Preparation Of Antifungal Cream

Saurabh Raj[1], Madhu Kushwaha[2], Dr. R. B. Goswami[3]
[1]*Student, Sagar Institute of Research Technology & Science-Pharmacy, Bhopal*
[2]*Assistant professor, Sagar Institute of Research Technology & Science-Pharmacy, Bhopal*
[3]*Director, Sagar Institute of Research Technology & Science-Pharmacy, Bhopal*

***Abstract*—Antifungal creams are semisolid topical formulations widely used for the treatment of fungal infections affecting the skin, nails, and mucosal tissues. Fungal infections caused by dermatophytes, yeasts, and molds have become increasingly common worldwide due to factors such as poor hygiene, immunosuppression, diabetes, prolonged antibiotic therapy, and environmental conditions. Topical antifungal therapy remains one of the most effective approaches for managing superficial fungal infections because it delivers the drug directly to the infected site while minimizing systemic side effects. Antifungal creams provide several advantages including ease of application, improved patient compliance, localized drug action, reduced toxicity, and enhanced therapeutic effectiveness.**

The preparation of antifungal crea" involves the incorporation of antifungal agents into suitable cream bases using appropriate pharmaceutical excipients. Commonly used antifungal drugs include clotrimazole, miconazole, ketoconazole, terbinafine, fluconazole, and itraconazole. The selection of an appropriate cream base plays a crucial role in determining the stability, spread ability, drug release, viscosity, and therapeutic efficacy of the formulation. Creams are generally classified as oil-in-water (O/W) emulsions or water-in-oil (W/O) emulsions depending on the nature of the continuous phase. Oil-in-water creams are commonly preferred for antifungal preparations because of their non-greasy nature, ease of washing, and better patient acceptability. The formulation process involves several important steps including selection of active pharmaceutical ingredients, excipients, emulsifying agents, preservatives, humectants, stabilizers, and penetration enhancers. The oil phase and aqueous phase are separately prepared and heated to appropriate temperatures before emulsification. Continuous stirring and homogenization are employed to obtain a stable and uniform cream formulation. Quality control tests such as pH determination, viscosity measurement, spreadability, drug content uniformity, microbial evaluation, stability studies, and in vitro drug release studies are essential to ensure product quality, safety, and efficacy.

Recent advances in topical drug delivery systems have led to the development of novel antifungal cream formulations containing nanoparticles, liposomes, microspheres, nano emulsions, and herbal extracts to improve drug penetration and therapeutic outcomes. These advanced systems enhance drug solubility, increase skin retention time, improve bioavailability, and reduce resistance associated with conventional formulations. Despite significant progress, challenges such as poor skin penetration, formulation instability, allergic reactions, and fungal resistance continue to affect antifungal therapy.

This review provides a comprehensive overview of the preparation, formulation principles, ingredients, methods of manufacture, evaluation parameters, therapeutic applications, advantages, limitations, and recent advancements in antifungal cream formulations. The report highlights the importance of pharmaceutical formulation strategies in improving the effectiveness and safety of topical antifungal therapy.

***Index Terms*— Topical drug delivery; Semisolid dosage form; Clotrimazole; Ketoconazole; Miconazole; Terbinafine; Fungal infections; Dermatophytosis; Candidiasis; Oil-in-water cream; Water-in-oil cream; Emulsion; Pharmaceutical formulation; Cream preparation; Topical antifungal therapy; Nanoemulsion; Liposomal cream; Nanoparticles; Drug release; Skin penetration; Pharmaceutical excipients; Stability studies; Spreadability; Antifungal agents; Topical formulations; Controlled drug delivery; Herbal antifungal cream; Pharmaceutical evaluation; Dermatological preparations.**

I. INTRODUCTION

Fungal infections are among the most common infectious diseases affecting humans worldwide. These infections are caused by various pathogenic fungi including dermatophytes, Candida species, Aspergillus species, and other opportunistic fungi. Superficial fungal infections primarily affect the skin,

hair, nails, and mucous membranes, whereas systemic fungal infections may involve internal organs and become life-threatening, particularly in immunocompromised patients. Factors such as poor personal hygiene, warm and humid climatic conditions, diabetes mellitus, prolonged antibiotic use, obesity, immunosuppression, and malnutrition significantly contribute to the increasing prevalence of fungal infections. (1,2)

