A Review Study on Anti-Fungalemulgel

Aamir Qayoom Rather, Mrs. Ranjana Joshi, Mrs. Nutan Mimrot, Dr. Revathi A Gupta

Institute of Pharmacy, Dr. A.P.J. Abdul Kalam University

ABSTRACT

According to the combined results of current research, the emulgel drug-delivery technology represents a substantial improvement over conventional topical antifungal formulations. Emulgels successfully overcome important limitations such low drug solubility, insufficient penetration, and inconsistent therapeutic response by combining the benefits of both emulsions and gels. Their superior rheological characteristics, ease of formulation, and better physicochemical stability all help to improve product uniformity and patient adherence. Additionally, emulgels promote better skin penetration and regulated drug release, which boosts antifungal effectiveness and speeds up clinical development. These characteristics demonstrate that emulgels are a strong, novel, and very successful approach to treating cutaneous fungal infections, with great promise for wider therapeutic uses.Keywords: cutaneous fungal infection, antifungal drugs, emulgel, and therapeutic.

INTRODUCTION

Topical Formulation-

Topical drug delivery can be defined as the application of a drug containing formulation to the skin to directly treat the cutaneous disorder. The topical drug delivery system is generally used where other routes (such as oral, sublingual, rectal, and parental) of drug administration fails or in local skin infection like fungal infection. Topical drug delivery is an attractive route for local and systemic treatment. A unique aspect of dermatological pharmacology is the direct accessibility of the skin as a target organ for diagnosis and treatment.

Classification of topical preparation.

Classification of topical drug delivery system-

Solid: Powders, Plasters Ointments,

Semi solid: Creams, Poultices, Gels, Pastes, Emulgel.

Liquid: Liniment, Lotions, solution, tinctures, Emulsions, Suspensions, Paints

Miscellaneous: Transdermal drug delivery systems, Tapes and Gauzes, Rubbing alcohols, Liquid cleanser, and Topical aerosol.

Advantages:

An increased dose of medication is applied where it is needed.

There are reduced side effect and toxicity to other organs compared to systemic medication.

Avoiding first pass metabolism.

Improving patients compliance.

Possible and easy self-medication.

Disadvantages:

-They can be time consuming to apply.

-The application may also be uncomfortable.

-Factors Affecting Topical Absorption of Drug-

Physiological Factors-

Skin thickness: Varies from epidermis to subcutaneous layer. Epidermis has high thickness about 100–150 µm. Skin on the sole and palm has a high rate of diffusion.Lipid content: It is an effective water barrier, percutaneous penetration increases when lipid weight in stratum corneum is low.Density of hair follicles: Hair follicle infundibulum has a large storage capacity about10 times more than the stratum corneum.

Density of sweat glands.
Skin pH: Sweat and fatty acid secreted from sebum influence the pH of the skin surface.Blood flow.
Hydration of skin: Can enhance permeation of drug.
Inflammation of skin: That disrupts the continuity of stratum corneum increases permeability.
Skin temperature: Increase in temperature gives rise to increase in the rate of skin permeation.

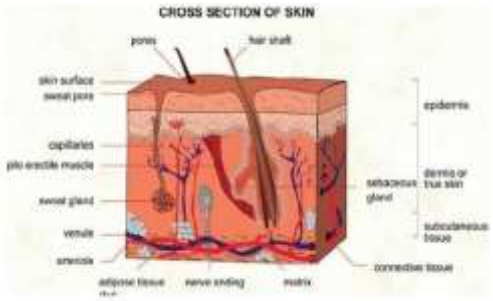
Physiochemical Factors-

- Partition coefficient.
- Degree of ionization (only unionized drugs gets absorbed well).
- Effect of vehicles.

Physiology of Skin-

Most of the topical preparations are meant to be applied to the skin. Hence, a basic knowledge of the skin and its physiology function are very important for designing topical dosage form. The skin of an average adult body covers a surface area approximately 2 m2 and receives about one-third of the blood circulating through the body. An average human skin surface is known to contain, on the average 40–70 hair follicles, and 200–300 sweat ducts on every square centimeter of the skin. The pH of the skin varies from 4 to 5.6. Sweat and fatty acid secreted from sebum influence the pH of the skin surface. The skin can be considered to have four distinct layers of tissue .

Structure and Physiology of the skin



Emulgel:

Emulgel is prepared both in oil- in- water and water- in- oil type emulsion mixed with gel. Oil- in- water type is used for lipophilic drugs and water- in- oil type is used for hydrophobic drugs' delivery. When gels and emulsions are used in a combined form, the dosage forms are referred to emulgel.Emulgel structure In the mid-1980's, Emulsion-gels have been gaining importance in pharmaceutical topical semisolid dosage forms. Emulgels are emulsions, either of the oil-in-water or water-in-oil type, which are gelled by mixing with a gelling agent.

Reason for selection of drug-

Suitable for formulation of emulgel in topical drug delivery system.

