Advanced Journal Of Dental & Medical Research Excellence

Volume-I (Issue 2) – Oct - Dec 2025 ISSN: 3107-8842

DEVELOPMENT AND FORMULATION OF NANOEMULGEL KETOCONAZOLE BY USING NATURA EXTRACT

Khushbhoo Bhamar[1]*, Akash Chauhan[2] Mr. Ramesh Pareek[3]

1. Research Scholar, Dept. of Pharmaceutics, Arya College of Pharmacy, Jaipur, Rajasthan
2. Research Scholar, Dept. of Pharmacology, Arya College of Pharmacy, Jaipur, Rajasthan
3. Associate Professor, Arya College of Pharmacy, Jaipur, Rajasthan

Corresponding Author:

Khushbhoo Bhamar

Research Scholar, Dept. of Pharmaceutics, Arya College of Pharmacy, Jaipur, Rajasthan

ABSTRACT

In order to improve therapeutic efficacy and skin compatibility, the current work focusses on the development and formulation of a nanoemulgel containing the antifungal drug ketoconazole using natural extracts. The benefits of both nanoemulsions and gels are combined in nanoemulgels, which provide better drug solubility, increased skin penetration, and prolonged drug release. Natural ingredients like coconut oil and aloe vera were added to this composition as biocompatible carriers and penetration enhancers. High-energy emulsification techniques were used to create the nanoemulsion, which was then incorporated into a Carbopol 940 gel base. Physical appearance, pH, viscosity, drug content, spreadability, in-vitro drug release, and antifungal efficacy were all assessed for the produced nanoemulgels.

In comparison to traditional gel formulations, the optimised formulation demonstrated greater antifungal activity, improved release profile, and good stability, according to the results. With better patient compliance and therapeutic potential, this innovative method offers a viable method for the topical administration of ketoconazole.

KEYWORDS-Aloe vera, Antifungal Activity, Carbopol 940, Coconut Oil, Ketoconazole, Natural Extracts, Topical Drug Delivery, Transdermal Delivery.

1. INTRODUCTION

The last two decades have seen unprecedented changes in the pattern of fungal infections in humans. These diseases have assumed a much greater importance because of their increasing incidence in persons with the acquired immunodeficiency syndrome AIDS in recipients of solid organ or haematopoietic stem cell transplants HSCT in persons with haematological malignancies and in other debilitated or immunocom promised individuals. Although gains have been made in the treatment and prevention of fungal infections, major changes in health care practices have resulted in the emergence of new atrisk populations. Fungi are a varied group of eukaryotic organisms that are essential to many ecological functions including breaking down organic matter and recycling nutrients. They can appear as single celled forms like yeasts or as multicellular filamentous structures such as molds. Fungi inhabit a wide range of environments including soil, water and living organisms like plants and animals they hold significant ecological and medical importanceFungi are believed to have appeared on Earth around a billion years ago making them some of the oldest living organisms and silent witnesses to the planet's ancient history. Fossil evidence suggests their presence dates back roughly 600 million years offering valuable insight into their early development and evolution. In those early days, fungi played a crucial role in shaping Earth's ecosystems[2]. By forming partnerships with the first land plants, they helped pave the way for life to thrive on land. One of the most important of these partnerships involved mycorrhizal fungi, which supported early plants by improving their ability to absorb nutrients from the soil. This relationship was key to helping plants establish themselves on the once-barren land setting the stage for the rich and diverse environments we see today.

1.2 The Modern Role of Fungi in Medicine and Technology:

Over the last few centuries, our view of fungi has changed dramatically. Once seen as oddities of nature they're now recognized as vital players in medicine industry and science fundamentally changing how we understand and use them in everyday life.

Antoni van Leeuwenhoek, often called the Father of Microbiology was one of the first people to truly glimpse the hidden world of microorganisms. Using microscopes he crafted himself he managed to observe yeast cells in detail something no one had seen before. At the time, this was a groundbreaking discovery.

2. AIM AND OBJECTIVE

2.1 Justification for Disease Selection

To address these limitations, novel delivery systems such as nanoemulgels have been explored. Nanoemulgels combine the advantages of nanoemulsions—such as enhanced drug solubility, stability, and bioavailability—with the ease of application and patient compliance of gels. The small droplet size in nanoemulsions promotes better penetration through the stratum corneum, while the gel matrix allows for sustained release and localization at the site of infection

2.2 Objectives

1. To formulate a nanoemulgel of ketoconazole for topical antifungal treatment.
2. To incorporate natural extracts as stabilizers, permeation enhancers, or therapeutic agents.
3. To improve the solubility and bioavailability of ketoconazole.
4. To enhance skin penetration and retention of the drug.
5. To achieve sustained and controlled drug release.