Topical antifungal therapy remains the preferred treatment for most superficial fungal infections due to its localized action and minimal systemic side effects. Antifungal creams are semisolid dosage forms designed for external application to the skin or mucosal surfaces. These creams deliver antifungal drugs directly to the site of infection, thereby improving therapeutic effectiveness and reducing systemic toxicity. Antifungal creams are commonly used in the treatment of conditions such as ringworm, athlete's foot, jock itch, candidiasis, and seborrheic dermatitis. (3,4,5)

Cream formulations are generally emulsions consisting of oil and water phases stabilized by emulsifying agents. Depending on the nature of the continuous phase, creams are classified into oil-in-water (O/W) creams and water-in-oil (W/O) creams. Oil-in-water creams are more commonly used for antifungal preparations because they are non-greasy, easily washable, cosmetically elegant, and provide better patient acceptability. Water-in-oil creams, on the other hand, are more occlusive and suitable for dry skin conditions. (6)

The effectiveness of antifungal creams depends on several formulation factors including drug solubility, skin penetration, stability, spreadability, viscosity, pH, and release characteristics. Selection of suitable excipients such as emulsifiers, preservatives, humectants, stabilizers, penetration enhancers, and antioxidants is essential to achieve a stable and therapeutically effective formulation. The preparation process typically involves separate heating of oil and aqueous phases followed by emulsification, homogenization, cooling, and packaging. (7,8)

Several antifungal agents are commonly incorporated into cream formulations, including clotrimazole, miconazole, ketoconazole, terbinafine, econazole, fluconazole, and nystatin. These agents act by inhibiting fungal cell membrane synthesis, disrupting membrane permeability, or interfering with fungal metabolism. Modern pharmaceutical research has also focused on the incorporation of herbal antifungal agents and nanotechnology-based systems to improve therapeutic performance and patient compliance. (9,10)

Recent advancements in topical drug delivery have introduced innovative approaches such as nanoemulsions, liposomal creams, microsponge systems, solid lipid nanoparticles, and polymeric nanoparticles for antifungal therapy. These advanced systems improve drug penetration through the stratum corneum, enhance drug retention within the skin, prolong drug release, and reduce dosing frequency. Nanotechnology-based antifungal creams have shown promising results in improving bioavailability and overcoming resistance associated with conventional topical formulations. (11,12)

Despite the advantages of antifungal creams, several challenges remain including poor penetration of certain drugs through the skin barrier, formulation instability, microbial contamination, allergic reactions, irritation, and emergence of resistant fungal strains. Therefore, continuous research is necessary to develop safer, more effective, and patient-friendly antifungal formulations. (13,14)

This review discusses the formulation principles, ingredients, methods of preparation, evaluation parameters, therapeutic applications, advantages, limitations, and recent developments in antifungal cream preparation. The report emphasizes the significance of pharmaceutical formulation techniques in enhancing the efficacy and quality of topical antifungal therapy. (15)

II. REVIEW OF LITERATURE

Extensive research has been carried out on antifungal cream formulations to improve the effectiveness, stability, patient compliance, and therapeutic performance of topical antifungal therapy. Various studies have focused on the development of semisolid formulations using synthetic and herbal antifungal agents along with advanced drug delivery systems to enhance skin penetration and controlled drug release. (16)

Allen LV reported that semisolid dosage forms such as creams, ointments, and gels are among the most widely used topical formulations because they provide localized drug action with minimal systemic side

effects. The study emphasized that cream formulations offer better patient acceptability due to their non-greasy texture, ease of application, and improved spread ability. (18)

Lachman, Lieberman, and Kanig discussed the importance of pharmaceutical excipients and formulation parameters in the preparation of stable topical creams. Their work highlighted that emulsifying agents, preservatives, humectants, and stabilizers play a significant role in determining the physical stability, viscosity, pH, and therapeutic efficacy of cream formulations.

