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Formulation and Evaluation of Luliconazole

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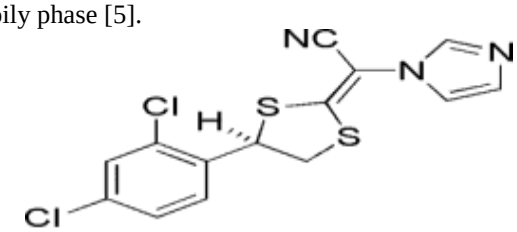
ABSTRACT
The aim of the present study was to develop an emulgel formulation of Luliconazole using carbopol 934 as a gelling agent. The Luliconazole has anti-Fungal activity. It acts by inhibiting lanosterol demethylase, which is major component of fungus cell wall. Emulgel has emerged as a promising drug delivery system for the delivery of hydrophobic drugs. The prepared emulgel were also evaluated for their physical properties, pH, drug content and rheological properties. Candida albicans was used as a model fungus to evaluate the antifungal activity of the prepared formulations. Stability studies revealed no significant differences in formulation. It was concluded that Luliconazole emulgel formulation (F3) prepared by using Carbapol 934 as gelling agent, emulsifying agent in its high level and liquid paraffin in its low level was the choice of formula, since it showed the highest drug release and antifungal activity.

KEYWORD- Luliconazole, Topical Gel, Antifungal, Topical Drug Delivery, Carbapol 934.

I. INTRODUCTION

Topical formulations apply a wide spectrum of preparations both cosmetic and dermatological, to healthy or diseased skin [1]. These formulations range in consistency from solid through semisolid to liquids. When gels and emulsions are used in a combined form, the dosage forms are referred to emulgel. [2, 3]As the name suggests they are the combination of emulsion micro-emulsion and gel. Novel polymers with complex fuctions as emulsifires and thickeners have been widely used due to their gelling capacity which allows the formulation of stable emulsion by decreasing surface and interfacial tension and also by increasing the viscosity of the aqueous phase. Oil/water and water/oil emulsions are used as vehicles to deliver various drugs to the skin [4]. Emulsion gels are has importance due to many reasons; they have better application property in comparison to classical formulation as creams and ointment, they have faster and more complete release of the drug from the vehicle to the skin, also they are convenient to apply on hairy skin due to the absence of greasiness and lack of residue upon application. They permit the incorporation of both aqueous and oleaginous ingredients, so hydrophobic or poorly water soluble drugs as antifungal agents are easily incorporated in such type of vehicles through the proper choice of the oily phase [5].



luliconazole

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STRUCTURE OF LULICONAZOLE

Luliconazole has anti-fungal activity. Luliconazole is inhibiting the enzyme lanosterol demethylase. Lanosterol demethylase is needed for the synthesis of ergo-sterol, which is a major component of the fungus cell membranes. For skin care and the topical treatment of dermatological diseases, a wide choice of vehicles including solid, semisolids and liquid Preparation is available to physician and patients. Within the major groups of semisolid preparations, the use of transparent emulgel has expanded, both in cosmetics and pharmaceuticals. Emulgel or jellified emulsion is stable one and better vehicle for hydrophobic or water insoluble drugs as Luliconazole. Also emulgel has a high patient acceptability since they possess the advantages of both emulsions and gels. Therefore, they have been recently used as vehicles to deliver various drugs to the skin. [6-7]

II. METHODOLOGY

MATERIAL AND METHOD

Luliconazole was obtained as a gift sample from A. S. Life Science, Haryana, India. Carbopol 940 was obtained from Loba chemicals Mumbai. Liquid paraffin, propylene glycol, ethanol

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was procured from Naprod life science, Mumbai. Methyl parabens and propyl parabens procured from Chem. Pure pvt.ltd. Mumbai. All other chemicals used were of analytical grade and were used without any further chemical modification.

PREFORMULATION STUDIES

Melting point determination:

The melting point of the sample is done to check the purity of the sample. Melting point is defined as the temperature at which a solid substance transits its state from solid to liquid. [10] Melting point of luliconazole was found by using the digital melting point apparatus from Remi Instrument.

Solubility analysis:

Solubility is defined as the ability of a solute to dissolve in a liquid (solvent) to form a homogeneous solution. Factors affecting solubility are; type of solvent used, temperature and pressure. [11] Solubility analysis was primarily performed in order to find out a suitable solvent to dissolve the API, lipid and excipients used for formulation preparation.

Partition Coefficient of the Drug:

Partition coefficient is the measure of the lipophilic and hydrophilic nature of a drug substance. It is defined as the extent to which a substance is distributed between two liquid phases, one being the aqueous phase and other being the oily phase. The majorly used phases are water and n-octanol (oil phase) in the ratio 1:1.

Determination of λmax of luliconazole in ethanol:

Stock solution of 100µg/ml was prepared by dissolving accurately weighed 100mg luliconazole in 100ml of ethanol. The dilution was scann ed from 400–200 nm with UV spectrophotometer using the blank solution as ethanol. The spectrum of absorbance versus wavelength was recorded on UVspectroscopy and analyzed for absorbance maximum and the highest absorbance was noted.

Calibration curve of λmax of luliconazole in ethanol:

Luliconazole (100mg) was dissolved in 100ml of ethanol solution in a volumetric flask. This solution of 100µg/ml was used to prepare aliquots of varying concentration of 2-20 µg/ml respectively. Absorbance of each of the solution was measured at 296 nm in UV-spectrophotometer using ethanol solution as blank and graph of concentration versus absorbance was plotted. The slope, straight line equation and correlation coefficient were obtained from the calibration curve intercept.