3. DRUG PROFILE

Table No. 1: List of content

S. No.	Component	Category	Function
1.	**HPMC**(Hydroxypropyl Methylcellulose)	Semi Synthetic Polymer	Gelling agent thickner, stabilizer, controlled-release agent

2	**Coconut Oil** (Virgin or Fractionated)	Natural Oil / Functional Excipient	Acts as oil phase; provides emollient and antifungal effects
3	**Carbopol 940**	Gelling Agent	Converts Nanoemulsion into gel for better skin adherence
4	**Propylene Glycol**	Co-surfactant / Penetration enhancer	Enhances drug solubility and skin penetration
5	**Tween 80** (Polysorbate 80)	Surfactant	Reduces interfacial tension; helps stabilize Nanoemulsion
6	**Triethanolamine**	pH Adjuster / Neutralizer	Adjusts pH to skin-compatible range
7	**Distilled Water**	Vehicle / Solvent	Forms the aqueous phase in the emulsion
8	**Ethanol** (optional)	Co-solvent / Penetration enhancer	Improves solubility and drug permeation
9.	**Methylparaben**	Preservatives	Prevents microbial contamination

A variety of functional excipients are included in the formulation of the ketoconazole nanoemulgel to improve skin compatibility, stability, and drug administration. While coconut oil functions as the oil phase with additional emollient and antifungal properties, HPMC works as a gelling agent and stabiliser. For improved skin adhesion, carbopol 940 turns the nanoemulsion into a gel. Ethanol and propylene glycol improve drug solubility and skin absorption by acting as penetration enhancers and co-surfactants. As a surfactant, Tween 80 lowers interfacial tension and stabilises the emulsion. Distilled water serves as the main aqueous solvent, and triethanolamine balances the pH to meet skin values. The inclusion of methylparaben as a preservative ensures formulation stability and safety by preventing microbiological contamination.

4. MATERIAL AND METHOD

Table2: List of Chemicals and Solvents.

S. No.	Name	Supplier / Manufacturer
1	ketoconazole	Torrent Pharma Pvt. Ltd.
2	Propylene Glycol	Signet Chemicals Pvt. Ltd., Mumbai
3	Carbopol 940	Central Drug House (P) Ltd., Mumbai

4	Triethanolamine	Central Drug House (P) Ltd., Mumbai
5	Span-80	Central Drug House (P) Ltd., Mumbai
6	Coconut Oil	Central Drug House (P) Ltd., Mumbai
7	Arachis oil	Central Drug House (P) Ltd., Mumbai
8	Methyl Paraben	Central Drug House (P) Ltd., Mumbai
9.	Tween 80	Central Drug House (P) Ltd., Mumbai

Table 3: Listof Instruments and Equipment

S. No.	Name	Manufacturer with model
01	Melting Point Apparatus	Sunbim, India
02	Digital Weighing Balance	Wensar Limited
03	UV Spectrophotometer	Shimadzu UV-1800
04	Differential Scanning Calorimeter (DSC)	Perkin Elmer, Pyris-1, DSC, USA
05	FTIR Spectrophotometer	Parkin Elmer India Ltd. New Delhi

5. EXPERIMENTAL WORK

5.1 Preformulation studies

1. Organoleptic Properties

Ketoconazole was evaluated for its physical characteristics. It appeared as a white to off-white crystalline powder, was odorless, and tasteless. These properties confirm its identification and are consistent with pharmacopeial standard

2. Melting Point Determination

The melting point of Ketoconazole was determined using a digital melting point apparatus and found to be approximately 152°**C**. This value confirms the purity and stability of the drug, as it matches the literature-reported melting point.

3. Solubility Studies

Solubility of Ketoconazole was tested in various solvents. The drug was practically insoluble in water but showed good solubility in organic solvents like methanol, ethanol, and propylene glycol, and in natural oils like coconut and arachis oil. This supports its suitability for an oil-based nanoemulsion system.