Barry BW extensively studied dermatological formulations and percutaneous absorption mechanisms. His research demonstrated that skin penetration of antifungal drugs depends on factors such as molecular size, lipid solubility, concentration gradient, and the presence of penetration enhancers. The study also explained the importance of the stratum corneum barrier in topical drug delivery. (19)

Patel and Patel evaluated various topical antifungal cream formulations and reported that oil-inwater creams provide superior spreadability, faster drug release, and better patient compliance compared to water-in-oil creams. Their findings showed that appropriate emulsifier concentration and homogenization techniques significantly improve formulation stability. (20)

Williams AC investigated transdermal and topical drug delivery systems and emphasized that advanced topical formulations can improve drug permeation through the skin barrier. The study suggested that penetration enhancers such as propylene glycol, ethanol, and surfactants can increase antifungal drug absorption and therapeutic effectiveness. (23)

Research conducted on clotrimazole cream formulations demonstrated effective treatment against dermatophytic infections including ringworm, athlete's foot, and candidiasis. Studies showed that clotrimazole creams possess broad-spectrum antifungal activity and good patient tolerability when formulated with suitable cream bases. (24)

Ketoconazole cream formulations have also been extensively investigated for the treatment of fungal skin infections and seborrheic dermatitis. Researchers observed that ketoconazole creams effectively inhibit fungal cell membrane synthesis and provide rapid symptomatic relief from itching, redness, and scaling. (25)

Several investigators have focused on terbinafine cream formulations due to their potent fungicidal activity. Studies indicated that terbinafine creams exhibit rapid onset of action and shorter treatment duration compared with conventional azole antifungal agents. The drug was found particularly effective against dermatophyte infections.

Miconazole nitrate cream formulations have been studied for their broad-spectrum antifungal and antibacterial properties. Researchers reported that miconazole creams show excellent therapeutic activity against Candida species and dermatophytes while maintaining good skin compatibility. (27)

Recent pharmaceutical research has increasingly focused on nanotechnology-based antifungal cream formulations. Nanoemulsion-based creams have shown enhanced drug solubility, improved skin penetration, and prolonged drug retention within the skin layers. These formulations also provide better physical stability and controlled drug release compared to conventional creams. (29)

Liposomal antifungal creams have gained considerable attention because liposomes can encapsulate both hydrophilic and lipophilic drugs while improving drug delivery to deeper skin tissues. Studies demonstrated that liposomal formulations reduce drug toxicity and enhance therapeutic efficacy through sustained release mechanisms.

Solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) have also been investigated for topical antifungal therapy. Researchers found that these systems improve antifungal drug bioavailability, enhance skin hydration, and prolong drug release while reducing irritation associated with conventional formulations.

Herbal antifungal cream formulations containing plant extracts such as neem, aloe vera, turmeric, tea tree oil, tulsi, and garlic have been studied for their natural antifungal properties. Several studies reported that herbal creams possess significant antifungal activity with fewer side effects and improved patient safety compared to synthetic formulations.

Microsponge drug delivery systems have emerged as another promising approach for antifungal cream preparation. Research indicated that microsponge-based creams provide controlled and sustained drug release, reduce irritation, and improve drug stability. These systems are particularly useful for prolonged topical therapy.

Studies on formulation evaluation parameters highlighted the importance of physicochemical characterization in ensuring product quality and stability. Parameters such as pH, viscosity, spreadability, drug content uniformity, extrudability, homogeneity, and microbial limit tests are essential for assessing the safety and effectiveness of antifungal cream formulations.

Stability studies conducted under different environmental conditions demonstrated that temperature, humidity, light exposure, and storage conditions significantly affect cream stability and drug potency. Proper packaging and storage conditions are therefore necessary to maintain product quality and shelf life. (30)

III. CLASSIFICATION OF ANTIFUNGAL CREAMS

a. Based on Type of Emulsion (31)

- Oil-in-Water (O/W) Creams
- Non-greasy
- Easily washable
- Better cosmetic appearance
- Preferred for topical antifungal therapy
- Water-in-Oil (W/O) Creams
- Greasy in nature
- Provide occlusive effect

IV. COMMON ANTIFUNGAL DRUGS USED IN CREAMS

Drug	Mechanism of Action	Therapeutic Use
Clotrimazole	Inhibits ergosterol synthesis	Ringworm, candidiasis
Ketoconazole	Alters fungal membrane permeability	Seborrheic dermatitis
Miconazole	Inhibits fungal cell membrane synthesis	Athlete's foot
Terbinafine	Inhibits squalene epoxidase	Dermatophytosis
Nystatin	Binds fungal cell membrane sterols	Candidiasis

