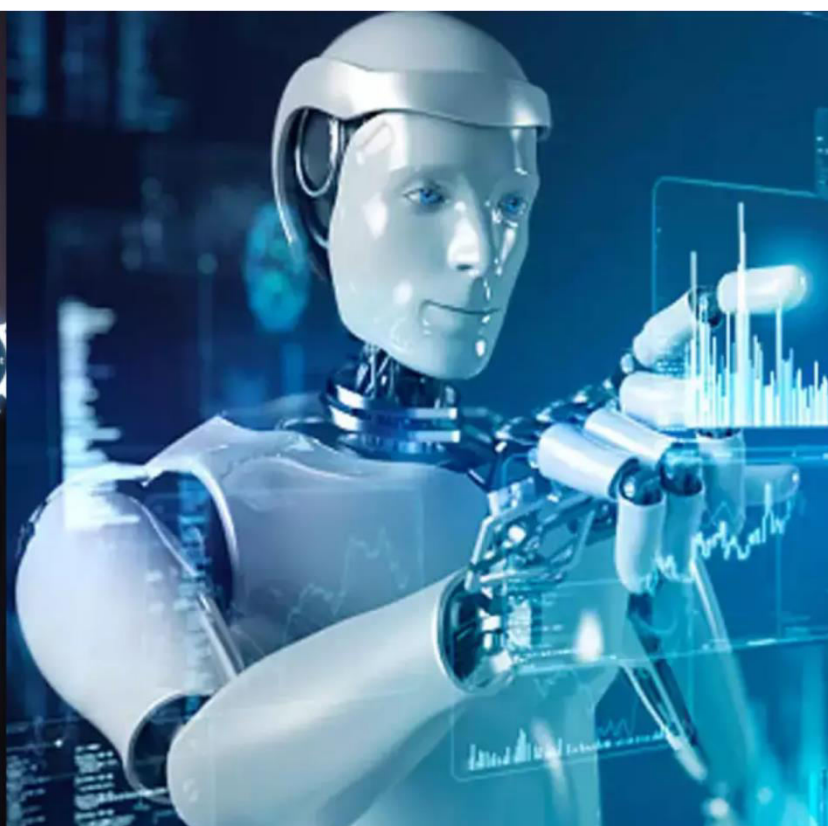




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Development of Antifungal Cream Containing Tolnaftate Liposomes

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ABSTRACT: Fungal infections being a widespread health issue can affect anyone regardless their age or health status and their topical treatments are common causing limited effectiveness by poor drug penetration and potential side effects. Topical drug delivery system is method used for administering medication through skin. Topical medication has several advantages as they escape the exposure to GIT reducing stomach discomfort and liver processing. This project report focuses on the development and evaluation of Anti-fungal cream embedded with Tolnaftate liposomes. Liposomes offer an optimistic solution by enhancing the drug delivery to targeted skin potentially increasing the efficacy and prominent side effects making them ideal for safe drug, genes or nutrients delivery to specific body parts.

Tolnaftate is a synthetic antifungal agent shows action by blocking the enzyme in selective and reversible way by disrupting the cell membrane integrity eventually leading to leakage and resulting in disfunction and death of fungi cell. Being a good Antifungal agent, it may even distort fungal growth(hyphae) and even inhibit further spread by mycelial development. The aim is to enhance the delivery of Tolnaftate, a commonly used anti-fungal drug, by encapsulating it in liposomes which are tiny, fat like vesicles that can improve drug penetration and retention into the skin. The study involves various stages like preformulation studies to assess drug properties, preparation of Tolnaftate- loaded liposomes, formulation of cream base, incorporation of liposomes into the cream, antifungal activity, stability studies, eukaryotic cytotoxic activity, in-vitro drug release study, drug release kinetics. Tolnaftate effectiveness against fungal infections is deep rooted but this project aims to enhance its delivery and efficacy through a novel liposomal cream formulation. The project seeks to develop an improved treatment for fungal skin infections by the coalescence of benefits of liposomes with the therapeutic action of Tolnaftate. Eventually this inventive liposomal cream would provide a more effectual and patient friendly solution encouraging higher and better therapeutic outcome.

