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FORMULATION AND INVITRO EVALUATION OFTERBINAFINE EMULGEL

M.S.Rani*, .T.Vijayendra, K.Sowjanya, Y.Ganga Sirisha, K.Naga Lakshmi, V.Vidya

Department of Pharmaceutics, JITS College of Pharmacy, Kalgampudi, Andhra Pradesh,India.

ABSTRACT

Terbinafine is categorized as synthetic allylamine antifungal drug and is successfully used to treat Fungal disorders. Terbinafine maximum wavelength is determined by UV-Visible spectrophotometer using 6.8 pH phosphate buffer and was detected to be 283 nm. Terbinafine emulgel was formulated using light liquid paraffin as oil phase and emulsifying agents tween 20 and span 20 for emulsion and incorporated into gel using HPMC and carbopol 934 polymers in different ratios.The optimized formulation F7 showed a shear thinning with thixotropic property with better spreadability, viscosity and in-vitro permeability compared to other formulations.In the study it was observed that the concentrations of tween20 spann 20 and light liquid paraffin has shown effect on viscosity, spreadability and in-vitro drug permeability. Increased amount of liquid paraffin showed suppress activity of tween 20 and span 20.The surface morphology of the optimized formulation was observed by Scanning Electron Microscopic study.Thus Terbinafine emulgel which could increase the drug permeability across the skin and fast release of the drug could be successfully achieved.

Key Words: Terbinafine, Carbopol, HPMC

Author for correspondence
M.S.Rani,
Department of Pharmaceutics,
JITS college of Pharmacy,
Kalgampudi, Andhra Pradesh, India.
Email id: msrani.jits01@gmail.com.

INTRODUCTION

Transdermal drug delivery system has been in existence for a long time. In the past, the most commonly applied systems were topically applied lotions, creams and ointments for dermatological disorders. The occurrence of systemic side-effects with some of these formulations is indicative of absorption of the drugs through the skin, which lead to the idea of TDDS. In a broad sense, the term transdermal delivery system includes all topically administered drug formulations intended to deliver the active ingredient into the general circulation. Transdermal therapeutic systems have been designed to provide controlled continuous delivery of drugs via the skin to the systemic circulation.Transdermal drug delivery system (TDDS) established itself as an integral part of novel drug delivery systems[2]. The novel Transdermal drug delivery is defined as self-contained, discrete dosage forms which when applied to the intact skin, deliver the drug through the skin at controlled rate to the systemic circulation[1].Transdermal delivery of medications was foreshadowed in earlier era as by the use of certain plasters and ointments. The mustard plaster, applied as a home remedy for severe chest congestion, may be considered an example. Powdered mustard seeds were mixed with warm water, and the resulting paste was spread on a strip of flannel, which was applied to the patient‟s chest with a cloth binding

wrapped around the body to hold the plaster in place. The history of plasters has been traced back to antiquity. In addition to mustard plasters, several other plasters were recognized in early 20th century editions of the United States Pharmacopeia (USP) and National Formulary (NF). At one time, Belladonna Plaster, containing 0.25 – 0.30% of belladonna root alkaloids, was believed to acttransdermally as an analgesic. Perhaps the most remarkable forerunner of modern transdermal medication was Strong Mercurial Ointment, used as a treatment for syphilis when Salvarsan and other arsenicals were in use, before the discovery of penicillin.For the first time use of transdermal drug delivery system was done by the USFDA in December 1979, which administered scopolamine for motion sickness [2].Semisolids serve as carriers for drugs that are topically delivered by way of the skin, cornea, rectal tissue, nasal mucosa, vagina, buccal tissue, urethral membrane, and external ear lining. Because of their peculiar rheological behavior, semisolids can adhere to the application surface for sufficiently long periods before they are washed off. This property helps prolong drug delivery at the application site. Drug delivery by means of semisolid dosage forms has seen new challenges in the past few years in terms of altered drug-release profiles as well as the enhanced stability of API [3, 4].Numbers of medicated products are applied to the skin or mucous membrane that either enhance or restore a fundamental function of skin or pharmacologically alter an action in the underlined tissues. Such products are referred as topical or dermatological products. Many widely used topical agents like ointments, creams lotions have many disadvantages. They have very sticky causing uneasiness to the patient when applied. Moreover they also have lesser spreading coefficient and need to apply with rubbing. And they exhibit the problem of stability also. Due to all these factors within the major group of semisolid preparations, the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparations. A gel is colloid that is typically 99% wt liquid, which is immobilized by surface tension between it and a macromolecular network of fibers built from a small amount of a gelating substance present. In spite of many advantages of gels a major limitation is in the delivery of hydrophobic drugs. So toovercome this limitation an emulsion based approach is being used so that even a hydrophobic therapeutic moiety can be successfully incorporated and delivered through gels [5].

