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TERBINAFINE HYDROCHLORIDE LOADED NIOSOME FORMULATION PREPARED VIA REVERSE PHASE EVAPORATION METHOD

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Abstract: Terbinafine is a lipophilic substance, and is slightly soluble in water, and according to the BCS, terbinafine and its hydrochloride salt, terbinafine hydrochloride belong to Class II. The purpose of this research was to prepare Terbinafine hydrochloride niosomes in a trial to enhance the desired drug delivery properties. The nonionic surfactant vesicles of Terbinafine hydrochloride were prepared with the lipid mixture consisted of cholesterol and span 20 using reverse phase evaporation technique and evaluated for their morphological characteristics, entrapment efficiency as well as in-vitro drug release profile. The percentage entrapment efficiency was found to be 95% and drug content was found to be 96.7%. Thus niosomes could be a promising carrier for Terbinafine hydrochloride with desired drug delivery properties.

Index Terms - Terbinafine hydrochloride, Niosome, Reverse Phase Evaporation Method

I. INTRODUCTION

Terbinafine hydrochloride (TbH) is a synthetic allylamine antifungal. It is highly lipophilic in nature and tends to accumulate in skin, nails, and fatty tissues. Like other allylamines, terbinafine inhibits ergosterol synthesis by inhibiting the fungal squalene monooxygenase, an enzyme that is part of the fungal cell wall synthesis pathway. TbH affects dermatophytes and some yeast, it is used orally for the treatment of dermatophyte infections of the skin and nails. It is commercially available in the pharmaceutical forms of creams, gels, tablets, sprays and solutions [1, 2].

The role of the novel drug delivery system is not only limited to a drug package convenience and ease of administration but along with this it is also needed to provide better therapeutic efficacy and safety by delivering the drug molecules to the target site in the most convenient manner. Drug delivery system using novel vesicular carrier, such as liposome or niosome, has distinct advantages over microspheres, nanoparticles, and other carriers in terms of better entrapment of drugs (payload characteristics), better target site specificity, and handling premature drug release (burst effect) [3].

Niosomes or non-ionic surfactants vesicles are microscopic lamellar structures formed on the admixture of a non- ionic surfactant, cholesterol and phosphate with subsequent hydration in aqueous media. Niosome can entrap both hydrophilic and lipophilic drugs, either in aqueous layer or in vesicular membrane, which is lipoidal in nature. Noisome are reported to attain and retain better stability than liposomes. They can prolong the circulation of the entrapped drugs because of the presence of nonionic surfactant here they possess better intrinsic targeting potential and propensity. Although liposomes have been studied as an effective vesicular drug delivery system for oral as well as transdermal routes for improving the absorption of the drugs, niosomes are preferred over liposomes due to their higher chemical stability, economy, and simple practical methods of preparation without the use of pharmaceutically unaccepted solvents [4]. There are different methods to prepare such nanocarriers while in this study the formulations were prepared by Reverse Phase Evaporation Technique.

II. EXPERIMENTAL:

Materials: The pure drug Terbinafine Hydrochloride was obtained as gift sample from YarrowChem Products, Mumbai. Span 20 was obtained from Continental Chemicals, Delhi. Cholesterol, Chloroform, Glycerine and other excipients were obtained from Fine ChemicalsLtd, Mumbai.

Methods:

Preparation of niosomes [5 ,6, 7]:

Accurately weighed TbH was dissolved in 10ml of Acetate buffer pH 5.5. Mixture of Chloroform and Diethyl ether was prepared. Accurately weighed 0.1gm of Cholesterol was dissolved in organic phase. Span 20 was added in this mixture. Then 1ml of aqueous phase containing drug was added in the mixture of organic phase. Then the mixture was covered and sonicated at 50^0C for 10 minutes. After the process of sonication white emulsion was formed. The emulsion was placed in Rotary vacuum evaporator and the organic phase was removed at60^0C for 15 minutes. The thin film formed was hydrated with 10ml of Acetate buffer pH 5.5 to produce aqueous niosomal suspension containing 10mg/ml drug. The niosomes vesicles were obtained after air drying.

Table1: Formulation Table for Niosomes

Sr.no	Ingredients	F1	F2	F3	F4
1.	Terbinafine Hydrochloride (mg/ml)	10	10	10	10
2.	Span 20 (ml)	0.5	0.2	0.1	0.1
3.	Cholesterol (mg)	100	100	100	100
4.	Chloroform (ml)	5	5	8	6
5.	Diethyl ether (ml)	5	5	2	4
6.	Acetate buffer pH 5.5 (ml)	20	20	20	20

Evaluation of Niosomes [8-11]:

Physical characterization-The particle size and shape of vesicles were examined using Electron microscope. The niosomes possessed spherical shape; the radius and surface area werealso determined.