KEYWORDS: Topical drug delivery system, Tolnaftate, liposomes, Anti-fungal cream.

I. INTRODUCTION

Fungal Infections also known as mycosis are diseases caused due to pathogenic fungi that colonize the hair, skin, nails, or internal organ of humans. Fungus is the microorganism which are tiny organisms that reside everywhere in our environment. Fungal infection can include superficial, cutaneous, subcutaneous, mucosal and systemic infection with varying degree of severity. Organisms such as candida spp. are part of human microbiota that cause opportunistic infections in individuals and life-threatening infection in immunodeficient patients such as HIV/AIDS or cancer patients receiving chemotherapy, are more susceptible to fungal infections. Although even healthy individual can get infected exclusively in warm and humid environment (e.g. Histoplasma, Blastomyces and Aspergillus) or through dermatophyte infection from direct contact with an infected person or animal. Some common Fungus which are responsible for fungal infection from include **Dermatophytes** are group of Fungus that live off of keratin, a substance in your hair and nails and the outer layer of your skin. Candida albicans, under certain conditions, it grows too much and cause itching, redness. Environmental Fungus. Fungal infection on normal skin, the outer layer (stratum corneum) act as an act as an effective barrier against invaders, but in some cases like minor cuts, scrapes, or continuous moisture can create entry points for fungi. In case of Dermatitis skin, provides a direct and easy entry point for fungal spores because of it include condition like eczema or atopic dermatitis its protective barrier is already compromised and inflamed. This condition makes skin significantly more vulnerable to secondary fungal infections (often referred to as colonization or overgrowth). “Staying aware about potential hazard and taking basic precautions or safety measures are key to protect both yourself and your family from these illnesses.”

II. ATERIALS AND METHODS

List of Materials:

Serial No.	Materials	Manufacturer
1.	Tolnaftate	Yarrow Pharm
2.	Albumin egg powder	GS LAB
3.	Cholesterol	GS LAB
4.	PEG	GS LAB
5.	Acetone	GS LAB
6.	Liquid paraffin	GS LAB
7.	Cetosteryl alcohol	GS LAB
8.	White bees wax	GS LAB
9.	Propyl paraben	GS LAB
10.	Borax	GS LAB
11.	Distilled water	GS LAB

Table 1. List of Materials

List of Equipment's:

Serial No,	Equipment	Manufacturer
1.	Digital Balance	Lab line shock center
2.	UV Visible Spectrometer	JASCO V-630
3.	Magnetic Stirrer	Bio Technics India
4.	Frame Diffusion Cell Apparatus	IIOP lab
5.	Hot Air Oven	Bio Technics lab

Table 2. List of Equipment's

Drug Profile: -

Tolnaftate is commonly used as antifungal treatment medication for variety of skin fungal infections. Also available as over the counter which are supplied in different forms like powder, cream, liquid, spray, liquid aerosols. Those are recognizable under brand names like Odor Eaters or Tinactin.

III. METHODOLOGY

➤ Preformulation studies

1. Melting point: - For determine the melting point, Thiele tube is used which is a specific glass tube with liquid paraffin. The one end of capillary tube is sealed with a small amount of drug being placed inside. A thermometer is attached and the capillary tube is interjected into Thieles tube filled with paraffin. As the paraffin is gently heated on Bunsen burner it starts to melt and the temperature is noted as drugs melting point. Before studying another sample, the paraffin must cool down to around 50°C.

2. Solution analysis: -

To check solubility of tolinaftate drug several solvents were used. Tolinaftate fails to dissolve in water and is more soluble in organic solvents like ethanol, methanol, ethyl aetate, chloroform, and diethyl ether.