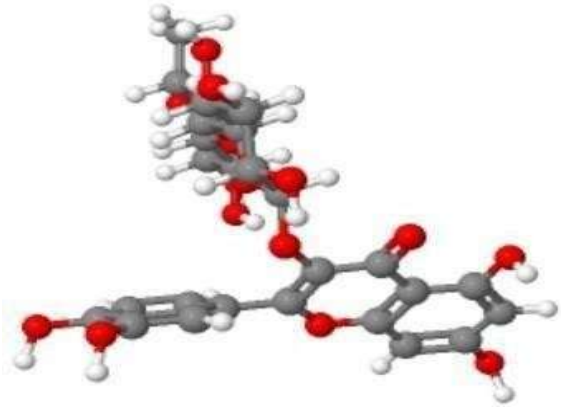
The skin is, however, a good barrier to drug permeation and drug flux is known to be low.In fact, drug absorption following application to the skin is so low that only a few drugs formulate for topical delivery.Treatment for the skin infection like psoriasis, fungal infection by avoiding first pas metabolism hence increasing bioavailability of the drug.

DRUG PROFILE-

Phytomelim is one of the phenolic compounds found in the invasive plant species, Carpobrotus edulis. Its name comes from the name of Ruta graveolens, a plant that also contains rutin. Various citrus fruit peels contain 32 to 49 mg/g of flavonoids expressed as rutin equivalents. Citrus leaves contain rutin at concentrations of 11 and 7 g/kg in orange and lime trees, respectively. In 2021, Samoan researchers identified rutin in the native plant, matalafi (Psychotria insularum).

Drug Name - Phytomelin

Structure



3-d structure of Phytomelin Synonyms- Phytomelin Rutin Rutoside Rutosido

EXPERIMENTAL WORK:

Preformulation Studies:-

Organoleptic properties-Determination of Melting point -Melting point of drug sample was determined by using melting point apparatus. Drug sample was filled in one end open capillary tube. The capillary was placed in melting point apparatus and gradually temperature rises when drug sample were melted the melting point of sample powder was recorded.

Determination of λmax By UV spectrophotometer-

100mg of Luliconazol sample were weighed and transferred to 100ml volumetric flask and adding 1:1 methanol: water as solvent upto the mark to give 1000µg/ml solution. 10ml of the above solution was pipetted out in a 100ml volumetric flask and diluted up to the mark.

Preparation of calibration curve of Luliconazol- Preparation of Standard Stock Solution:

transferred to a 100ml volumetric flask and volume was made upto the mark to give 100µg/ml solution as standard working solution.

Preparation of Working Solutions:

A series of concentrations ranging from 2-20µg/ml. was prepared by pipetting out 0.2, 0.4, 0.6, 0.8, 1, 1.2, 1.4, 1.6, 1.8 and 2ml of standard working stock solution to different 10ml volumetric flasks. 1:1 methanol: water was added upto the mark to give 2-20µg/ml working solutions of Luliconazol.

Partition Coefficient-

The partition coefficient determination of Luliconazol was performed using n-octanol as the oil phase and water (1:1) as the aqueous phase. The two phases were mixed in equal quantities (50 ml) by adding 50 mg of drug in a separating funnel and was saturated with each other at room temperature for 24 hour to separate the two phases. The test compound in each phase was sample and quantitated using UV spectroscopy.

Fourier-transform infrared(FTIR) spectroscopy-

Preparation of Emulsion-

The oil phase of the emulsion was prepared by first Cetostearyl alcohol is melted then mixed Oleic acid, Span 80 and Methyl salicylate while the aqueous phase was prepared by dissolving Tween 80 in purified water. Preservative Propyl paraben dissolve in Propylene glycol. Drug was dissolve in ethanol and both solutions were mixed with the aqueous phase. Both the oily and aqueous phases were separately heated to 70℃ to 80℃, the oily phase were added to the aqueous phase with continuous stirring until cooled to room temperature.

Finally the emulgel was prepared by mixing of both gel and emulsion in 1:1 ratio

Drug Content Determination-

The drug content of Luliconazol emulgel was measured by dissolving a known weight of the emulgel formulation (1 gram) in 100 ml flask and adding 1:1 methanol: water, appropriate dilutions were made and the resulting solution was then filtering. Absorbance was measured at 299nm using UV- Spectrophotometer (Shimadzu UV 1800). Drug content was calculated using the slope and the intercept obtained by linear regression analysis of standard calibration curve.

In - Vitro Release Study-

The study was carried out using the modified USP apparatus type II. 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

Stability Studies-

The prepared Luliconazol emulgel were packed in aluminium tubes (5 gram) and subjected to stability studies at 25°C/60% relative humidity (RH) and 40°C/75% RH for period of 1 month. Samples were withdrawn at time intervals of 15 days and evaluated for physical appearance, pH, rheological properties, drug content and drug release.

RESULT AND DISCUSSION-

Preformulation Studies-

Organoleptic properties-

The drug was studied for their organoleptic properties like colour, odour, taste, crystallinity and pH observation was recorded.

Organoleptic Properties of Luliconazol

Melting point-

Melting point of drug was determined by capillary method was found to be 147℃ (Table 7). The observed value was identical to the reported value i.e. 149℃. The observed melting point confirmed the drug as Luliconazol.