Entrapment efficiency-It is defined as the percentage amount of drug which is entrapped by the noisome. The free drug is removed by centrifugation method. Then % entrapment efficiency is determined by following formula-

% Entrapment efficiency = Total drug added – Free drug / Total drug added ×100

Drug content- The formulations were analysed by UV-visible spectroscopy at wavelength determined in preformulation studies and % drug content was calculated. The following formula was used

% Drug content = Drug content / Label claim x 100

In-vitro dissolution profile of niosomes In-vitro dissolution profile of niosomes was carried out using USP type II dissolution apparatus. The powdered niosomal vesicles were placed in 900ml medium Acetate buffer pH 5.5 and were rotated at 50rpm. The assembly was maintained at 37 ± 0.5^0C. The sample was withdrawn at time interval of 10 minutes and the same amount was replaced by medium Acetate buffer, maintaining the sink condition. The sample was withdrawn until 95% of drug was dissolved. The sample was then filtered using Whatman filterpaper and was diluted further with medium. The absorbance was measured using UV-visible spectroscopy. The absorbance determines the saturation point where maximum drug is dissolved.

Stability study-Stability of drug is defined as the ability of the formulation to remain within its physical, chemical, therapeutic and toxicological specifications mentioned in ICH. The objective of this study is to prove the quality of formulation which varies with time effect of variety of environmental conditions such as temperature, humidity and light.

Specifications of ICH-

Long-term testing: 25^0C ± $20\ ^0$C / 60% RH ± 5% for 12 months

Accelerated testing: 40^0C ± 2^0C / 75% RH ± 5% for 6 months

To determine the stability of niosomes, the batches were stored in airtight container. The sealedvials were kept at different temperatures. Surface characteristics and % drug content were parameters for evaluation of stability studies. The accelerated stability testing was performed for 1 month.

III. RESULTS AND DISCUSSION

Physical Characterization-The niosomes possessed spherical shape and large unilamellar vesicles were formed of size 0.1-10µm.

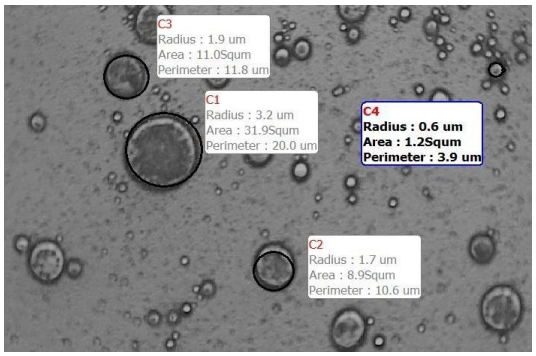

Figure 1: Microscopy of niosomes

Entrapment efficiency- In the formulation of niosomes total drug added was 10mg. After centrifugation, the free drug was separated and weighed 0.5mg. Using formula, % Entrapment efficiency was found to be 95%. It states that maximum drug was entrapped in the vesicles.

Drug content- The % Drug content was found to be 96.7% by UV-visible spectroscopy.

In-vitro dissolution profile of niosomes –

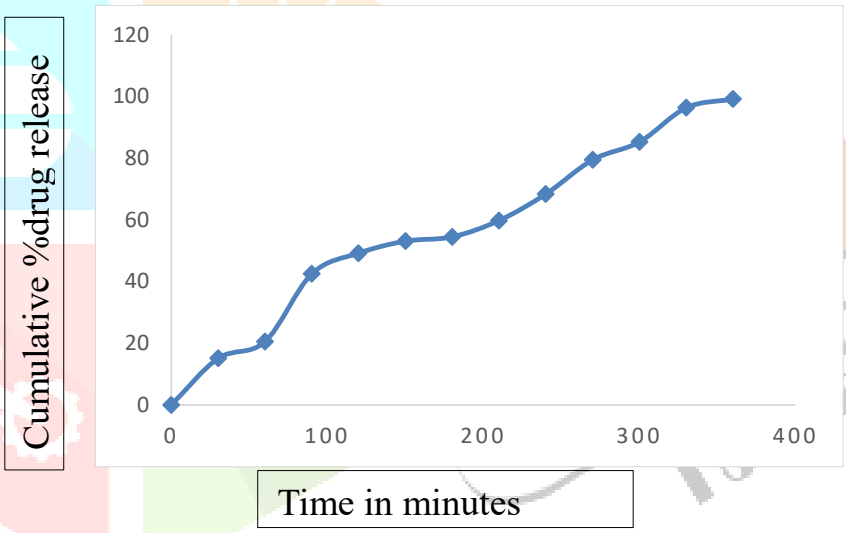

Figure 2: In-vitro drug release of Niosomes of Terbinafine hydrochloride

The dissolution of niosomes showed that, was there was >70 % drug release in four hours. It states that, niosomes possessed controlled drug delivery system, as the drug is released slowly.Thus, niosomes increases the bioavailability of drug in the system.

