WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A Review On Topical Anti-Fungal Formulations

Neelam Brinda Gouri [1], Dr.M. Sunitha Reddy [2]

[1, 2] Department of Pharmaceutics, Center for pharmaceutical sciences, UCEST, Jawaharlal Nehru Technological University, Kukatpally, Hyderabad, Telangana-500085 Email- brindagourineelam28@gmail.com

A B S T R A C T

Fungus-induced skin infections are the most common skin health issue worldwide. Fungal infections are commonly treated with topical or systemic antifungal therapy. Topical fungal therapy is usually advised since it provides customised therapy with fewer side effects.[1] Many antifungal medications are available on the market in different topical formulations (such as creams, ointments, and powders) for local dermatological therapy[2].Currently, these antifungal drugs are offered for sale in standard dosage forms as sprays, gels, lotions, and creams.

Keywords: Topical formulations, Antifungal, Fungal infections, Posaconazole, Emulgel, Gel.

Introduction

Fungi that cause infections are mycotic infection or fungal infection, they are caused by Dermatophytes, Yeast, Moulds. They usually effect skin, hair, nails, mouth, throat, lungs, urinary tract, mucous membrane also other parts of body Dermatophytes results in Tinea corporis,Tinea cruris, Tinea faciei, Tinea mannum, Tinea pedis. Yeast results in Candida intertigo and pityriasis versicolor, Moulds result in Tinea nigra and nail infections, Fungi obtains nutrition from keratinized materials,so they are typically responsible for fungal infection of skin, scalp, nails Fungal infections are common where the moisture is present and have lot of friction. They are serious in case of diabetes and weekened immune system.
To treat such infections there are anti-fungal drugs, that are available in the form of oral dosage forms, parentrals, and mostly topical formulations. This review article focuses on Topical antifungal agents.
Topical anti-fungal treat fungal infections which when applied onto skin, nails, hair, vaginally, inside mouth. Topical formulation that are available are creams, gels, lotions, ointments, Shampoos, Sprays, Tinctures, Powders.
The most prevalent problem with skin health globally is fungus-induced skin infections. Topical or systemic antifungal treatment is frequently used to treat fungal infections. Due to its tailored therapy and lower side effects, topical fungal therapy is typically recommended. Because of their unique structural and functional characteristics, advanced topical carriers solve biopharmaceutical problems with traditional drug delivery vehicles, such as inadequate bioavailability and poor retention. Evidence from the literature suggests that topical nanocarriers containing antifungal drugs exhibit optimal therapeutic efficacy while posing the least amount of harm. Topical anti-fungal medications are frequently delivered via nanocarriers such as solid-lipid nanoparticles, microemulsions, liposomes, niosomes, microsponge, nanogel, nanoemulsion, and micellar forms. The new techniques used in topical carriers to enhance the therapeutic efficacy of antifungal medications are outlined in this review.

Advantages.

1. No First pass metabolism.
2. Easy and convenient to apply.
3. Sustained drug delivery.
4. very low incidence of drug interactions.
5. very low systemic side effects and complications due to limited systemic absorption.
6. relatively low cost of therapy
7.Economical and simple to use.
8.Eliminating potential risks and drawbacks associated with intravenous therapy as well as the various conditions of absorption, such as changes in pH, the presence of enzymes, the time it takes for the stomach to empty, etc.
9. Continuous drug input leads to efficacy with a reduced total daily dosage of the medicine.
10. Prevents changes in medication levels between and among patients.
11.The effortlessness of discontinuing medication when essential.

12.A comparatively broad application range when compared to the nasal or buccal cavities
13.Possibility of more targeted medicine delivery to a particular location.
14.Preventing intestinal incompatibility.
15.Making use of medications with a brief biological half-life and a limited window of therapeutic application.
16.Optimizing the pharmacological and physiological reaction.
17.Boost commitment from patients.

Limitations

1) The patient feels uncomfortable when they are applied because they are quite sticky.

2) They also require rubbing in application due to their lower spreading coefficient.

3) They also show signs of fragility.

4) It is possible for drugs and/or excipients to trigger skin irritation or contact dermatitis.

5) Some medications have poor skin permeability.

6) The potential for allergic responses.