PREPARATION OF LULICONAZOLE

Preparation of emulsion: In this o/w emulsion, the oily phase was prepared by dissolving Span 20 in light liquid paraffin while the aqueous phase was prepared by dissolving Tween 20 in purified water. Methyl paraben was dissolved in propylene glycol whereas drug was dissolved in methanol and both solutions were mixed with the aqueous phase. Both the phases were heated separately to 70° to 80°C; then the oily phase was added to the aqueous phase with continuous stirring until cooled to room temperature.

Preparation of gel:

The gel was prepared by dispersing Carbopol 940 in purified water with constant stirring at a moderate speed and then the pH was adjusted approximately to 6 using tri-ethanol amine. Finally, the emulgel was prepared by mixing both the gel and emulsion in 1:1 ratio. The composition of different formulations has been discussed in Table 1:

Evaluation

1. Physical Appearance and pH Determination:

The prepared Luliconazole emulgel were inspected visually for their colour, homogeneity, Consistency and pH. The pH values of 1% aqueous solutions of the prepared emulgels were measured by a pH meter (Orion Research, Inc., USA). [12]

2. Drug Content Determination: The drug content of Luliconazoleeemulgel was measured by dissolving a known weight of the emulgel formulation (one gram) in 100 ml methanol, appropriate dilutions were made and the resulting solution was then filtering using millipore filter (0.45 µm). Absorbance was measured at 296 nm using UVspectrophotometer (Shimadzu UV 1800). [11] Drug content was calculated using the slope and the intercept obtained by linear regression analysis of standard calibration curve.

3.Rheological Studies:

The viscosity of different Luliconazole emulgel formulations was determined at 25˚C using a Brookfilled Viscometer. Viscosity was measured by using spindle (52).

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4.Skin Irritation Test (Patch Test):

A set of 8 rats was used in the study. The emulgel was applied on the properly shaven skin of rat. Undesirable skin changes, i.e., change in colour, change in skin morphology were checked for a period of 24 h.

5. Spreading Coefficient:

Spreading coefficient was determined by apparatus suggested by Mutimer. It consists of a wooden block, which is attached to a pulley at one end. Spreading coefficient was measured on the basis of 'Slip' and 'Drag' characteristics of emulgels. A ground glass slide was fixed on the wooden block. An excess of emulgel (about 2 g) under study was placed on this ground slide. The emulgel preparation was then sandwiched between this slide and second glass slide having same dimension as that of the fixed ground slide. The second glass slide is provided with the hook. Weight of 500 mg was placed on the top of the two slides for 5 min to expel air and to provide a uniform film of the emulgel between the two slides. Measured quantity of weight was placed in the pan attached to the pulley with the help of hook. The time (in s) required by the top slide to cover a distance of 5 cm was noted. A shorter interval indicates better spreading coefficient.

6. In-Vitro Release Studies:

The study was carried out using the modified USP apparatus type II (Hanson SR8-plus 80, USA). Two grams of each emulgel was spread on the cellophane membrane previously soaked overnight in the dissolution medium. The loaded membrane was stretched over a glass cup of diameter 3 cm, and then the cup was immersed in 100 ml of the dissolution medium (25%v/v DMF in 0.02N HCl) to maintain sink condition, the temperature was maintained at 37±0.5°C with paddle agitation speed 50 rpm. An aliquot of 5 ml was withdrawn at different intervals of time. The withdrawn samples were replaced by equal volumes of fresh release medium. The samples were assayed using spectrophotometer at λ max 296 nm. The effect of gelling, the liquid paraffin concentration and emulsifying agent concentration was studied. [5].

7. Antifungal Activity Studies:

The prepared emulgel formulations were tested against candida albican strain using agar cup method. Cups of 10mm diameter were made aseptically in savoured dextrose agar after being inoculated with the tested fungal suspension strain (106cfu/ml) by spreading on the agar surface The cups were filled with each prepared formulation by sterile syringe. The zone of inhibition of each cup was observed and the radius of the zone of inhibition was measured. [17]

8. Stability Studies:

The prepared Luliconazole emulgel were packed in aluminium tubes (5 grams) and subjected to stability studies at 25°C/60% relative humidity (RH) and 40°C/75% RH for period of 3 months. Samples were withdrawn at time intervals of 15 days and evaluated for physical appearance, pH, rheological properties, drug content and drug release. [18]

9. Stability Study

All the prepared emulgel formulations were found to be stable upon storage for 2 months, no change was observed in their physical appearance, pH, rheological properties and drug content.

III. CONCLUSION

The main goal of the study was to formulate an antifungal luliconazole emulgel for topical route of administration to treat patients suffering from Candida albicans, Malassezia spp., and Aspergillus Luliconazole has been concluded to be a drug of BCS Class II (low soluble and high permeable drug). The present work focused on preparing luliconazole emulgel by employing varied concentrations of methanol, propylene glycol, liquid paraffin, span and tween to form an appropriate formulation. The prepared emulsions were loaded into the hydrogel made up of Carbopol 934 in order to get the required emulgel. As resulted all the preparations, F1-F4 was found to be suitable in all preparations and formulation F3 was most stable. All the formulations were stored at room temperature 25-35°C and then observed for 1 month. Stored formulations were observed for phase separation and related substances (bacterial growth). None of the formulation showed phase separation and bacterial growth. The % drug release studies revealed that formulation F3 showed the maximum amount of drug release within five hours. Hence, from all the preparations prepared, F3 was chosen to be the best one. According to the findings, it can be concluded that that luliconazole emulgel can prove to be an effective and more efficient system for topical fungal treatment as compared to the traditional

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luliconazole systems that are commercially available.

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