Stability study -As per ICH guidelines the niosomes were subjected to light, temperature andhumidity for 1 month. It was observed that there was no change in physical and chemical characteristics of niosomes and no degradation was observed.

IV. CONCLUSION

Terbinafine Hydrochloride -loaded niosomes were formulated by the Reverse phase evaporation technique and evaluated for their *in-vitro* drug release profile by using UV method. The evaluation of niosomes for particle size, entrapment efficiency, in-vitro dissolution studies and accelerated stability testing indicate that the formulation F3 is the optimistic preparation of niosomes having higher entrapment efficiency and drug release. In conclusion, the niosomal formulation could be a promising delivery system for Terbinafine Hydrochloride with controlled drug release profiles.

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REFERENCES

1. Tagliari,MP. Kuminek,G. Borgmann,SHM Bertol, CD. Cardoso, SG. Stulzer, HK. 2010. Terbinafine: Optimization of a LC method for quantitative analysis in pharmaceutical formulations and its application for a tablet dissolution test. Quim. Nova, 33(8):1790-1793. DOI:10.1590/S0100-40422010000800029
2. Karekar, P. Salunkhe,N. Yadav,A Bangar,D. Yadav, D. 2014. Modulation of Physico-Chemical Properties of Terbinafine HCl by Using Solid Dispersion Technique. Research J. Pharm. and Tech, 7(4):450-453.
3. Asthana,GS. Sharma,PK. Asthana, A. In Vitro and In Vivo Evaluation of Niosomal Formulation for Controlled Delivery of Clarithromycin. Hindawi Publishing Corporation Scientifica, Volume 2016, Article ID 6492953, 10 pages http://dx.doi.org/10.1155/2016/6492953.
4. Ahuja,N. Saini,V. Bishnoi,VK Garg,A. Hisoria,M. Sharma, J. Nepali, K. 2008. Formulation and evaluation of lansoprazole niosome Rasayan J. Chem, 1(3): 561-563.
5. Sharma R, Dua JS, Prasad DN, Kaushal S, Puri A.2019. Formulation and Evaluation of Clindamycin phosphate Niosomes by using Reverse Phase Evaporation Method, Journal of Drug Delivery and Therapeutics, 9(3-s):515-523http://dx.doi.org/10.22270/jddt.v9i3-s.289.
6. Ramadan,WM. Singh, AP. 2009. Preparation of Acyclovir Loaded Non-ionic Surfactant Vesicles (Niosomes) Using Reverse Phase Evaporation Technique. Research J. Pharm. and Tech.2 (4): 793-795.
7. M. Zarei, D. Norouzian, B. Honarvar, M. Mohammadi, H. Ebrahimi Shamabadi and A. Akbarzadeh, 2013. Paclitaxel Loaded Niosome Nanoparticle Formulation Prepared via Reverse Phase Evaporation Method: An in vitro Evaluation. Pakistan Journal of Biological Sciences, 16: 295-298. DOI: 10.3923/pjbs.2013.295.298
8. Kondoros BA, Jójárt-Laczkovich O, Berkesi O, Szabó-Révész P, Csóka I, Ambrus R, Aigner Z.2022. Development of Solvent-Free Co-Ground Method to Produce Terbinafine Hydrochloride Cyclodextrin Binary Systems; Structural and In Vitro Characterizations. Pharmaceutics. 14(4):744. doi: 10.3390/pharmaceutics14040744
9. Kumar P; Kumar V. 2013. Formulation and evaluation of Econazole niosomes. Scholars Academic Journal of Pharmacy, Vol 2(3), pp315-318.
10. Irene T; Elessy A. 2018. Formulation development and evaluation of niosomal gel of combined antifungal agents. International Journal of Pharmacy, Vol 8(3), pp3-20.
11. Mohite M; Kumbhar T (2019) Preparation and evaluation of ketoconazole niosomal gel drug delivery system by ultrasonication method. World Journal of Pharmaceutical Research, Vol 8, Issue 6, pp1303-1318.