Determination of λmax is 299nm

Preparation of calibration curve-The wavelength of maximum absorbance, λmax for Luliconazol in distilled water and methanol (1:1) was determined with the help of UV-Visible Spectrophotometer.

Qualitative solubility of Luliconazol

Where,FTIR Spectrum of Luliconazol was obtained by scanning the drug in the range of 4000 to 400cm-1. Major peaks observed were as 3114.75, 3075.75 & 3040.00cm-1, minor peaks observed were as 7.59.29 & 1101.04cm-1 whose presence resembled the structure of Luliconazol. Observed FTIR spectra and standard value were as depicted in Fig. 18. The observed value was within the range or very close to the characteristic peaks of standard value confirming drug as Luliconazol.

Evaluation Parameter-

Physical appearance-

Emulgel formulations were white viscous creamy preparation with a smooth homogeneous texture and glossy appearance. Result has been discussed in table

Physical Parameter of formulation

pH Determination-

pH of prepared Emulgel was measured by using pH meter. The pH of the emulgel formulation was in the range of 5.76-6.238 which considered acceptable to avoid the risk of skin irritation upon application to skin.

pH of emulgel formulation

Rheological Studies-Viscosity of different formulations was determined at 25℃ using Brookfield viscometer was measured by using spindle 61 and rpm 10.

Viscosity (mPas) of Luliconazol Emulgel

Drug content determination-

The drug content of different emulgel formulations was estimated by using UV spectrophotometer at 200-400 nm range. The release of drug through prepared formulation was found to be 96.82, 97.64, 97.62 and 98.02 respectively.

Drug content of Luliconazol emulgel formulation

In-Vitro Release studies- the release of the drugs from emulsified gel formation can be ranked in the following decending order.Data for in vitro cumulative % drug release data of formulations F1-F4.In-vitro cumulative % drug release of formulation F1–F4.

Antifungal activity study-

The antifungal activity of Luliconazol emulgel was studied (Table). The zone of inhibition was measure for antifungal activity of drug. The greatest activity was observed in F3 formulation i.e. 49.4mm and the lowest activity were found in F1.

Antifungal activity of Luliconazol emulgel

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.

CONCLUSION-

In the coming years, topical drug delivery will be used extensively to impart better patient compliance. Since emulgel is helpful in enhancing spreadability, adhesion, viscosity and extrusion, this novel drug delivery become popular. Moreover, they will become a solution for loading hydrophobic drugs in water soluble gel bases for the long term stability.

REFERENCES-

Ashara kalpesh, Soniwala moinuddin, & Shah ketan, “Emulgel: A novel drug delivery system”, Journal of Pakistan Association of Dermatologists, 2016; 244-249

Phad R. Anil, Dilip Tanaji & Ganapathy R. Sundara, “Emulgel: A Comprehensive Review for Topical Delivery of Hydrophobic Drugs”, Review article, 2018

Panwar A.S., Upadhyay N., Bairagi M., Gurjar S. and Jain D.K., “Emulgel: A review”, Asian Journal of Pharmacy and Life Science, 2011

Redkar R. Mayuresh, Dr. Patil Sachinkumar and Rukari G. Tushar, “Emulgel: A modern tool for topical drug delivery”, World Journal of Pharmaceutical Research, 31 march 2019, 586-597.

Bhatt Preeti and G. Gnanaranjan, “Emulgel: A Novel Formulation Approach Fir Topical Delivery Of Hydropobic Drugs”, International Research Journal of Pharmacy, 2013, 4(2)

Bhowmic Debjit, Gopinath Harish, Pragati B. Kuma and Sampath K.P.Kumar, “Recent Advances In Novel Topical Drug Delivery System”, The pharma innovation, 2016

Buhse Luchinda, Goutam Mamta, Kibbe Arthur and Turujman Saleh, “Topical Drug classification”, International journal of pharmaceutics, March 1017

Ueda T. Clarence, Shah P. Vinod, Kailas Thakkar, “Topical & Transdermal Drug Products”, Pharmacopeia forum volume 35(3), may-june 2009

Vats S, Saxena C, Easwari TS, and Shukla VK, " Emulsion Based Gel Technique: Novel Approach for Enhancing Topical Drug Delivery of Hydrophobic Drugs" International journal of pharmaceutical science and research, 2014; 3: 649-60

Sharma S., "Topical preparations are used for the localized effects at the site of their application by virtue of drug penetration into the underlying layers of skin or mucous membrane", Pharmaceutical reviews, 2008; 6: 1.

C. Surver and F.A. Davis, "Bioavailability and Bioequivalence, Dermatological and Transdermal Formulation", Marcal Dekker, New York, 2002; 323- 327.

Prakash Raj Eugine leo & Balakrishnan Sangameswaran, "Short review- Emulgel", Journal of Comprehensive Pharmacy, 2015

Akbari Sweeta, Nour Abdurahman hamid, "Emulsion types, stability mechanisms and rheology: A review", International Journal of Innovative Research and Scientific Studies, 20