4. Compatibility Studies (FTIR Analysis)

Fourier Transform Infrared (FTIR) spectroscopy was used to evaluate compatibility between Ketoconazole and formulation excipients, including natural oils and polymers. No significant shifts or disappearance of characteristic peaks were observed, indicating chemical compatibility.

5. Differential Scanning Calorimetry (DSC)

DSC was used to assess the thermal behavior of Ketoconazole. A sharp endothermic peak near 152°C confirmed the purity and crystalline nature of the drug. No additional peaks suggested there was no drug-excipient interaction, supporting its thermal stability in the formulation.

5.2 Formulation table

Table 4: nanoemugel (API containing)

Ingredients (% w/w)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ketoconazole	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
HPMC	0.5	1.0	2.0	-	-	-	-	-	-
Coconut Oil	-	-	-	2.5	3.5	5.0	-	-	-

Carbopol 940	-	-	-	-	-	-	1.0	1.5	2.0
Tween 80	10.0	10.0	10.0	12.0	12.0	12.0	15.0	15.0	15.0
Triethanolamine (TEA)	pH 6.5–7.0	pH 6.5–7.0	pH 6.5–7.0	pH 6.5–7.0	pH 6.5–7.0	pH 6.5–7.0	pH 6.5–7.0	pH 6.5–7.0	pH 6.5–7.0
Methylparaben	0.1	0.1	0.1	0.15	0.15	0.15	0.2	0.2	0.2
Distilled Water	87.4	86.9	85.9	83.35	82.35	80.85	81.8	81.3	80.8

6.RESULT

6. ANALYTIC PROFILE OF ACTIVE DRUG (DSC & FTIR)

a) **Ketoconazole:** The DSC thermogram of Ketoconazole is shown in Figure 1. The DSC thermogram of Ketoconazole showed sharp peak at 162^0C**.** The IR spectra obtained was elucidated for important chromophore groups. The IR spectra showed peaks at 3640, 1450, 1057, 1250, 810 and 690 cm^{-1}.