7) Applicable exclusively to medications whose actions depend on extremely low plasma concentrations.

8) Drugs may be denatured by an enzyme in the epidermis.

9) Drugs with greater particle size are challenging for the skin to absorb.

RESEARCH ARTICLES ON ANTIFUNGAL TOPICAL FORMULATIONS

1**) TOPICAL ANTIFUNGAL BIGELS:FORMULATION ,CHARACTERIZATION AND EVALUATION**

Bigels with antifungal substances, ciclopirox olamine and terbinafine hydrochloride, were made of hydrogel and oleogel,they were found to be physically stable at room temperature for 6 months, Amount of drug release was found to be reduced when oleogel concentration increased, All the formulations showed great inhibition of microsporum canis, Thus, bigels are promising dosage form for topical use.

2**)FORMULATION AND EVALUATION OF FLUCANAZOLE TOPICAL GEL**

This study was designed to formulate fluconazole for treating fungal infection on skin, this gel was formulated using different concentration of Carbopol 940, HPMC E4M, Methyl cellulose ,Pectin, Pluronic P407. 10 formulations were prepared. The results of in vitro drug release and permeation studies showed that highest values was from F3 .

3)FORMULATION AND EVALUATION OF ANTIFUNGAL NON-AQUEOUS MICROEMULSION FOR TOPICAL DRUG DELIVERY OF GRISEOFULVIN

Emulsions are water-in-oil or oil-in-water type, but emulsions may contain polar liquid as one of the phase .The study was to design a stable non-aqueous microemulsions using cosmetically approved ingredients .A non aqueous system was obtained with glycerin and olive oil stabilized by glycerol mono stereate with co surfactant. Results proved that non aqueous microemulsions can be used as vehicle for poorly water soluble drug,and oleogels

4) FORMULATION AND EVALUATION OF TOPICAL ANTIFUNGAL GEL CONTAINING ITRACONAZOLE

The gel was formulated by changing polymer ratio, Various formulations were prepared using carbapol and HPMC.The formulation was evaluated for % yield, spreadability, extrudability, wash ability and viscosity in vitro drug release study, skin irritation study, stability testing. Results indicated that the concentration of carbopol-934 and HPMC K4M significantly affects drug release and rheological properties of the gels

5)FORMULATION AND EVALUATION OF TOPICAL ANTIFUNGAL FLUCONAZOLE GEL USING ALOE VERA GEL

This gel was formulated using natural polymer that is aloe vera gel, along with two different gelling agents that is carbopol and HPMC. From among all the developed formulation F1 show better drug diffusion, good rheological properties, pH of F5formulation is sufficient to treat the skin infection. Result indicated that the concentration of aloe Vera significantly affected drug release and rheological properties of the gel.

6)PREPARATION AND EVALUATION OF VORICONAZOLE OINTMENT FOR TOPICAL DELIVERY

Voriconazole 5% ointment was prepared using water soluble ointment base, The method of preparation used was fusion method-in this process higher melting point substance should be melted first and add then other ingredients of the bases in order of their melting point, PEG4000 was melted and added to PEG400 and PEG600 by fusion method, results showed that the PEG ointment formulations exhibited better voriconazole release formulation.

7)FORMULATION, DEVELOPMENT AND EVALUATION OF EMULGEL OF GRISEOFULVIN

Griseofulvin Emulgel to enhance the permeation of drug through topical delivery. The system was formulated using Carbopol 940 as gelling agent, DMSO as penetration enhancer, Corn oil as oil phase. Different concentration of surfactants and gelling agent was used in various formulations . release of drug was increased with increase in concentration of Smix and decreased with increase in concentration of carbopol 940.

8) FORMULATION AND EVALUATION OF ANTIFUNGAL CREAM OF CHLORPHENESIN

Its an oil in water cream formulation, in which oil phase was prepared by mixing stearic acid with different oils such as coconut oil, liquid paraffin with different concentrations in different formulations, similarly aqueous phase was prepared by glycerine with aloe vera gel with different concentrations.