3. UV-Visible Spectrophotometer Study: -

a. Preparation of Stoch Solution:

- 10 mg of Tolnaftate is dissolved in 100 ml of ethanol.
-

b. Procedure:

- Take 1 ml of stock solution and dilute it to 10 ml with ethanol in a volumetric flask.
- From this solution, take 1 ml again and dilute it up to 10 ml.
- Measure the absorbance of final solution using a UV-Visible Spectrophotometer.
- Ethanol shows interaction with tolinaftate, and the maximum absorbance (A_{max}) is noted at 257 nm.

4. Compatibility studies: -

a. Preparation of samples: -

- API and excipients were precisely weighed and mixed in 1:1 ratio.
- The mixture was filled into multiple vials, ensuring each vial had a uniform composition.

b. Storage condition and duration; -

- Closed vials: Some vials were sealed tightly to avert any external environmental factors from influencing the mixture.
- Open vials: some vials were left open to environment to assess the impact of exposure to air, moisture, and potential contaminants.
- Both vials were stored under room temperature for a period of 4 weeks.

c. Observation and analysis:

- Samples from both open and closed vials were examined and studied at regular intervals that is weekly for over 4-week period.
- Physical, chemical and organoleptic properties were evaluated including its Appearance (color, clarity), degradation or interaction, etc.

Liposome preparation:

Formulation table:

Ingredients	Quantity with (with drug)	Quantity (blank/without drugs)	Role
Tolnaftate	200mg	-	API
Albumin egg powder	200mg	200mg	Stabilizer
Cholesterol	100mg	100mg	Permeability enhancer
PEG	250mg	250mg	Stabilizer
Acetone	5ml	5ml	solubilizer
Distilled water	10ml	10ml	Vehicle

Table 3. Formulation Table for Liposomes

- Liposomes were prepared using both blank (without drug) and drug loaded (with drug) formulation to examine structural characteristics from microscopic analysis. Both mixtures were exposed to ultrasonication to achieve constant dispersion of particles. The microscopic analysis resulted that drug containing had more structured and particle rich field, while the blank liposomes showed fewer particles, considering the absence of API.

Cream base preparation:

Ingredients	Quantity	Role
Liquid paraffin	2ml	Emollient
Cetosteryl alcohol	0.5ml	Emulsifier
White beeswax	1gm	Stiffening agent
Propyl paraben	q. s.	Preservative
Borax	1gm	Emulsifier
Distilled water	5.5gm	Vehicle

Table 4. Cream Base Preparation



Figure 1. Cream Base Preparation

Incorporation of liposome into cream base:

- Liposome dispersion was slowly introduced into cream base with gentle stirring
- Use of mechanical or overhead stirrer was done to avoid vehicle rupture
- After 15-20 min mixing, homogenous state forms.

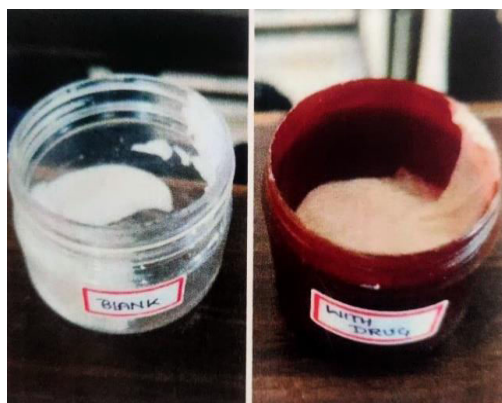


Figure 2. Final Formulation



Figure 3. Microscopic Image

(FINAL FORMULATION)

Evaluations of liposomes-based cream: -

1. Organoleptic test:

- Organoleptic evaluation was performed to ensure that products meet quality standard and are appealing to customers.
- Appearance: it was performed to evaluate visual appearance of cream focusing on factors like texture, color and consistency.
- Odor: examined the aroma of cream focusing on any unpleasant or unusual odor.
- Texture: The consistency, smoothness, effortless and smooth spreading.

2. pH Value:

- The pH range is an important factor used to determine the stability, compatibility and effectiveness with skin.
- The pH range for creams rely on the specific product specifications, but 5.5 to 7.0 is generally considered an optimal pH range of skin creams.

