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Nanoemulsions: A Promising Approach for Antifungal Therapy

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Abstract : Fungal infections present a significant global health challenge, necessitating the development of innovative therapeutic strategies. Nanoemulsions have emerged as a promising approach for enhancing the efficacy of antifungal agents. This review provides a comprehensive overview of the application of nanoemulsions in antifungal therapy. We discuss the composition and characteristics of nanoemulsions, mechanisms of antifungal action, recent advancements, and future prospects. Nanoemulsions offer numerous advantages, including improved drug solubility, enhanced bioavailability, and targeted drug delivery, making them an attractive platform for combating fungal infections. This review highlights the potential of nanoemulsions to revolutionize antifungal therapy and pave the way for more effective treatment strategies.

IndexTerms **- Nanoemulsions, Antifungal therapy, Drug delivery, Targeted delivery, Topical formulations.**

I. INTRODUCTION

Fungal infections pose a significant global health threat, affecting millions of individuals worldwide and contributing to substantial morbidity and mortality. Despite the availability of antifungal medications, the emergence of drug-resistant fungal strains and limitations of conventional formulations have underscored the need for innovative therapeutic approaches. Nanoemulsions have emerged as a promising strategy for enhancing the efficacy of antifungal agents and overcoming existing challenges in fungal infection treatment[1].Nanoemulsions are colloidal dispersions composed of nanoscale droplets of one immiscible liquid dispersed within another immiscible liquid, typically stabilized by surfactants or co-surfactants. These formulations offer several advantages for drug delivery, including enhanced drug solubility, improved bioavailability, and targeted delivery to the site of infection. The small droplet size and unique physicochemical properties of nanoemulsions facilitate rapid drug release and interaction with fungal pathogens, leading to enhanced antifungal activity[2].

In this review, we provide a comprehensive overview of the application of nanoemulsions in antifungal therapy. We discuss the composition and characteristics of nanoemulsions, mechanisms of antifungal action, recent advancements, and future prospects. By highlighting the potential of nanoemulsions to revolutionize antifungal therapy, this review aims to contribute to the development of more effective treatment strategies for fungal infections[3].

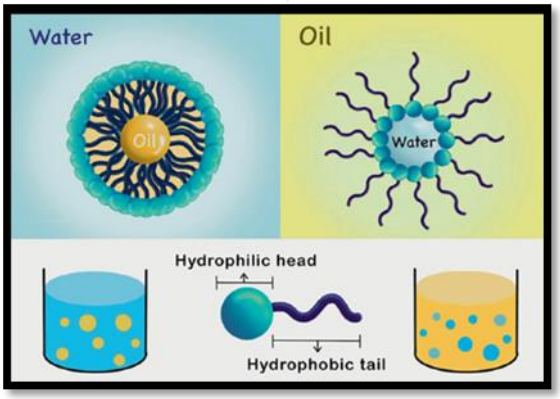

Fig 1: Nanoemulsion

II. NANOEMULSIONS: COMPOSITION AND CHARACTERISTICS

The composition of nanoemulsions plays a crucial role in determining their stability, biocompatibility, and therapeutic efficacy. Typically, nanoemulsions consist of three main components: the dispersed phase, continuous phase, and stabilizers. The dispersed phase contains the active pharmaceutical ingredient (API) or drug, which may be hydrophobic or hydrophilic, depending on its solubility characteristics. Commonly used dispersed phases include oils such as medium-chain triglycerides (MCTs), soybean oil, or essential oils with inherent antimicrobial properties. The continuous phase, often an aqueous solution, provides the bulk of the formulation and facilitates the dispersion of the dispersed phase[4]. Stabilizers, including surfactants and co-surfactants, prevent the

coalescence and aggregation of droplets, thereby maintaining the stability of the nanoemulsion. Surfactants such as Tween, Span, and lecithin are commonly employed for this purpose.

The characteristics of nanoemulsions are determined by several factors, including droplet size, polydispersity index (PDI), zeta potential, and viscosity. The droplet size of nanoemulsions typically ranges from 10 to 200 nanometers, with smaller droplets exhibiting higher stability and greater surface area for drug interaction. The PDI reflects the uniformity of droplet size distribution, with lower values indicating a more monodisperse formulation. Zeta potential, a measure of the electrostatic repulsion between droplets, influences the colloidal stability of nanoemulsions, with higher absolute values indicating greater repulsion and enhanced stability[5]. Viscosity affects the flow behavior and ease of administration of nanoemulsions, with lower viscosity formulations being preferred for topical applications.

Several methods are available for the preparation of nanoemulsions, including high-energy and low-energy techniques. High-energy methods, such as high-pressure homogenization and ultrasonication, generate nanoemulsions by applying mechanical forces to disrupt the dispersed phase into smaller droplets. Low-energy methods, such as phase inversion temperature (PIT) and spontaneous emulsification, rely on phase transitions or self-assembly to form nanoemulsions without the need for extensive energy input[6].