MATERIALS AND METHODS

Formulation of Terbinafine emulgel

Gel preparation [6-8]

The composition of Terbinafine emulgel 2% w/v was shown in the formulation code table. The carbopol gel was prepared by dispersing 0.25g of carbopol 934 in purified water with constant stirring at a moderate speed and soaked overnight. The gel was obtained by neutralizing the dispersion with tri ethanol amine and pH is adjusted to 6.5 and purified water was added to adjust the weight to 50ml.In case of Hydroxy Propyl Methyl cellulose gel was prepared by dispersing HPMC in hot purified water (80^0C) and the dispersion was cooled, then weight was adjusted to 50ml with purified water.

Emulsion preparation:

The oil phase of emulsion was prepared by dissolving span 20 in light liquid paraffin and heated upto 70^0-80^0C.Aqueous phase was prepared by dissolving tween 20 and drug in 5ml ethanol and heated upto 70^0-80^0C. Methylparaben, propylparaben were mixed in propylene glycol and glutaraldehyde and this added this mixture was dissolved in aqueous phase.Then oil phase was mixed slowly with aqueous phase and final volume is made with purified water.

Emulgel preparation:

The obtained emulsion was mixed with the gel and volume was adjusted to 50ml with water and subjected to homogenization for 45 minutes to get Terbinafine emulgel 2% w/v.

In-vitro drug permeation study

In-vitro permeation study was carried out using keisharychein cell having capacity of 18ml volume. Egg membrane was isolated and used for the study. 5ml of emulgel was spread evenly on to the egg membrane. The egg membrane was clamped between donor and receptor compartment. The receptor compartment was filled with 16ml of 6.8pH phosphate buffer maintained at 37ºC and stirred by using magnetic stirrer. The sample (2ml) was collected at

suitable time intervals and analyzed for drug content by UV-Visible Spectrophotometer 1700 (Shimadzu, Japan) at 283nm after appropriate dilutions as discussed earlier.

RESULTS AND DISCUSSION

The viscosities of all the formulations were measured using Brookfield viscometer at 10 rpm using spindle 6, it was found that all the formulations were followed shear thinning effect with thixotropic property. It was observed that the viscosity of the formulation increases with increase in emulsion-gel ratio.Drug content of all the formulations were carried out as per procedure stated in the methodology section. Drug content of all the formulations was found to be in the range 97.54%-99.90% as indicates in the table-1.

Table-1 Drug content determination

S.no	Formulation code	Mean%
1	F1	98.41
2	F2	99.15
3	F3	98.02
4	F4	99.47
5	F5	98.83
6	F6	97.54
7	F7	98.74
8	F8	99.90

The in-vitro permeation studies of all the formulations were carried out using Keisharychein as described in the methodology section using egg membrane as a permeation membrane for the study. The comparitive cumulative percentage drug permeation data of all the formulations F1 to F8 were shown in the table-2 and plots in the fig-1 respectively. The optimized formulation F7 containing maximum concentration of span 20 and tween 20 showed highest % drug permeation at the end of 12 hrs and hence this formulation was selected as optimized formulation for further study. It was revealed that span 20 and tween 20 concentration was having positive effect on the drug permeation through the membrane.