3. Eukaryotic cytotoxic activity:

- This experiment was done to evaluate cytotoxic effect of cream formulation on yeast cells, stimulating its antifungal activity. This assessment was helpful to examine the formulation's therapeutic efficacy in resisting to fungal infections.

Methodology:

• Preparation of test tube:

•

Test tube	Composition
1) Blank	Saline water + yeast granules
2) Drug	Saline water + yeast granules + API
3) Formulation	Saline water + yeast granules + liposomal cream

Table 5. Composition of Eukaryotic Cytotoxic Activity Models

1. Incubation and observation:

- The test tubes were incubated and observed microscopically after 24 and 48 hours to analyze the effect on yeast cells.

2. Invitro permeability testing:

- The purpose was to evaluate permeability of Tolnaftate through a membrane stimulating human skin by using Franz Diffusion Apparatus.

Methodology:

It was done by few steps like Membrane Selection (Egg peel used to mimic human skin), Receptor Compartment (phosphate buffer solution was used as stimulating physiological condition which was of pH 7.4), Sample Collection, Quantification (UV spectroscopy was utilized to quantify the amount of tolnaftate that was permeated through membrane)

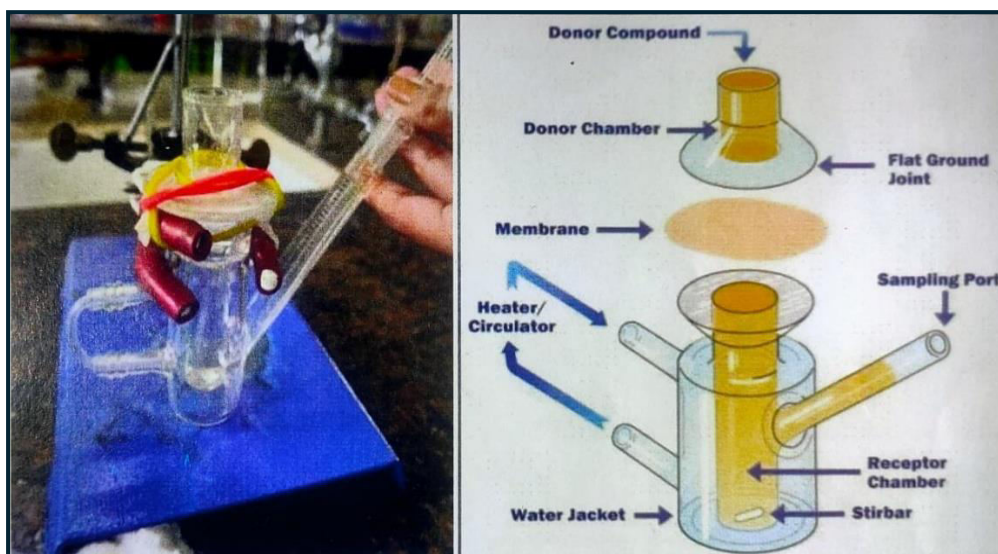


Figure 4. Franz Diffusion Cell Apparatus

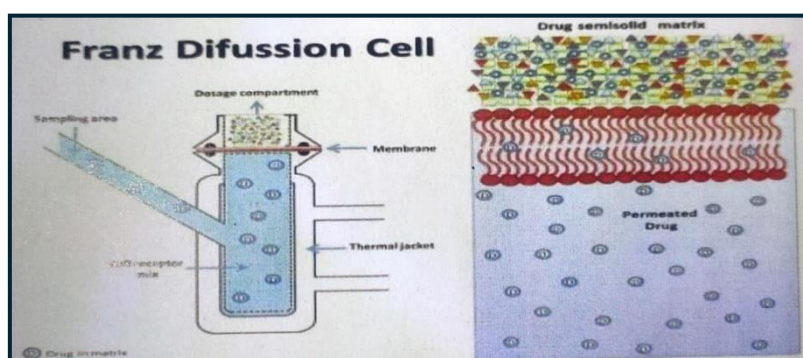


Figure 5. Franz Diffusion Cell Release

IV. RESULT



Figure 6. Drug Release Kinetic Models: Comparative Analysis

Time (Hr.)	Cumulative % drug released	% drug remaining	Square root time	Log Cumu % drug remaining	Log time	Log Cumu % drug released	% Drug released	Cube Root of % drug Remaining (Wt.)
0	0	100	0.000	2.000	0.000	0.000	100	4.642
0.5	3.899	96.101	0.707	1.983	-0.301	0.591	3.899	4.580
1	9.388	90.612	1.000	1.957	0.000	0.973	5.489	4.492
1.5	14.676	85.324	1.225	1.931	0.176	1.167	5.288	4.402
2	17.181	82.819	1.414	1.918	0.301	1.235	2.505	4.359
2.5	22.325	77.675	1.581	1.890	0.398	1.349	5.144	4.267
3	33.553	66.447	1.732	1.822	0.477	1.526	11.228	4.050

0	0	100	0.000	2.000	#NUM!	#NUM!	-33.553	4.642
0	0	100	0.000	2.000	#NUM!	#NUM!	0	4.642

Table 6. Results of In-Vitro Drug Release Study (Diffusion Study)

Drug release kinetics:

1. Zero order kinetics:

The Zero-order model which describes system where the rate of process has been constant and independent of by the amount or concentration of substance involved. This states that the rate of process remains same constant despite the input. Dosage does not follow the zero-order drug release.

2. First order kinetics