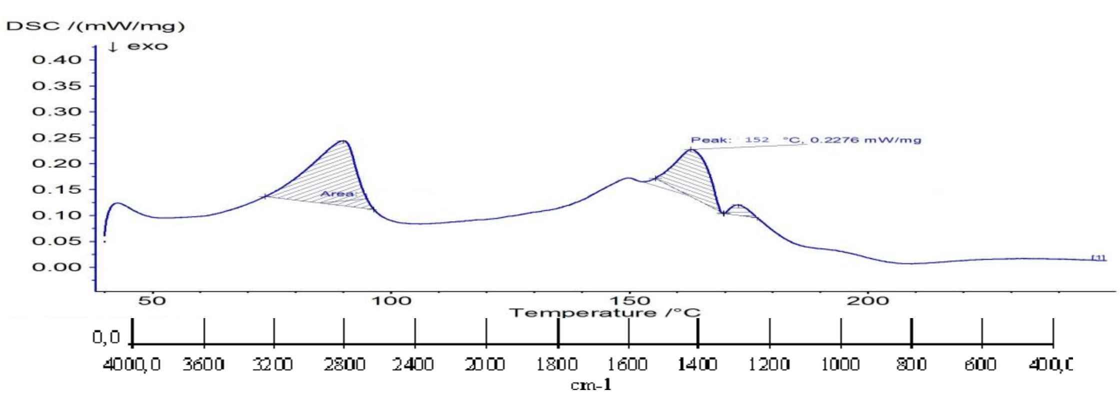

Figure 1: DSC Thermogram of Ketoconazole

6.4 DSC OF NANOEMULGEL FORMULATION

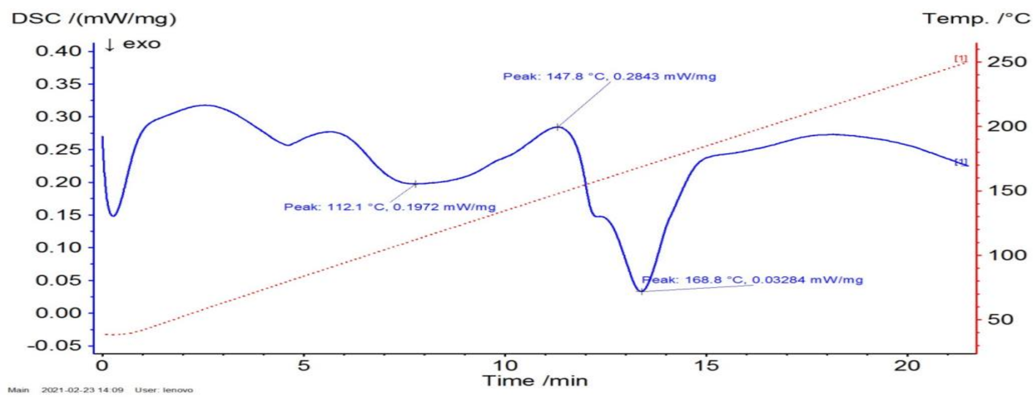

Fig. 2 DSC Nanoemulgel Formulation

6.7 STANDARD CURVE OF KETOCONAZOLE

The Ketoconazole was characterized in methanol as solvent by measuring absorption spectrum using Shimadzu UV Visible Spectrophotometer. The drug exhibited λmax at 272 nm when scanned between 180-400 nm. Standard curve of Ketoconazole was obtained by plotting absorbance values at different concentrations of the drug UV- spectrophotometer. The standard plot was made with concentration (µg /ml) on X axis and Absorbance on Y axis.

7.7.1 Preparation of Calibration curve of Ketoconazole inDMSO:

Table-5 Absorbance of Ketoconazole in DMSO

Concentration	Absorbance (272 nm)
0.0	0
2.0	0.125±0.003
4.0	0.259±0.002
6.0	0.384±0.003
8.0	0.528±0.002
10.0	0.653±0.003
12.0	0.786±0.001

All values are expressed as mean (± SD), $n = 3$

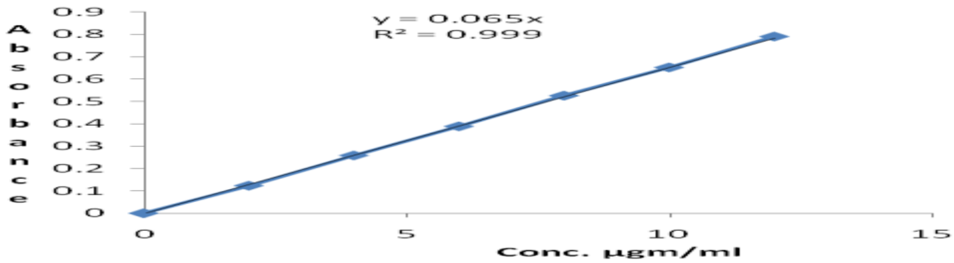

Fig.3: Standard curve of ketoconazole

Formulation Name	Zeroorder	Firstorder	Higuchi	KorsymerPeppas
F8	R^2	R^2	R^2	R^2
	0.9892	0.9971	0.9488	0.9989

Discussion: mathematical models are commonly used to predict the release mechanism and compare release profile. For all optimized formulations, the % drug release vs time (zero order), log% drug remaining vs time (first order), log% drug release vs square root of time (higuchi plot) and log fraction drug releasevs log time (korsmeyerpeppas) were plotted. Considering the determination coefficient, Korsmeyermodelfit the release data.

7.CONCLUSION

The goal of the current study was to improve the local therapeutic efficacy of ketoconazole, an antifungal medication that is poorly soluble in water, and to avoid hepatic first-pass metabolism by developing and thoroughly evaluating nanoemulgel formulations of the drug. By combining the benefits of emulsions and gels, nanoemulgels enable improved medication penetration through the skin as well as a stable, non-greasy, and patient-acceptable dose form for topical use. Using variable quantities of gelling agents (HPMC, Carbopol 940), oil phase (Coconut oil), and surfactants (Tween 80), nine distinct formulations (F1 to F9) were created. To find the best candidate for efficient skin administration of ketoconazole, these formulations underwent extensive preformulation, physicochemical, and in vitro release tests.

