Scholars Academic Journal of Pharmacy (SAJP) **ISSN 2320-4206**
Sch. Acad. J. Pharm., 2013; 2(4):315-318

(An International Publisher for Academic and Scientific Resources)
www.saspublisher.com

Research Article

Formulation and Evaluation of Econazole Niosomes

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Abstract: This article to investigate the effectiveness of using Niosomes in a transdermal drug delivery system for Econazole. Topically applied Niosomes can increase the longer action on the skin (stratum corneum and epidermis), while reducing the systemic absorption of the drug. Econazole is a imidazole antifungal agent used in the treatment of Candida infections, fungal infections. Econazole Niosome was prepared by Thin Film Hydration Technique by varying the cholesterol and surfactant ratios as 1:1, 1:2, 1:3, 1:4 Each formulation was evaluated for drug release. The release showing required amount of drug release per day as well as extended for the required day is the optimized formulation. Hence, B formulation is the optimized one.

Keywords: Niosomes, transdermal drug delivery, cholesterol, span 80 and Econazole,

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INTODUCTION

Niosomes are non-ionic surfactant vesicles ,capable of forming vesicles & entrapping hydrophilic and hydrophobic molecule [1,2]. Niosomes are uni or multilamellar vesicles formed from synthetic, non ionic surfactant of alkyl or di-alkyl poly glycerol ether class, offering an alternatively to liposome as drug carriers. Niosomes can entrap solutes in a manner analogous to liposomes, are relatively more stable in vitro and can improve the stability and duration of action of entrapped drug as compared to the stability of conventional dosage forms [3]. Niosomes characteristics such as lamellarity. Niosomes offer several advantages such as higher chemical stability, contact time and skin penetration enhancing properties .Better targeting of drugs to the infected organ scan be achieved by niosomal formulation due to the presence non-ionic surfactants with lipids. The presence of nonionic surfactants increase the permeability of Econazole through the biological membrane and also reduces the systemic toxicity of anti-infective drugs [4].

Drug deposition, vesicle size and entrapment efficiency were the key parameters involved in formulation of topical Niosomes. The number of formulation and processing variables are involved during niosome preparation may affect these parameters and hence the performance of the formulation. Factorial design and response surface methodology is an important statistical tool to study the effect of several factors influencing responses by varying them simultaneously by carrying out limited number of experiments [5].

MATERIEALS AND METHODS

Econazole gift sample was obtained from Cipla pharmaceutical ltd .Hyderabad. Cholesterol, Span received from natco pharma ltd. Hyderabad. Ingredients used were AR grade. Triton X– was supplied by Loba Chemicals, Mumbai.

Formulation of Econazole Niosome

Niosome was prepared by Thin Film Hydration Technique. Accurately weighed quantity of cholesterol and span 80 were dissolved in chloroform – methanol mixture (1:1 v/v) in 100 ml round bottom flask. The weighed quantity of drug is added to the solvent mixture. The solvent mixture was removed from liquid phase by flash evaporation at 60oC to obtain a thin film on the wall of the flask at a rotation speed of 150 rpm. The complete removal of residual solvent can be ensured by applying vacum. The dry lipid film was hydrated with 5 ml phosphate buffer saline of pH 7.4 at a temperature of 60 ± 2o C for a period of 1hour until the formation of Niosomes. The ratios of the formulations were 1:1, 1:2, 1:3, 1:4 of cholesterol : span 80 . The batch codes were A1 to A4.

Removal of unentrapped [6] drug from Niosome by dialysis method. Niosome suspension was placed in 3cm x 8cm long dialysis bag whose molecular weight cut off was 12,000. The dialysis bag was then placed in 250 ml beaker containing phosphate buffer saline of pH 7.4 with constant stirring by means of a magnetic stirrer. Dialysis was carried out for 24 hour by replacing the buffer with fresh for every 3 hours [7, 8].

Size analysis

By optical microscopy

A drop of niosome suspension was placed on a glass slide and it was diluted. A cover slip was placed over the diluted niosome suspension [9] and evaluated the average vesicle size and shape by an ordinary optical microscope using a recalibrated ocular eye piece micrometer [10].

Percentage Encapsulation of drug [11]

Vesicles containing Econazole were separated from unencapsulated drug by dialysis [12]. Niosomal preparation of 0.5 ml was taken after dialysis. To this 0.5 ml of 10% triton X – 100 was added and incubated for 1 hour[12]. The triton X–100 was added to lyse the vesicles in order to release the encapsulated Econazole. Then it was diluted with phosphate buffer saline solution (pH 7.4) [4] and filtered through whatmann filter paper. The filtrate was measured spectrophotometrically at 424 nm using phosphate buffer and triton X – 100 mixture as blank. From the absorbance value, the concentration of drug in mcg/ml was found using the standard curve [13].

$$\% \text{ drug loading (PDL)} = \frac{\text{Total Drug Added (mg)}}{\text{Entrapped drug (mg)}}$$

In vitro release study for niosomal formulations and analysis by UV method

Niosomal preparation was taken in a dialysis membrane of 5 cm length and suitably suspended in a beaker containing 200 ml of diffusion medium (Phosphate buffer saline pH 7.4). The medium was maintained at a temperature of 37 ± 0.5°C [5]. It was stirred by means of magnetic stirrer at a constant speed. Sample of 2 ml (diffusion medium) was withdrawn at every 24 hours for 8 days and replaced the diffusion medium, so that the volume of diffusion medium was maintained constant at 200 ml. The samples were measured spectrophotometrically at 424 nm. The release was compared with a marketed Econazole gel.