First order model was also used to denote the absorption as well as elimination, despite that it is difficult to devise this mechanism.

3. Korsemeyer-Peppas kinetics

Korsemeyer – Peppas model is to find out the mechanism of drug release first 60% drug release data was fitted in Korsemeyer and Peppas Model.

4. Higuchi kinetic

The Higuchi Model is a foundational model in field of controlled drug delivery examining release of drugs from a solid matrix depending on how the drug diffuses out over time.

Diffusion-Driven Release:

The Higuchi model focuses on Fickian diffusion concept, in which the drug moves from higher concentration area in matrix to lower concentration area in surrounding medium.

Square Root of Time:

The model was used to forecast that the amount of drug released is proportional to square root of time. It conveys that the rate of release is not constant but decreases gradually over time.

Regression analysis:

Linear regression analysis helps to find out how well Higuchi Model fits experimental data. A high R² value shows a good fit stating that the Higuchi model precisely predicts the drug release behavior. When cumulative percents of drug release was plotted as function of square root of the time at which they were obtained, and nearly straight-line plot was obtained. Coefficient of linear regression of line was R² = 0.8703 and it follows diffusion mechanism.

5. The Hixson-Crowell Kinetics:

The Hixson-Crowell model showed highest R²=0.9623 value in release data indicating it as an effective model for describing diffusion in formulation.

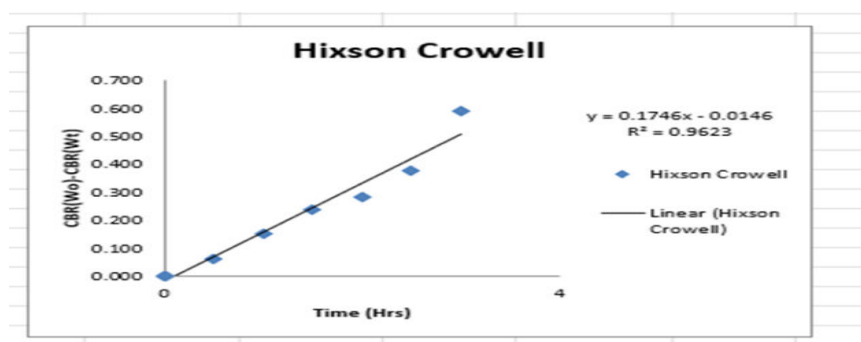


Figure 6. Hixson-Crowell Model for Drug Release Kinetics

V. DISCUSSION

The Liposomal Tolnaftate cream showed prominent improvement on how well drug works specifically by helping it absorb better in skin. By incorporating the drug in fat-based bubbles known as Liposomes. It has become more stable and is protected from breakdown too quickly and is released slowly over time. In lab, the cream properties like particle size and stability were carefully adjusted to make certain that it spreads evenly and penetrates into skin effectively. The test showed that the drug stays longer on skin indicating fewer applications resulting in better patient compliance. This type of targeted delivery additionally reduces the side effects since less amount of drug goes into the bloodstream. Altogether these results Suggest that liposomal cream which could be strong as well as safe option for treating fungal skin infection having good potential for future medical use.