9)FORMULATION AND EVALUATION OF TOPICAL DELIVERY OF ANTIFUNGAL DRUG BIFONAZOLE USING MICROEMULSION BASED GEL

Microemulsions are transparent systems and typically consists of oil, surfactant, cosurfactant and aqueous phase, they are thermodynamically stable and droplet size <0.5 ,They are advantageous over traditional gels and creams , in this article microemulsion based gel formulation was prepared using xanthum gum. It was evaluated by checking its pH, spreadability, rheological studies and *in-vitro* drug release studies. Bifonazole microemulsion showed good invitro drug release

MECHANISM OF ACTION OF ANTI-FUNGALS

a. ECHINOCANDINS-Cyclic lipopeptide antibiotics that interfere with fungal cell wall synthesis by inhibition of β-(1,3)D-glucan synthase .Loss of cell wall glucan results in osmotic fragility.
Uses- It treats fungal infections caused by Aspergillus and candida species
Drugs-Caspofungin, Micofungin, Anidulafungin

b. POLYENES- Binds to ergosterol in the plasma membrane of sensitive fungal cells, form pores disrupt membrane function, allowing electrolytes and small molecules to leak from cell, resulting in cell death
Drugs- Amphoterecin B, Nystatin
Uses-

1. Amphotericin B- The drug of choice for Cryptococcal meningitis, Mucormycis and invasive fungal infection
2. Nystatin- treats mucosal, cutaneous, vaginal, esophageal candida infections

c. HETEROCYCLIC BENZOFURAN- Binds to polymerized microtubules and inhibit fungal mitosis .
Drugs- Griseofulvin
Uses- It is used only for dermatophytosis ,for Nails,Hair,Large Body Surface

d. ANTIMETABOLITE-drug is converted into cytostatic fluorouracil that interacts as 5-fluorouridine triphosphate with RNA biosynthesis and disturbs the building of certain essential protiens
Drugs-flucytocin
Uses-treats serious infection caused by susceptible strains of candida and also treats chromomycosis

e. AZOLES- Azole inhibit enzyme lanosterol 14α-demethylase;the enzyme necessary to convert lanosterol to ergosterol. Depletion of ergosterol in fungal membrane disrupts the structure and many function of fungal membrane leading to inhibition of fungal growth.
Drugs- ketoconazole,clotrimazole,fluconazole,itraconazole
Uses-

1. Ketoconazole-Topical and systemic antifungal, antiandrogenic and anti-glucocorticoid
2. Clotrimazole-Treats fungal infections, such as vaginal yeast infections, ,thrush and ringworm
3. Fluconazole-Drug of choice for cryptococcus neoformans after therapy with amphotericin B, for most candidemias, and for coccidioidomycosis.
4. Itraconazole-Drug of choice for treatment of blastomycosis, sporotrichosis, para coccidioidomycosis , and histoplasmosis

f. ALLYLAMINES- Inhibits squalene epoxidase, resulting in the blocking of the biosynthesis of ergosterol ,an essential component of fungal cell

membrane

Drugs- Terbinafine ,Butenafine ,Ciclopirox, Tolnafate

Uses

1.Terbinafine-Drug of choice for treating dermatophytosis and especially oonychomycoses

2.Butenafine- Active against Trichophyton, Epidermophyton And Malassezia

3.Ciclopirox- Redness , Irritation , Burning, Blistering or swelling at a site of application

LIST OF MARKETED TOPICAL ANTI-FUNGAL FORMULATIONS

S.no	DRUG NAME	BRAND NAME	STRENGTH
1	MICONAZOLE	MICOGEL CREAM	2%
		DAKLARIN CREAM	2%
		DAKLARIN GEL	2%
2	CLOTRIMAZOLE	CANAZOLE CREAM	1%
		CANDID GEL	1%
		CANDID CREAM	1%
		CANDID LOTION	1%
		LOTRIMIN AF CREAM	
3	OXYCANAZOLE	OXISTAT	1%
		ZODERM	1%
		ZODERM T CREAM	1%
4	LULICONAZOLE	LULIFIN CREAM	1%
		LULICAN	1%
		LULIFORD	1%
		LULIZ	1%
		LULIGEE	1%
5	BUTENAFINE	FINTOP CREAM	1%
		BUTOP CREAM	1%
6	TOLNAFATE	TINADERM CREAM	10MG
		TINACTIN	
7	TERBINAFINE	LAMISIL	1%
		TERBITOTAL	1%
		TERBINAFORCE	1%
8	NAFTIN	NAFTIFINE	2%
9	CICLOPIROX	CICLODAN	1%
		CANDIDOX	1%
		CICLOCIDAL CREAM	1%
10	KETOCONAZOLE	KERAGLO AD SHAMPOO	2%
		KENZ	2%
		KZ LOTION	2%
		KEVON LOTION	2%
		KERAGLO AD CREAM	2%
		KETOSCALP CREAM	2%