8. REFERNCES

1. Kumar P, Hussain Z, Chandra P, Diksha, Raj V, Verma N, Singh A. Nanoemulgel: An Innovative Carrier for Drug Delivery of Poorly Water-soluble Drugs. Current Nanomedicine. 2025 Apr;15(2):157-72.
2. Qayyum T, Shabbir A, Ullah N, Sarwar A, Aziz T, Alharbi NK, Alshehri F, Shami A, Asmari FA, Alwethaynani MS, Al-Joufi FA. Microbial evaluation of Melaleuca alternifolia essential oil for its antifungal activity against Trichophyton violaceum and its synergistic effects with ITZ and KTZ. Archives of Dermatological Research. 2025 Mar 30;317(1):654.
3. Prajapati SK, Jain A, Bajpai M. Lipid-based nanoformulations in onychomycosis therapy: addressing challenges of current therapies and advancing treatment. RSC advances. 2025;15(10):7799-825.
4. Wagh P, Karnik H, Kuchekar A, Chaudhari G, Gawade A. Design and evaluation of emulgel with a polyherbal basis for topical delivery.
5. Wagh P, Karnik H, Kuchekar A, Chaudhari G, Gawade A. Design and evaluation of emulgel with a polyherbal basis for topical delivery.
6. Waghmare ND, Hiwe KA, Bakal RL, Hatwar PR, Khansole NG, Saware US. Emulgel: A Novel Topical Drug Delivery System. Asian Journal of Pharmaceutical Research and Development. 2025 Apr 15;13(2):82-91.
7. Shukla M, Narain S, Kumar A, Dikshit A. Dermal Delivery of NanoFormulations: An Emerging Technology in Dermatological Conditions. BioNanoScience. 2025 Jun;15(2):215.
8. Hake G, Mhaske A, Shukla R, Flora SJ. Copper-Induced Neurodegenerative Disorders and Therapeutic Potential of Curcumin-Loaded Nanoemulsion. Toxics. 2025 Jan 29;13(2):108.
9. Soomro RB, Soomro AB, Wassan SM, Abbasi F, Memon I. Advancements in Early

Diagnosis and Personalized Treatment Strategies for Skin Diseases: A Meta-Analysis of Interdisciplinary Approaches Combining Dermatology, Genetics, and Immunology.

10. Jadhav VS, Thorat VG, Gawali PV, Rathi BR. A Review on Topical Emulgel. International Journal of Research in Pharmacy and Allied Science. 2025 Jan 1;3(6):1-9.
11. Bakhatwar M, Kola M, Prathyusha B, Aleti R, Neha T, Anusha M, Rupini S. Therapeutic Herbal Gels: A Pharmaceutical Perspective. Trends in Pharmaceuticals and Nanotechnology (e-ISSN: 2582-4457). 2025 Feb 7:1-1.
12. Mahapatra M, Mohapatra S, Jena GK. Nanostructured Lipid Carriers: A Revolutionary Approach in Antifungal Drug Delivery. Biomedical Materials & Devices. 2025 Feb 4:1-7.
13. Adwani G, Bharti S, Kumar A. Nano-Enhanced Antifungal Therapy in Diabetic Patients with Candidiasis. BioNanoScience. 2025 Jun;15(2):230.
14. Seenivasan R, Halagali P, Nayak D, Tippavajhala VK. Transethosomes: A Comprehensive Review of Ultra-Deformable Vesicular Systems for Enhanced Transdermal Drug Delivery. AAPS PharmSciTech. 2025 Jan 17;26(1):41.
15. Gomes GS, Casarini TP, Gazzi R, Aguirre TA, Paese K, Contri RV. Polymeric Nanoparticles Applied to Skin Diseases. InNovelNanocarriers for Skin Diseases 2025 Feb 10 (pp. 279-316). Apple Academic Press.
16. Alburyhi MM, Yahya TA, Saif AA, Noman MA. FORMULATION AND EVALUATION OF LORNOXICAM MICROSPONGE-BASED GEL AS A TRANSDERMAL DRUG DELIVERY SYSTEMS.
17. Kandekar U, Lotake S, Pandit A, Sayare A, Ghode P. Optimization of invasomal gel of miconazole nitrate for the treatment of topical fungal infections. Journal of Drug Delivery Science and Technology. 2025 Feb 1;104:106450.
18. Singh VK, Patel HA. A Unique Strategies for Psoriasis Management: Utilizing Nanoemulsion Based Insitu-Gel Formulation for Topical Administration of MometasoneFuroate. Cuestiones de Fisioterapia. 2025 Feb 3;54(3):3448-60.