Table 1: Composition of Formulations

Ingredients	A1	A2	A3	A4
Econazole (mg)	1mg	1mg	1mg	1mg
Cholesterol (mg)	100umg	100umg	100umg	100umg
Span 80 (mg)	100umg	200umg	300umg	400umg

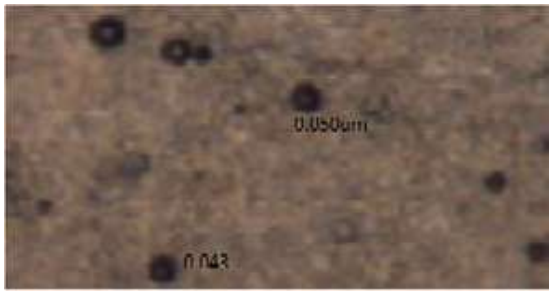

Fig. 1: Econazole Loaded Niosomal Gel

Table 2: Percentage Entrapped Drug & Percentage Drug Release

Formulation code	Chole:span80	Percentage entrapped drug	%Drug release
A1	1:1	62.5%	70.10%
A2	1:2	71%	77.89%
A3	1:3	88.23%	82.18%
A4	1:4	98%	92.10%

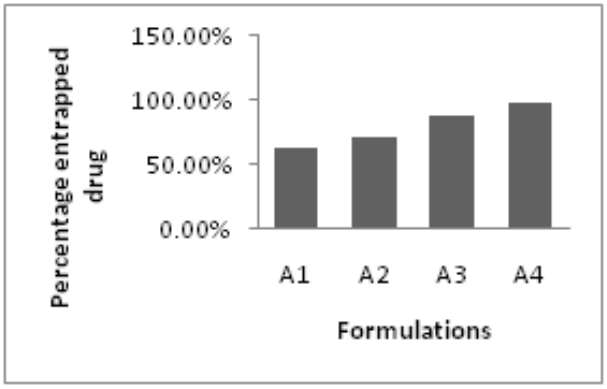

Fig. 2: Percentage Entrapped Drug in Various Formulations

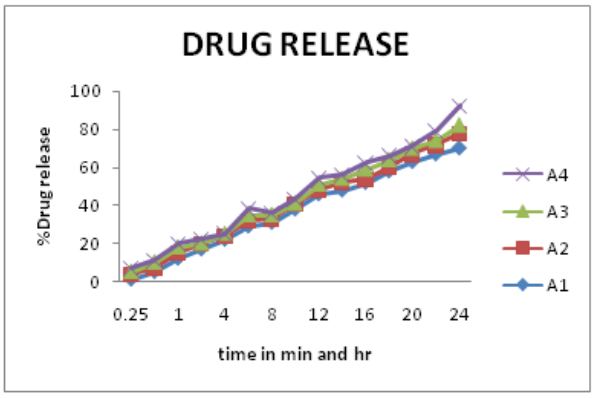

Fig. 3: Percentage Drug Release in Time of 24 Hr

RESULTS AND DISCUSSION

Formulation of Econazole Niosomes

Based on the above optimized parameters, Econazole Niosomes were prepared by varying the cholesterol and surfactant ratios as 1:1, 1:2, 1:3,1:4 Each formulation was evaluated for percentage of drug entrapment and for their cumulative drug release.

Removal of entrapped dug

As the amount of surfactant increased, the amount of dialyzed Econazole was also increasing 1:4 ratio indicates that concentration of surfactant used should be optimum so that more amount of drug can be in the encapsulated form for an extended release. Among all the formulations, the dialyzed quantity of batch A3 (Cholesterol: Span 80= 1 : 4) was maximum .The result indicated more amount of Econazole in an encapsulated form.

Size analysis

Size analyzed performed by optical microscopy. Niosomes have spherical in nature.

Entrapment efficiency

After the removal of un entrapped drug by dialysis, the entrapment efficiency of all the formulations was studied. The various factors like lipid concentration, drug to lipid ratio, cholesterol content will change the entrapment efficiency. The lipophilicity also influences the entrapment of drug.

The formulation A4 with Cholesterol and Span 80 in the ratio of 1:4 showed entrapment efficiency of 98%. The formulation A1, Cholesterol: span80 = 1: 1 showed low entrapment efficiency among all formulations. It showed entrapment of 62.5%.

In vitro release study by UV

In vitro release was found to be biphasic as the release was controlled by the dialysis membrane and the lipid bilayer. Incorporation of cholesterol affected the release rate of the encapsulated drug.

A formulation with 1:1 cholesterol: span 80 ratio has shown only 70.10 % drug release in a 20 hours period. In formulation with 1:4 cholesterol: span 80 ratio, the concentration of span was increased and it has shown 92.10 % drug release in 24 hours.

In C formulation with 1:3 CHOL: SA ratio has shown 82.18 % drug release in 22 hours. The release showing required amount of drug release per day as well as extended for the required day is the optimized formulation. Hence, A4 formulation is the optimized one.

Kinetics of drug release

The optimized formulation A4 was subjected to graphical treatment to assess the kinetics of drug release. A plot of concentration versus time showed linearity in optimized formulation of Econazole Niosome. Hence it follows zero order kinetics. Higuchi's plot confirms that the release is diffusion mediated.

CONCLUSION

An effort was made to formulate the Econazole Niosomes and incorporate the Niosomes into the gel. From the results of the present experiments it may be concluded that formulation A4 containing 1:4. was showing high percentage of entrapment and desired sustained release of Econazole. Hence A4 formulation was the optimized one. The optimized formulation A4 was found to follow zero order release pattern which was revealed by the linearity shown from the plot of time versus drug release.

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