VI. CONCLUSION

This project successfully developed and evaluated a novel antifungal cream containing Tolnaftate- loaded liposomes, focusing to restructure the treatment of fungal skin infections. Recognizing the limits of poor drug penetration of traditional cream, we utilized liposomes to significantly strengthen tolnaftate's delivery and retention within skin. The research included careful preparation of stable liposomes and their seamless incorporation into suitable cream base. Meticulous testing, including stability studies including drug release profiles, confirmed the formulations integrity and efficacy. The enhanced antifungal activity has been enhanced was demonstrated while proving its superior performance. Ultimately, this innovative liposomal cream provides enhanced effectiveness and patient- friendly solution by ensuring improver drug penetration and sustained release. Promising higher localized drug concentration, leading to better therapeutic outcomes for individuals suffering from fungal skin infections.

REFERENCES

1. Darshini, D., et al. "Formulation and Evaluation of Liposomal Cream Containing Tolnaftate." *Journal of Drug Delivery and Therapeutics*, vol. 15, no. 1, Jan. 2025, pp. 13-18. DOL.org (Crossref), <https://doi.org/10.22270/jddt.v15i1.6944>
2. John DF, Yunus AA, Chigbo UJ, Paul US, Jkenna E. Tolnaftate loaded liposomes-design, and in-vitro evaluation. *Universal Journal of Pharmaceutical Research* 2016;1(2): 29-31. <http://doi.org/10.22270/ujpr.v1i2.R6>
3. Dimov, Nikolay, et al. "Formation and Purification of Tailored Liposomes for Drug Delivery Using a Module-Based Micro Continuous-Flow System." *Scientific Reports*, vol. 7, no. 1, Sept. 2017, p. 12045. DOI.org (Crossref), <https://doi.org/10.1038/s41598-017-11533-1>.
4. Shaw, Tapan Kumar, et al. "Research-Based Findings on Scope of Liposome-Based Cosmeceuticals: An Updated Review." *Future Journal of Pharmaceutical Sciences*, vol. 8, no. 1, Nov. 2022, p. 46. DOL.org (Crossref), <https://doi.org/10.1186/s43094-022-00435-3>.
5. Kurban, A. K., et al. "Clinical Evaluation of Tolnaftate. A Double-Blind Study of a Topical Antifungal Agent." *Dermatology*, vol. 133, no. 6, 1966, pp. 482-86. DOL.org (Crossref), <https://doi.org/10.1159/000254371>.
6. Miles. William J. "Tinea Nigra: Report of Two Cases and Results of Treatment With Tolnaftate." *Archives of Dermatology*. vol. 94, no. 2. Aug. 1966, p. 203. DOI.org (Crossref), <https://doi.org/10.1001/archderm.1966.01600260095015>
7. Dash, Alekha K. "A Liquid Chromatographic Method for the Determination of Tolnaftate in Pharmaceutical Formulations." *Journal of Pharmaceutical and Biomedical Analysis*, vol. 11, no. 9. Sept. 1993, pp. 847-53. DOL.org (Crossref), [https://doi.org/10.1016/0731-7085\(93\)80079-G](https://doi.org/10.1016/0731-7085(93)80079-G).
8. AbouSamra, Mona Mahmoud, and Alaa Hamed Salama. "Enhancement of the Topical Tolnaftate Delivery for the Treatment of Tinea Pedis via Provesicular Gel Systems." *Journal of Liposome Research*, vol. 27, no. 4. Oct. 2017, pp. 324-34. DOI.org (Crossref), <https://doi.org/10.1080/08982104.2016.1239634>.
9. Ayres, Samuel. "Erythrasma: Response to Tolnaftate, an Antifungal Medication." *Archives of Dermatology*, vol. 97, no. 2, Feb. 1968, p. 173. DOI.org (Crossref). <https://doi.org/10.1001/archderm.1968.01610080077014>.
10. Department of biochemistry Ahmadu Bello University, P. M. B. 1045, Samaru, Zaria, Kaduna, Nigeria, and Dingwoke Francis John. "TOLNAFTATE LOADED LIPOSOMES- DESIGN, AND IN-VITRO EVALUATION." *Universal Journal of Pharmaceutical Research*, Dec. 2016, pp. 48-53. DOL.org (Crossref). <https://doi.org/10.22270/ujpr.v1i2.R6>.
11. "Tolnaftate." *BMJ*, vol. 3, no. 5568, Sept. 1967, pp. 785-785. DOL.org (Crossref), <https://doi.org/10.1136/bmj.3.5568.785>.