19. Dubey P, Kumar A, Vaiphei KK, Basrani S, Jadhav A, Wilen CE, Rosenholm JM, Bansal KK, Chakravarti R, Ghosh D, Gulbake A. A poly-δ-decalactone (PDL) based nanoemulgel for topical delivery of ketoconazole and eugenol against Candida albicans. Nanoscale Advances. 2024;6(21):5322-36.
20. Ain S, Ain Q, Chauhan S, Yadav M, Singh SV, Kumar B. PREPARATION AND EVALUATION OF KETOCONAZOLE NANOGEL FOR TOPICAL APPLICATION.
21. AZHAR M, MISHRA A. REVIEW OF NANOEMULGEL FOR TREATMENT OF FUNGAL INFECTIONS. International Journal of Pharmacy and Pharmaceutical Sciences. 2024.
22. Sethi SK, Goel H, Chawla V. Nanoemulsion Based Supramolecular Drug Delivery systems for Therapeutic Management of Fungal infections. Drug Delivery Letters. 2024 Mar 1;14(1):2-15.
23. Aldeeb RA, Ibrahim SS, Khalil IA, Ragab GM, El-Gazar AA, Taha AA, Hassan DH, Gomaa AA, Younis MK. Enhancing collagen based nanoemulgel for effective topical delivery of Aceclofenac and Citronellol oil: Formulation, optimization, in-vitro evaluation, and in-vivo osteoarthritis study with a focus on HMGB-1/RAGE/NF-κB pathway, Klotho, and miR-499a. Drug Delivery and Translational Research. 2024 Nov;14(11):3250-68.
24. Detroja MA, Dhinoja MM, Gajera SB. Development and Evaluation of Ketoconazole Serum.
25. Khan BA, Haq SU, Khan MK, Khan MS, Menaa F. Fabrication of lornoxicam loaded into curcumin reinforced nanoemulgel: In-vitro characterization and in-vivo anti-inflammatory potential. Journal of Drug Delivery Science and Technology. 2024 Oct 1;100:106090.
26. Ahmad I, Farheen M, Kukreti A, Afzal O, Akhter MH, Chitme H, Visht S, Altamimi AS, Alossaimi MA, Alsulami ER, Jaremko M. Natural oils enhance the topical delivery of ketoconazole by nanoemulgel for fungal infections. ACS omega. 2023 Jul

26;8(31):28233-48.

27. Phagna M, Badhwar R, Singh M, Alhalmi A, Khan R, Noman OM, Alahdab A. Development and Characterization of Terbinafine-Loaded Nanoemulgel for Effective Management of Dermatophytosis. Gels. 2023 Nov 12;9(11):894.
28. Lavate S, Chaudhari S. Formulation and Evaluation of Voriconazole Loaded Nanoemulgel for the treatment of Onychomycosis.
29. Naksuriya O, Nitthikan N, Supadej K, Kheawfu K, Khonkarn R, Ampasavate C, Intasai N, Monton C, Kiattisin K. Approach for development of topical ketoconazole-loaded microemulsions and its antifungal activity. Trends in Sciences. 2023 Sep 10;20(12):7046-.
30. Padhy S, Sahoo BM, Kumar BV, Patra CN. Development, Characterization and Evaluation of Nanoemulgel Used for the Treatment of Skin Disorders. Current Nanomaterials. 2021 Apr 1;6(1):43-57.
31. Kammoun AK, Khedr A, Hegazy MA, Almalki AJ, Hosny KM, Abualsunun WA, Murshid SS, Bakhaidar RB. Formulation, optimization, and nephrotoxicity evaluation of an antifungal in situ nasal gel loaded with voriconazole–clove oil transferosomal nanoparticles. Drug Delivery. 2021 Jan 1;28(1):2229-40.
32. Aithal GC, Narayan R, Nayak UY. Nanoemulgel: A promising phase in drug delivery. Current pharmaceutical design. 2020 Jan 1;26(2):279-91.
33. Prajapati D, Patel TJ. FORMULATION, DEVELOPMENT AND CHARACTERIZATION OF LULICONAZOLE NANOEMULGEL FOR TOPICAL DELIVERY. Pharma Science Monitor. 2021 Oct 1;12(4).
34. Siddiqui A, Jain P, Alex TS, Ali MA, Hassan N, Haneef J, Naseef PP, Kuruniyan MS, Mirza MA, Iqbal Z. Investigation of a minocycline-loaded nanoemulgel for the treatment of acne rosacea. Pharmaceutics. 2022 Oct 28;14(11):2322.
35. Aljohani AA, Alanazi MA, Munahhi LA, Hamroon JD, Mortagi Y, Qushawy M, Soliman GM. Binary ethosomes for the enhanced topical delivery and antifungal efficacy of

ketoconazole. OpenNano. 2023 May 1;11:100145.

