Research Article *Cuestiones de Fisioterapia* *Pharmaceutics*

FORMULATION AND EVALUATION OF MICCONAZOLE LOADED TRANSFEROSOME PATCHES TO TREAT FUNGAL DISEASE

Venkata ramana Godishala[1], Jeganath S[2]*

[1]Research Scholar, Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Pallavaram, Chennai-600117, India.
[2]Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Pallavaram, Chennai-600117, India.

Abstract
The research work was carred out to develop a transferosomalpatchesloaded miconazole for fungal treatment. Variousformulations of transfersomes were prepared and evaluated. Prepared patcheswere prepared and evaluated for pH measurement, weight uniformity, folding endurance, thickness, moisture loss and drug release study, weight uniformity was found that 19.913(mg), folding endurance was found to be>150 , thickness of patches was found to be 138.5(mm), moisture loss was 0.681.By Frans diffusion cell method the drug absorption will be ensured and found to be 227nm.
Keywords: transferosomes, patches, miconazole, evaluation

Introduction

Transfersomes are unnaturally prepared vesicles that act as natural cell vesicles. Through this similarity, they are suitable for targeted drug delivery. Transfersomes consist of highly elastic lipid bilayers. These vesicular systems are more elastic than liposomes, which help to penetrate the skin more effectively. [4-5] A transfersome is a highly elastic and stress- responsive. The water-filled colloidal particles are the vesicles.These vesicles act as a reservoir for sustained release of the formulations. In transdermal formulations, they act as a rate-controlling membrane, it help to regulate the systemic drug absorption. [6-9]

Transferosomes are composed of phospholipids such as phosphatidylcholine, which self-assemble into a lipid bilayer in an aqueous environment. To improve the elasticity and permeability of the lipid bilayer, a bilayer-softening agent (edge activator) is added. [10].

Fungal infections are common infectious disease. In humans, fungal infections occurs,it takes over zone of the body and is much for immune system to handle. The happening of fungal infections is increasing nowadays, some patients with immunodeficiency conditions. These infections are the common reason to seek treatment at dermatology clinics. Many antifungal drugs are available in the market to treat fungal infections; their therapeutic effectiveness is in limit because their toxicity and physicochemical properties.

Transfersomes are a novel drug delivery system that can transport both high-molecular and low-molecular drugs through the skin pores. They exhibit high deformability that weakens the lipid bilayer. Because of their greater flexibility, transfersomes will help to easily penetrate the skin more stably than liposomes and can pass through skin pores [11-12].

Miconazole is used to treat different fungal infections such as jock itch and ringworm. For the tinea virsicolor it is more effective if the fungal infection occur that causes a change in the skin color; it will cause darker patches on areas like the neck, chest, arms, or legs. Miconazole is the azole group of antifungal drugs. The growth of fungi will be inhibited[13].

MATERIAL AND METHOD:

MATERIALS:

Miconazoleobtained from pharmaceutical company as a gift sample. Soya PC was acquired from Himedia Laboratory, Mumbai. Ethanol, Glycerin, PEG, HPMC E15 and polyvinylpyrrolidone (PVP)purchased from Raksh Bio Science Private Limited Chennai. The double distilledwater is used for the formulation.

METHOD:

Preparation of miconazole loaded transfersomes:

Soya PC was dissolved in ethanol, and the solution was heated in a water bath at 30 °C. The drug solution prepared and added in double-distilled water. Before the process, the solution heated to 30 °C, the ethanolic lipid solution was added slowly by continuous stirring with a magnetic stirrer at the required rpm. The mixture was stirred for an additional 5 minutes, and the prepared allowed to cool at room temperature for 45 minutes[14].

Preparation of transdermal patch:

By using the solvent casting method, the miconazole loaded transfersome patches will be formulated using aluminum foil. For the formulation, the different polymer ratio of HPMC and PVA was used. Glycerine and PEGwere added as plasticizer [15].

Table 1: Formulation of transferosomes patches

Formulation	Polymerratio HPMC E50 AND PEG	Plasticizer (30%W/W)	solvent
F1	1:2	GLYCERINE	WATER
F2	1:3	GLYCERINE	WATER
F3	1:1	PEG	WATER
F4	2:1	PEG	WATER
F5	3:1	PEG	WATER

EVALUVATION:

Drug content:

The amount of drug weight equivalent to 100 mg for the transfersomal formulation was placed in a beaker and mixed with 20 mL of methanol. The formulation gets stirred and then filtered using Whatman filter paper No.1.After the filtration take 1.0 mL is transferred into a 10 mL volumetric flask and diluted with ethanol. The solution was absorbed using UV spectrophotometer at itsλmax227nm[16].