12. Barren-Bee. K. J. et al. "The Mode of Antifungal Action of Tolnaftate" Medical Mycology, vol. 24, no. 2, Jan. 1986, pp. 155-60 DOL.org (Crossref), <https://doi.org/10.1080/02681218680000221>
13. Amsel, Lewis P., et al. "Comparison of in Varo Activity of Undecylenic Acid and Tolnaftate against Athlete's Foot Fungi." Journal of Pharmaceutical Sciences, vol. 68, no. 3. Mar. 1979. Pp. 84-85. DOL.org (Crossref). <https://doi.org/10.1002/jps.2600680338>.
14. Robinson, Harry M. "Tolnaftate, a Potent Topical Antifungal Agent." Archives of Dermatology, vol. 91, no. 4, Apr. 1965, p. 372. DOL.org (Crossref). <https://doi.org/10.1001/archderm.1965.01600100088024>.
15. Environmental College, Department of Technology, University of Mosul-Iraq, and Nief Rahman Ahmed. "Estimation of Tolnaftate in Pharmaceutical Preparations Samples." Journal of Infectious Diseases & Case Reports, Sept. 2020, pp. 1-3. DOL.org (Crossref), [https://doi.org/10.47363/JJDSCR/2020\(1\)114](https://doi.org/10.47363/JJDSCR/2020(1)114).
16. Pérez, R. González, et al. "Allergic Contact Dermatitis from Tolnaftate." Contact Dermatitis, vol. 32, no. 3, Mar. 1995, pp. 173-173. DOL.org (Crossref). <https://doi.org/10.1111/j.1600-0536.1995.tb00811.x>.
17. "Tolnaftate Used in Treatment of Dermatomycoses." JAMA, vol 190, no. 12, Dec. 1964, p. 38. DOL.org (Crossref), <https://doi.org/10.1001/jama.1964.03070250086049>.
18. Noguchi, T. "Teratogenesis Study of Tolnaftate, an Antitrichophyton Agent." Toxicology and Applied Pharmacology, vol. 8, no. 3, May 1966, pp. 386-97. DOL.org (Crossref), [https://doi.org/10.1016/0041-008X\(66\)90049-4](https://doi.org/10.1016/0041-008X(66)90049-4).
19. Sastry, C. S. P., et al. "Spectrophotometric Methods for the Determination of Tolnaftate." Talanta, vol. 40, no. 4. Apr. 1993, pp. 571-76. DOL.org (Crossref). [https://doi.org/10.1016/0039-9140\(93\)80019-N](https://doi.org/10.1016/0039-9140(93)80019-N).
20. Salim, Edward F., and Wilbur S. Felker. "Qualitative and Quantitative Tests for Tolnaftate." Journal of Pharmaceutical Sciences, vol. 56, no. 7, July 1967, pp. 886-87. DOL.org (Crossref), <https://doi.org/10.1002/jps.2600560720>.
21. Ayyangar, N. R., et al. "AN ALTERNATIVE METHOD FOR TOLNAFTATE." Organic Preparations and Procedures International, vol. 22, no. 1, Feb. 1990, pp. 128-30. DOL.org (Crossref), <https://doi.org/10.1080/00304949009356685>
22. Gregoriadis, Gregory, editor. Liposome Technology: Liposome Preparation and Related Techniques. 0 ed., CRC Press, 2016. DOL.org (Crossref), <https://doi.org/10.1201/9780849397264>.