36. Ahmad MZ, Ahmad J, Alasmary MY, Akhter S, Aslam M, Pathak K, Jamil P, Abdullah MM. Nanoemulgel as an approach to improve the biopharmaceutical performance of lipophilic drugs: Contemporary research and application. Journal of Drug Delivery Science and Technology. 2022 Jun 1;72:103420.
37. KHUDHAIR AS, SABRI LA. Preparation and evaluation of topical hydrogel containing ketoconazole-loaded bilosomes. ACTA Pharmaceutica Sciencia.;62(4).
38. Ranpise HA, Gujar KN, Pawar SC, Awasthi R, Dua K, Mathure D, Madan JR. Formulation, optimization, and evaluation of ketoconazole loaded nanostructured lipid carrier gel for topical delivery. Drug Delivery Letters. 2020 Mar 1;10(1):61-71.
39. Vartak R, Menon S, Patki M, Billack B, Patel K. Ebselennanoemulgel for the treatment of topical fungal infection. European Journal of Pharmaceutical Sciences. 2020 May 30;148:105323.
40. MENDONSA D, KOLAND M, SM S. Self nano emulsifying drug delivery system of ketoconazole for topical administration. International Journal of Pharmaceutical Research (09752366). 2020 Jan 2.
41. Dar MJ, Khalid S, Varikuti S, Satoskar AR, Khan GM. Nano-elastic liposomes as multidrug carrier of sodium stibogluconate and ketoconazole: A potential new approach for the topical treatment of cutaneous Leishmaniasis. European journal of pharmaceutical sciences. 2020 Mar 30;145:105256.
42. Noronha LL, Ferreira PG, GS Lima C, Borba-Santos LP, Rozental S, de Moraes M, Silva FC, Ferreira VF, Futuro DO. Formulation and evaluation of a novel itraconazole-clotrimazole topical emulgel for the treatment of sporotrichosis. Current Pharmaceutical Design. 2020 Apr 1;26(14):1566-70.
43. Sadozai SK, Khan SA, Karim N, Becker D, Steinbrück N, Gier S, Baseer A, Breinig F, Kickelbick G, Schneider M. Ketoconazole-loaded PLGA nanoparticles and their synergism against Candida albicans when combined with silver nanoparticles. Journal of

Drug Delivery Science and Technology. 2020 Apr 1;56:101574.

44. Mokale V, Naik S, Khatal T, Sonawane SH, Potoroko I. Formulation development and in vitro multimedia drug release study of solid self-microemulsifying drug delivery system of ketoconazole for enhanced solubility and pH-independent dissolution profile. InEncapsulation of Active Molecules and Their Delivery System 2020 Jan 1 (pp. 211-231). Elsevier.

45. Tungadi R, Wicita P. Formulation, optimization, and characterization of snakehead fish (OphiocephalusStriatus) powder nanoemulgel. Brazilian Journal of Pharmaceutical Sciences. 2020 Mar 16;56:e17337.

46. Wu X, Yu Q, Wu J, Li T, Ding N, Wu W, Lu Y, Zhu Q, Chen Z, Qi J. Ionic liquids containing ketoconazole improving topical treatment of T. Interdigitale infection by synergistic action. International Journal of Pharmaceutics. 2020 Nov 15;589:119842.

47. Aggarwal R, Targhotra M, Kumar B, Sahoo PK, Chauhan MK. Treatment and management strategies of onychomycosis. Journal de mycologiemedicale. 2020 Jun 1;30(2):100949.

48. Noronha LL, Ferreira PG, GS Lima C, Borba-Santos LP, Rozental S, de Moraes M, Silva FC, Ferreira VF, Futuro DO. Formulation and evaluation of a novel itraconazole-clotrimazole topical emulgel for the treatment of sporotrichosis. Current Pharmaceutical Design. 2020 Apr 1;26(14):1566-70.

49. Waghule T, Gorantla S, Rapalli VK, Shah P, Dubey SK, Saha RN, Singhvi G. Emerging trends in topical delivery of curcumin through lipid nanocarriers: effectiveness in skin disorders. AapsPharmscitech. 2020 Oct;21:1-2.

50. Huang L, Huang XH, Yang X, Hu JQ, Zhu YZ, Yan PY, Xie Y. Novel nano-drug delivery system for natural products and their application. Pharmacological Research. 2024 Mar 1;201:107100.