Uniformity of weight:

This test was performed to evaluate whether each patch contains a uniform amount of drug without

variation. From the each batch, five patches were taken and weighed using a digital balance, and the average weight of the patches was noted. [16].

Moisture loss:

To evaluate the stability of the patches under dry conditions. The patches get placed in a desiccator before the weight of the patches is noted. After three days, the patches were removed from the desiccator and weighed. The percentage of moisture loss is calculated.

$$\% \text{ Moisture loss} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Thickness:

The uniformity of the drug was measured by thickness of the patches.By using micrometer screw the thickness was determined**.**

Folding endurance:

Folding endurance was evaluated to determine the ability of the patches to withstand repeated folding. It was measured by repeatedly folding a small strip of the film at the same place until it broke. The number of times the film could be folded at the same point without breaking. The average of five readings was taken.

***In vitro* dissolution studies:**

The in-vitro diffusion study was performed using a Franz Diffusion Cell. The membrane was connected to one end open cylinder serve as the donor. The formulated patch was placed on the membrane with the receptor medium containing tear fluid. The fluid was maintained at a temperature of 37°C and by using magnetic stirrer the solution get mixed. At required time intervals, withdrawn 1ml sample from the receptor compartment and it get absorbedby using a UV spectrophotometer at 227 nm.

Stability studies:

The studies were conducted for one month. There was no degradation of the patch and drug content was uniform and there were no major changes in drug release.

RESULT AND CONCLUSION:

Uniformity of weight:

This test is to ensure that each patches contains the efficient amount of drug without any drastic deviation. The weight of the patches F1 to F5 tends to be in the range of 19.915 to 24.605 mg.

Moisture loss:

The percentage moisture loss in the range of 0.532% to 0.697%.The concentration of hydrophilic polymer decrease the moisture loss will decrease.

Thickness:

The average thickness of patches of F1 to F5 is in 138.2 to 181.47.The formulation 4 has lesser thickness compare to other formulation.

Folding endurance:

The folding endurance of the formulation is in the range of 145 to 150.

Table no:2 data for various parameters

Formulation	Weight Uniformity(mg)	Folding endurance	Thickness (mm)	Moisture loss
F1	20.029	>145	170.4	0.531
F2	24.311	>147	176.3	0.544
F3	24.601	>145	181.6	0.571
F4	19.913	>150	138.5	0.681
F5	20.259	>150	148.9	0.696

***In vitro* dissolution studies:**

The evaluation tests showed that all formulations has good drug release. Among other formulation, the P4 formulation has better drug release.

Table no 3: Data for various physicochemical parameters

Time	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	20	20	27	29	28
2	30	35	34	36	35
3	40	46	48	49	48
4	50	57	52	54	52
5	60	75	80	88	85