V. INGREDIENTS USED IN ANTIFUNGAL CREAM PREPARATION

- Active Pharmaceutical Ingredient (API)
- Antifungal drug
- Oil Phase Components
- Stearic acid
- Cetyl alcohol
- Liquid paraffin
- Beeswax
- Aqueous Phase Components
- Purified water
- Glycerin
- Propylene glycol
- Emulsifying Agent
- Tween 80
- Span 80
- Sodium lauryl sulfate
- Preservatives
- Methyl paraben
- Propyl paraben
- Stabilizers and Antioxidants
- EDTA
- BHT

Ingredient	F1 (15 g)	Quantity F2 (15 g)	F3 (15 g)
Leave extract of Pongamia pinnata	1.5 g	2 g	2.5 g
Neem oil	0.5 ml	0.5 ml	0.5 ml
Stearic acid	2 g	1.5 g	1.5 g
Potassium hydroxide	1.5 g	1 g	1 g
Sodium carbonate	1.5 g	1.5 g	1.5 g
White soft paraffin	1.5 g	1.5 g	1.5 g
Methanol	1.5 g	1.5 g	1.5 g
Glycerin	2 ml	2 ml	2 ml
Methyl paraben	1.5 g	1.5 g	1.5 g
Rose oil	0.5 ml	0.5 ml	0.5 ml
Distilled water	q.s	q.s	q.s

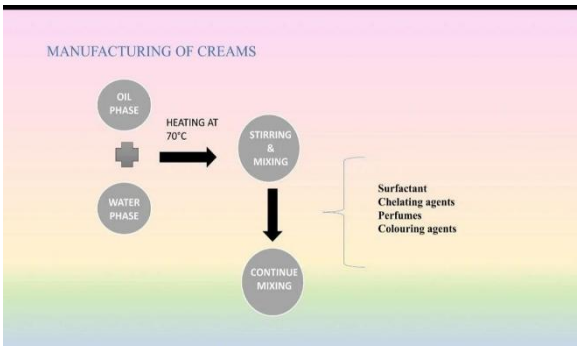
VI. METHOD OF PREPARATION

Step 1: Preparation of Oil Phase

Oil-solble ingredients such as stearic acid, cetyl alcohol, beeswax, and liquid paraffin are weighed and heated to 70–75°C.

Step 2: Preparation of Aqueous Phase
Water-soluble ingredients including water, glycerin, preservatives, and emulsifiers are dissolved and heated separately to the same temperature.

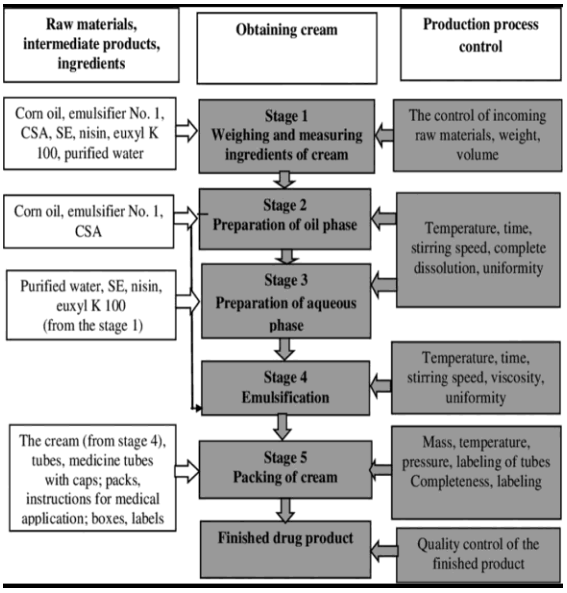
Step 3: Emulsification
The aqueous phase is slowly added to the oil phase with continuous stirring to form an emulsion.



Step 4: Drug Incorporation
The antifungal drug is dissolved or dispersed into the cream base under continuous mixing.

Step 5: Homogenization
The cream is homogenized to achieve uniform consistency and particle distribution.