23. Odds. Frank C., et al. "Antifungal Agents: Mechanisms of Action." Trends in Microbiology, vol. 11, no. 6, June 2003, pp. 272-79. DOL.org (Crossref). [https://doi.org/10.1016/S0966-842X\(03\)00117-3](https://doi.org/10.1016/S0966-842X(03)00117-3).
24. Khashaba, P. Y., et al. "Analysis of Some Antifungal Drugs by Spectrophotometric and Spectrofluorimetric Methods in Different Pharmaceutical Dosage Forms." Journal of Pharmaceutical and Biomedical Analysis, vol. 22, no. 2, Mar. 2000, pp. 363-76. DOL.org (Crossref), [https://doi.org/10.1016/S0731-7085\(99\)00280-0](https://doi.org/10.1016/S0731-7085(99)00280-0).
25. S. Deeksha, et al. "Comparative Study of Liposomes. Transfersomes and Ethosomes as Carriers for Enhancing Topical Delivery of Tolnaftate: In Vitro Evaluation." Research Journal of Pharmacy and Technology, June 2024, pp. 2661-68. DOL.org (Crossref). <https://doi.org/10.52711/0974-360X.2024.00417>.
26. Ryder, N. S., et al. "Ergosterol Biosynthesis Inhibition by the Thiocarbamate Antifungal Agents Tolnaftate and Tolciclate." Antimicrobial Agents and Chemotherapy, vol. 29, no. 5, May 1986, pp. 858-60. DOL.org (Crossref), <https://doi.org/10.1128/AAC.29.5.858>.
27. Albasri, Omar Waleed Abduljaleel. "Formulation and Assessment of Tolnaftate Microsponges for Topical Medication Deliverance." South Asian Research Journal of Pharmaceutical Sciences, vol. 6, no. 06, Nov. 2024, pp. 176-82. DOL.org (Crossref). <https://doi.org/10.36346/sarjps.2024.v06i06.001>.
28. Priya, Sneha, et al. "Tolnaftate-Loaded Ethosomal Gel for Topical Delivery: Formulation and In Vitro Evaluation." Journal of Health and Allied Sciences NU, vol. 15, no. 01, Jan. 2025, pp. 026-31. DOL.org (Crossref), <https://doi.org/10.1055/s-0044-1787293>.
29. Department of biochemistry Ahmadu Bello University. P. M. B. 1045. Samaru, Zaria, Kaduna, Nigeria, and Dingwoke Francis John. "TOLNAFTATE LOADED LIPOSOMES-DESIGN, AND IN-VITRO EVALUATION." Universal Journal of Pharmaceutical Research, Dec. 2016, pp. 48-53. DOL.org (Crossref). <https://doi.org/10.22270/ujpr.v1i2.R6>.
30. Meier-Davis, Susan R., et al. "Enhancing the Skin Flux of Tolnaftate Utilizing the Novel Excipient, Dodecyl-2-N, NDimethylaminopropionate (DDAIP)." Journal of Pharmaceutics & Drug Delivery Research, vol. 01. no. 01, 2012. DOL.org (Crossref). <https://doi.org/10.4172/2325-9604.1000102>.
31. Schmid. M. H., and H. C. Korting. "Therapeutic Progress with Topical Liposome Drugs for Skin Disease." Advanced Drug Delivery Reviews, vol. 18, no. 3, Feb. 1996, pp. 335-42. DOL.org (Crossref), [https://doi.org/10.1016/0169-409X\(95\)00019-4](https://doi.org/10.1016/0169-409X(95)00019-4).



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