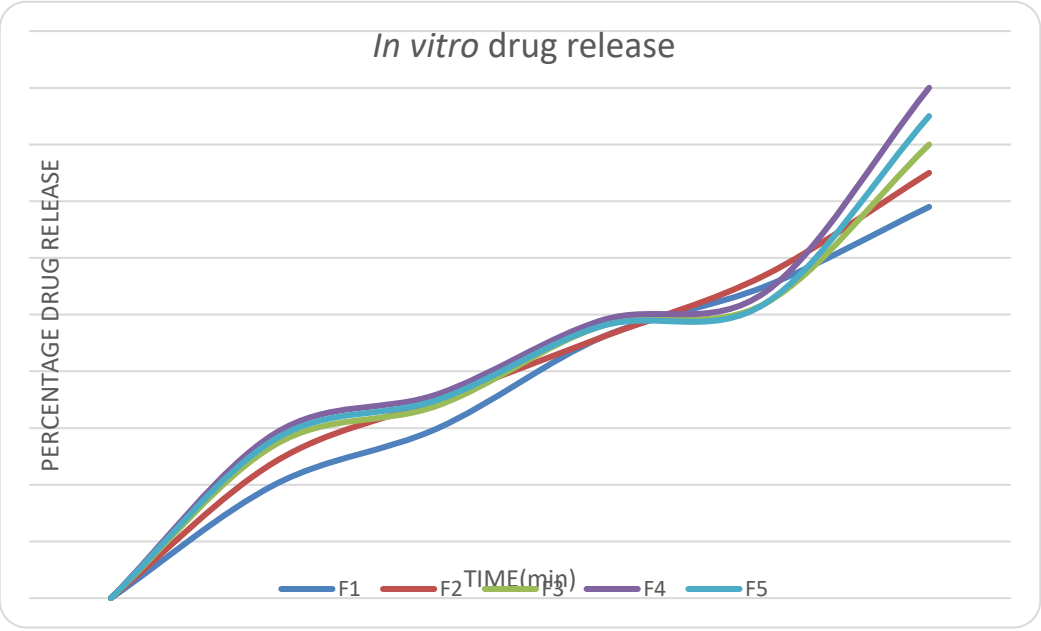

Figure 1: Comparative invitro drug diffusion data for F1-F5

CONCLUSION:

Transfersomal patches were prepared and evaluated. Based on the study results, the P4 formulation containing HPMC E15 and PVP in a 2:1 ratio with PEG, along with a transferosomal formulation of soya PC, was identified as the best formulation compared to the others. It showed satisfactory results in parameters such as percentage drug content, moisture loss, weight uniformity, folding endurance, thickness, and drug release. The formulation exhibited a drug release of 84%, which is higher and considered better when compared to the oral bioavailability of the drug.

REFERENCES

1. Irfan M, Verma S, Ram A. Preparation and characterization of ibuprofen loaded transferosomes as a novel carrier for transdermal drug delivery system. Asian j Pharm. clin resear, 2012; 162-165.
2. Trommer, H., & Neubert, R. H. H. (2006). Overcoming the stratum corneum: the modulation of skin penetration: a review. *Skin pharmacology and physiology*, *19*(2), 106-121.
3. El Zaafarany GM, Awad GAS, Holayel SM, Mortada ND. Role of edge activators and surface charge in developing ultra deformable vesicles with enhanced skin delivery. Int J Pharm, 2010; 164-172.
4. Cevc G, Grbauer D, Schatzlein A, Blume G. Ultraflexible vesicles, transferosomes, have an extremely low pore penetration resistance ant transport therapeutic amounts of insulin across the intact mammalian skin. BiochemBiophys Act, 1998; 201-215.
5. El-Maghraby GM, Williams AC. Vesicular systems for delivering conventional small organic molecules and larger macromolecules to and through human skin. Expert Opin Drug Deliv, 2009; 149-163.
6. Walve JR, Bakliwal SR, Rane BR, Pawar SP. Transferosomes: A surrogated carrier for transdermal drug delivery system. Int J App Bio Pharm Tech, 2011; 201-214.
7. Cevc G, Blume G. Lipid vesicles penetrate into intact skin owing to transdermal osmoticgradient and hydration force. BiochemBiophys Act, 1992; 226-332.
8. Jain NK. Advances in Controlled and Novel Drug Delivery. CBS Publishers and Distributers First edition2001. New Delhi, 426-451.
9. Paul, A, Cevec G. Non-invasive Administration of Protein Antigens. Epicutaneous with Bovin Serum Albumine, Vaccine Research, 1998; 145-164.
10. Bovin Serum Albumine, Vaccine Research, 1998; 145-164. 10. Panchagnula R. “Transdermal delivery of drugs”. Indian Journal Pharmacology, 1997; 140-156.
11. Cevc G. “Isothermal lipid phase”, Transitions Chemistry and Physics of Lipids, 1991; 293-299.
12. Modi CD, Bharadia PD. “Transferosomes: New Dominants for Transdermal Drug Delivery”. Am. J. PharmTech Res., 2012; 71-91.
13. Sheo DM, Shweta A, Vijay KT, Ram CD, Aklavya S, Ghanshyam M. “Enhanced Transdermal delivery of indinavir sulfate via transferosomes”. Pharmacie Globale (IJCP), 2010; 1-7.
14. Neha Thakur, Prabhat Jain, Vivek Jain. Formulation, development and evaluation of transferosomal gel. Journal of drug delivery and therapeutics, 2018; 8(5): 168-177.
15. Lei W, Yu C, Lin H, Zhou X (2013). Development of tacrolimus loaded transfersomes for deeper skin penetration enhancement and therapeutic effect improvement in vivo. Asian J Pharm. 8(6),336–345.
16. Guo F., Wang J., Ma M., Tan F., Li N (2015). Skin targeted lipid vesicles as novel nano-carrier of ketoconazole: characterization, in vitro and in vivo evaluation. J. Mater. Sci. Mater. Med. 26,175.