Step 6: Cooling and Packaging
The prepared cream is cooled to room temperature and packed into suitable containers. (33,34)



VII. EVALUATION PARAMETERS

- Physical Evaluation
- Color
- Odor
- Appearance
- Homogeneity
- pH Determination
- Ensures compatibility with skin pH.
- Viscosity Measurement
- Determines consistency and spreadability.
- Spread ability Test
- Evaluates ease of application on skin.
- Drug Content Uniformity
- Determines uniform distribution of antifungal drug.
- Stability Studies
- Performed to assess formulation stability under different storage conditions.
- Microbial Limit Test
- Ensures absence of microbial contamination.
- In Vitro Drug Release Study
- Determines release profile of drug from cream formulation.

VIII. ADVANTAGES OF ANTIFUNGAL CREAMS LOCALIZED DRUG ACTION (34)

- Reduced systemic side effects (35)
- Improved patient compliance (36)
- Easy application
- Controlled drug release
- Better therapeutic effectiveness
- Reduced dosing frequency

IX. LIMITATIONS OF ANTIFUNGAL CREAMS

- Limited skin penetration
- Possible skin irritation (37)
- Allergic reactions
- Poor stability of some formulations
- Risk of microbial contamination
- Drug resistance development

X. RECENT ADVANCES

- Nanoemulsion-Based Creams
- Improve drug solubility and penetration. (38)
- Liposomal Creams
- Enhance drug retention and controlled release.
- Nanoparticle-Based Creams
- Increase bioavailability and antifungal activity.(39)
- Herbal Antifungal Creams
- Contain natural plant extracts with antifungal properties.
- Microsponge Drug Delivery Systems (40)
- Provide sustained drug release.

XI. CONCLUSION

Antifungal creams are important topical dosage forms widely used for the treatment of superficial fungal infections. Proper selection of antifungal agents, excipients, and formulation methods plays a crucial role in determining the safety, stability, and therapeutic efficacy of the final product. Advances in pharmaceutical technology and nanotechnology have significantly improved the effectiveness of antifungal cream formulations by enhancing drug penetration, controlled release, and patient compliance. Although challenges such as resistance, stability issues, and skin irritation remain, ongoing research continues to improve topical antifungal therapy through innovative drug delivery approaches.

REFERENCES

[1] Allen LV. *Pharmaceutical Dosage Forms and Drug Delivery Systems*. Philadelphia: Lippincott Williams & Wilkins.

[2] Lachman L, Lieberman HA, Kanig JL. *The Theory and Practice of Industrial Pharmacy*. 3rd ed. Philadelphia: Lea & Febiger.

[3] Ansel HC. *Introduction to Pharmaceutical Dosage Forms*. Philadelphia: Lea & Febiger.

[4] Remington JP. *Remington: The Science and Practice of Pharmacy*. Philadelphia: Lippincott Williams & Wilkins.

[5] Martin A. *Physical Pharmacy and Pharmaceutical Sciences*. Philadelphia: Lippincott Williams & Wilkins.

[6] Aulton ME. *Pharmaceutics: The Design and Manufacture of Medicines*. Edinburgh: Churchill Livingstone.

[7] Sinko PJ. *Martin's Physical Pharmacy and Pharmaceutical Sciences*. 6th ed. Philadelphia: Lippincott Williams & Wilkins.

[8] Barry BW. *Dermatological Formulations: Percutaneous Absorption*. New York: Marcel Dekker.

[9] Patel RP, Patel MM. Preparation and evaluation of topical formulations.

[10] Williams AC. *Transdermal and Topical Drug Delivery Systems*. London: Pharmaceutical Press.

[11] Gupta AK, Cooper EA. Update in antifungal therapy of dermatophytosis. Mycopathologia. 2008;166(5-6):353-367.

[12] Havlickova B, Czaika VA, Friedrich M. Epidemiological trends in skin mycoses worldwide. Mycoses. 2008;51(Suppl 4):2-15.

[13] Benson HAE. Transdermal drug delivery: Penetration enhancement techniques. Curr Drug Deliv. 2005;2(1):23-33.

[14] Benson HAE, Watkinson AC. *Topical and Transdermal Drug Delivery: Principles and Practice*. Chichester: Wiley.

[15] Naik A, Kalia YN, Guy RH. Transdermal drug delivery: Overcoming the skin's barrier function. Pharm Sci Technol Today. 2000;3(9):318-326.

[16] Eccleston GM. Functions of mixed emulsifiers and emulsifying waxes in dermatological lotions and creams. Colloids Surf A Physicochem Eng Asp. 1997;123:169-182.