Table-2 % cumulative drug release data for F1 to F8

	% Cumulative drug release							
Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	5.17	5.56	4.10	5.18	6.01	3.94	8.80	5.76
2	12.02	8.61	7.25	7.93	13.42	6.15	16.51	7.51
3	16.54	13.25	10.93	12.45	25.08	9.37	29.72	11.05
4	25.16	19.13	12.28	17.62	32.75	11.20	38.64	16.54
5	33.47	26.58	23.68	26.01	38.62	22.46	47.38	25.93
6	41.31	34.40	28.41	32.85	45.27	25.34	55.13	30.24
7	49.67	42.79	33.06	42.56	56.91	29.81	63.02	38.85
8	58.46	49.83	37.12	46.42	62.84	34.65	70.61	40.69
9	60.02	52.32	42.62	49.83	68.56	40.65	77.54	45.65
10	68.32	59.82	49.53	52.64	76.85	46.74	83.45	52.25
11	74.60	63.25	53.62	57.45	80.25	50.15	85.05	55.48
12	76.77	69.53	60.31	62.06	84.32	58.09	89.97	63.42

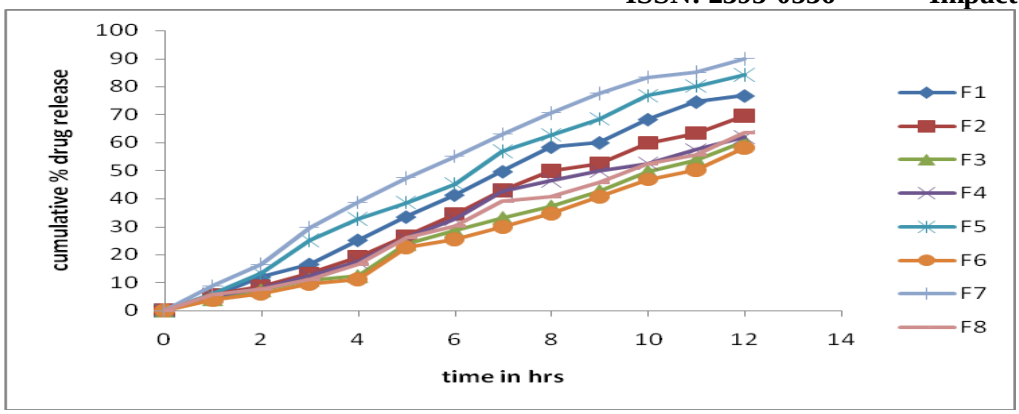

Fig-1 In vitro drug permeation graph

The drug release kinetics was studied with invitro drug permeation data for all the formulations F1 to F8 and results were stated in the table, the best fit model for selected formulation F7 were found to be Zero order model with non-fickian diffusion (Table-3).

Table-3 Release kinetics of optimized formulation

	ZERO	**FIRST**	**HIGUCHI**	**PEPPAS**
	% CDR Vs T	**Log % Remain Vs T**	**%CDR Vs √T**	**Log C Vs Log T**
Slope	7.757527473	-0.14226443	29.57298225	1.343816675
Intercept	4.671758242	2.272945911	-15.3200226	0.639814304
Correlation	0.990176129	-0.82109574	0.976979985	0.908588553
R 2	0.980448767	0.674198227	0.95448989	0.825533159

CONCLUSION

Terbinafine is categorized as synthetic allylamine antifungal drug and is successfully used to treat Fungal disorders. On this contest, emulgel was formulated using carbopol 934 and HPMC, liquid paraffin as oil phase, emulsifying agents like tween 20 and span 20 and propylene glycol as permeation enhancers.On basis of quality of emulgel produces total eight formulations F1 to F8 were selected. They were evaluated for physical appearance, pH, rheological study, spreadability, drug content and in-vitro drug permeation study.Prior to formulation drug polymer interaction studies were carried by FTIR and found to me compatible and to find out the maximum wavelength of mitrazapine UV-Visible spectroscopy was used using 6.8 pH phosphate buffer.The effect of formulation variables on the drug permeation kinetics and the increased permeation of emulgel formulation in contrast to optimized formulation were also studied.Thus, the formulated emulgel had a distinct advantage over existing conventional dosage form in that the drug permeation was found to be rapid across the skin and hence the increased therapeutic response by bypassing 1st pass metabolism and with no gastro intestinal problems and patient compliance.

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