		KETOFORD	**2%**
		KETO SOAP	**2%**
		KETAFUNG	**2%**
		KETOCIP	**2%**
		KETOSTAR	**2%**
			2%

CONCLUSION:

Surface fungal infections affecting the skin, nails, and mucous membranes are commonly treated using topical antifungal medications. There are a number of important aspects that contribute to these treatments' efficacy. Topical antifungal formulations minimize systemic side effects and maximize local medication concentration by delivering the active component directly to the infection site. These drugs are available as creams, ointments, gels, sprays, and powders, among other forms. This diversity enables treatment of various infections and patient preferences to be flexible. Topical antifungals work well against a variety of fungi, including dermatophytes, yeasts, and molds. Examples of these include azoles (e.g., clotrimazole, miconazole) and allylamines (e.g., terbinafine, naftifine). They function by rupturing the fungi's cell wall or membrane, which results in cell death

REFERENCES

1. Recent Advances In Topical Carriers Of Anti-Fungal Agents by Abhinava garg, Ganti.S.Sharma, Amit.K.Goyal, Goutham Gosh, Sudham Chakra Si,
2. Formulation And Evaluation Of Antifungal Cream Of Chlorphenesin Original Article Veena S.1*, Surinder Kaur2, Gururaj Kulkarni2021[2]
3. Formulation And Evaluation Of Topical Delivery Of Antifungal Drug Bifonazole Using Microemulsion Based Gel Formulations. Journal Article**:** World Journal Of Pharmacy And Pharmaceutical Sciences (Wjpps),2013. Manisha Karpe Manisha Karpe, Vilasrao Kadam Vilasrao Kadam, Nikhil Mali Nikhil Mali, Vruti Patel Vruti Patel, Namrata Jadhav Namrata Jadha
4. Single V, Saini S, Joshi B, Rana AC, "Emulgel: A new platform for topical drug delivery" International Journal of Pharma and Bio Sciences, 2012; 3(1):485-498.
5. "Ketoconazole Monograph for Professionals". Drugs.com. American Society of Health-System Pharmacists. Retrieved 23 March 2019.
6. Ankur Jain et al. "Development and characterization of ketoconazole emulgel for topical drug delivery- a research". Pelagia research library Der Pharmacia sinica, 2010, Volume 1(3): 221-231.
7. Madaan V, Chanana A, Katarian M. K., Bilandi A, 2014. Emulsion technology and recent trends in emulsion applications. International research journal of pharmacy. . Issue 5, Vol 7, p.p 533-539
8. Yadav S, Mishra M, Tiwari A, and Shukla A. Emulgel: A novel approach for enhanced topical drug delivery. Int J Curr Pharm Res 2017;9:15-9.
9. Kumar Manish, Shanthi Nithya And Mahato Arun, "Qualitative and Quantitative Methods for Determination of Drug Luliconazole", International journal of research in advent technology, 2018
10. 10)Deepak Chandra Sharma et al. "Desin and characterization of apermilast loaded emulgel for topical treatment- a research". International journal of pharmacy and biological sciences 2018, volume 8: 552- 562. Swati verma, et al.
11. Formulation and evaluation of ketoconazole nanoemulgel– a research". World journal of pharmacy and pharmaceutical science, 2016, volume 5(2):899-911.
12. FORMULATION, DEVELOPMENT AND EVALUATION OF TOPICAL EMULGEL OF GRISEOFULVIN PALLAVI A.MHATRE *, RAJESHWARI N. PATIL, RACHANA S.KUMAR An International Journal of Advances in Pharmaceutical Sciences ,2014
13. Formulation & evaluation of voriconazole ointment for topical delivery Rajesh Asija*, Prem Chand Dhaker, Nitin Nama, Journal of Drug Discovery and Therapeutics Available Online at www.jddt.in,2015