[17] Date AA, Naik B, Nagarsenker MS. Novel drug delivery systems: Potential in improving topical delivery of antiacne agents. Skin Pharmacol Physiol. 2006;19(1):2-16.

[18] Müller RH, Radtke M, Wissing SA. Solid lipid nanoparticles and nanostructured lipid carriers in cosmetic and dermatological preparations. Adv Drug Deliv Rev. 2002;54(Suppl 1):S131-S155.

[19] Souto EB, Müller RH. Cosmetic features and applications of lipid nanoparticles. Int J Cosmet Sci. 2008;30(3):157-165.

[20] Korting HC, Schäfer-Korting M. Carriers in the topical treatment of skin disease. In: Schäfer-Korting M, editor. *Handbook of Experimental*

Pharmacology. Vol. 197. Berlin: Springer; 2010. p. 435-468.

[21] Pandey S, Patel DK, Thakur R, Mishra DP, Maiti P, Haldar C. Anti-inflammatory and antimicrobial activities of herbal-based cream formulations. Int J Pharm Sci Rev Res. 2014;26(2):45-50.

[22] Kokate CK, Purohit AP, Gokhale SB. *Pharmacognosy*. Pune: Nirali Prakashan.

[23] Swarbrick J, Boylan JC. *Encyclopedia of Pharmaceutical Technology*. New York: Marcel Dekker.

[24] Lieberman HA, Rieger MM, Banker GS. *Pharmaceutical Dosage Forms: Disperse Systems*. New York: Marcel Dekker.

[25] Singh M, Sharma R, Banerjee UC. Biotechnological applications of cyclodextrins in food and pharmaceutical industries. Biotechnol Adv. 2002;20(5-6):341-359.

[26] Kapoor D, Patel M, Vyas RB, Lad C. Formulation and evaluation of antifungal cream containing fluconazole. Int J Drug Dev Res. 2011;3(4):18-25.

[27] Patel JK, Patel RP, Amin AF, Patel MM. Formulation and evaluation of mucoadhesive antifungal gel for oral candidiasis. Int J Pharm. 2007;350(1-2):276-282.

[28] Nair AB, Kumar A, Jacob S, Al-Dhubiab BE, Attimarad M, Harsha S, et al. Dermal and transdermal drug delivery systems: Current and future prospects. Curr Drug Deliv. 2020;17(4):357-378.

[29] Vyas SP, Khar RK. *Controlled Drug Delivery: Concepts and Advances*. New Delhi: Vallabh Prakashan.

[30] Mishra B, Patel BB, Tiwari S. Colloidal nanocarriers: A review on formulation technology, types and applications toward targeted drug delivery. Nanomedicine. 2010;6(1):9-24.

[31] Shinde AJ, Garala KC, More HN. Development and characterization of liposomal drug delivery system for nystatin. Int J Pharm Pharm Sci. 2012;4(2):351-357.

[32] Kaur IP, Garg A, Singla AK, Aggarwal D. Vesicular systems in ocular drug delivery: An overview. Int J Pharm. 2004;269(1):1-14.

[33] Pardeike J, Hommoss A, Müller RH. Lipid nanoparticles (SLN, NLC) in cosmetic and pharmaceutical dermal products. Int J Pharm. 2009;366(1-2):170-184.

[34] Elzayat EM, Samy AM, Hafez AA. Formulation and optimization of itraconazole topical cream using factorial design. AAPS PharmSciTech. 2012;13(2):325-333.

[35] Basha BN, Prakasam K, Goli D. Formulation and evaluation of topical antifungal gel containing terbinafine hydrochloride. Int J Drug Dev Res. 2011;3(4):93-102.

[36] Patel D, Chaudhary SA, Parmar B, Bhura N. Transdermal drug delivery system: A review. Pharma Innov J. 2012;1(4):66-75.

[37] Rieger MM. *Harry's Cosmeticology*. New York: Chemical Publishing Company.

[38] Florence AT, Attwood D. *Physicochemical Principles of Pharmacy*. London: Pharmaceutical Press.

[39] Jain NK. *Controlled and Novel Drug Delivery*. New Delhi: CBS Publishers and Distributors.

[40] Sharma PP. *Cosmetics: Formulation, Manufacturing and Quality Control*. New Delhi: Vandana Publications.