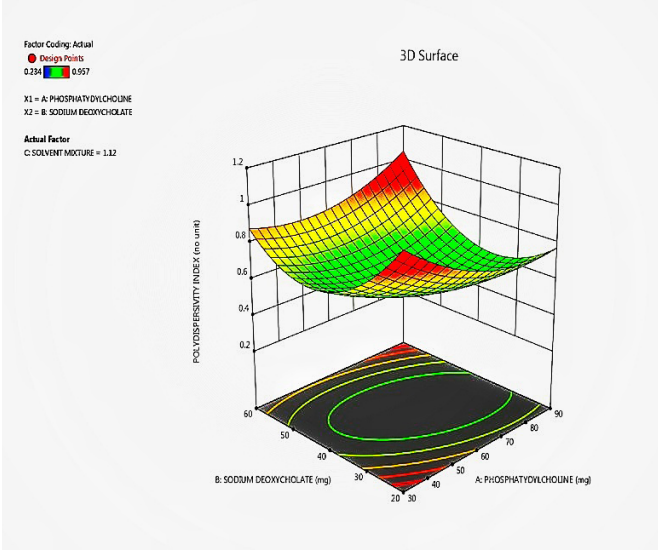


Figure 3: Effect of an independent variable on the formulation of a tamoxifen-loaded transferosomal gel is shown in a 3D response surface plot.

To evaluate the individual and interacting effects on the responses, 3D surface plots were created as figured in Figure 3.

- The 3D surface diagram also ensures the same effect shown in the interaction graph for the responses such as particle size, percentage entrapment efficiency, and polydispersity index at 24 hours.[20-26]

CONCLUSION

According to the *in-vivo* skin deposition investigations, transferosomes, as opposed to drug solutions, enhanced drug penetration and accumulation in the epidermis and deep skin due to their edge activation and deformation. Additionally, a skin irritation trial using the improved formulation of tamoxifen citrate-loaded transferosomal gel revealed skin tolerability. The promising potential of transferosomal gel for the topical distribution of tamoxifen citrate was demonstrated by the results in the conclusion.

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AUTHORS CONTRIBUTIONS

Each author contributed equally.

CONFLICT OF INTERESTS

Stated none

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