Overall, nanoemulsions offer numerous advantages for drug delivery and antimicrobial therapy, including enhanced solubility, stability, and targeted delivery of drugs to infection sites. By optimizing the composition and characteristics of nanoemulsions, researchers can develop highly effective formulations for the treatment of fungal infections and other medical conditions[7].

III. Antifungal Agents in Nanoemulsions

Antifungal agents formulated in nanoemulsions represent a promising approach for the treatment of fungal infections due to their enhanced solubility, stability, and bioavailability. These nanostructured delivery systems offer several advantages over conventional antifungal formulations, including improved drug penetration into fungal cells, sustained release kinetics, and reduced adverse effects[8].

Azole antifungals, such as fluconazole and itraconazole, have been successfully incorporated into nanoemulsions to enhance their antifungal activity. By encapsulating these drugs within nanoscale droplets, their aqueous solubility is increased, leading to improved drug permeation across biological barriers and enhanced efficacy against fungal pathogens. Additionally, nanoemulsions can protect encapsulated antifungal agents from degradation and premature clearance, thereby prolonging their therapeutic effects[9].

Amphotericin B, a potent antifungal agent with poor aqueous solubility and significant nephrotoxicity, has also been formulated in nanoemulsions to overcome these limitations. By encapsulating amphotericin B within lipid-based nanoemulsions, its solubility is improved, reducing the risk of nephrotoxicity and enabling targeted delivery to fungal infection sites. Furthermore, nanoemulsion-based formulations of amphotericin B have demonstrated enhanced antifungal activity and reduced toxicity compared to conventional formulations.

Essential oils, such as tea tree oil and cinnamon oil, which possess inherent antifungal properties, have been incorporated into nanoemulsions for topical applications. These natural compounds exhibit broad-spectrum antifungal activity and can effectively inhibit the growth of various fungal species[10]. Nanoemulsion-based delivery systems enhance the stability and skin penetration of essential oils, making them promising candidates for the treatment of superficial fungal infections.

IV. Mechanisms of Antifungal Action

Antifungal action within nanoemulsion drug delivery systems involves several mechanisms that contribute to the enhanced efficacy of antifungal agents against fungal pathogens:

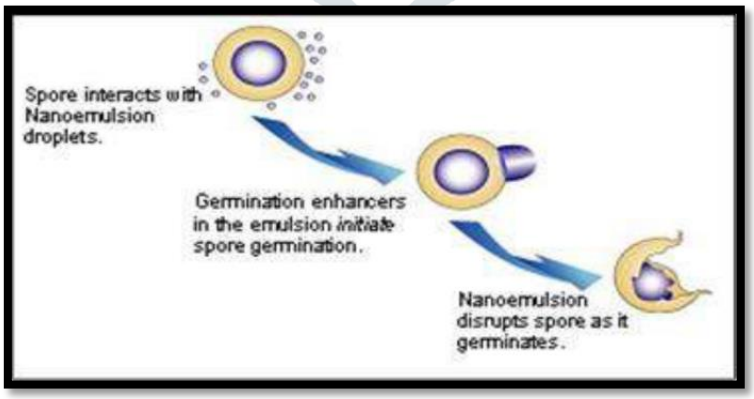

Fig 2: Nanoemulsion mechanism of action against spores

- Increased Drug Solubility: Nanoemulsions enhance the solubility of antifungal drugs, particularly those with poor aqueous solubility, by encapsulating them within nanoscale droplets. This increased solubility ensures better dispersion of the drug within the formulation and facilitates its interaction with fungal cells.
- Enhanced Drug Penetration: Nanoemulsions improve the penetration of antifungal agents into fungal cells by reducing their particle size and increasing their surface area. This allows for more efficient diffusion of the drug through fungal cell membranes, ultimately enhancing its intracellular accumulation and antifungal activity[11].
- Targeted Drug Delivery: Nanoemulsions can be engineered to target specific fungal infection sites, thereby minimizing off-target effects and maximizing therapeutic efficacy. Functionalization of nanoemulsions with ligands or antibodies that

recognize fungal cell surface antigens enables selective drug delivery to infected tissues, reducing systemic exposure and potential toxicity.

- Disruption of Fungal Cell Membranes: Some nanoemulsion formulations exert their antifungal effects by directly disrupting fungal cell membranes. The small size of nanoemulsion droplets allows them to penetrate fungal cell walls and interact with membrane lipids, leading to destabilization and eventual lysis of fungal cells[12].
- Synergistic Effects with Other Antifungal Agents: Nanoemulsions can be used to encapsulate multiple antifungal agents, leading to synergistic effects that enhance their overall antifungal activity. Combination therapy within nanoemulsion formulations allows for the simultaneous delivery of multiple drugs with complementary mechanisms of action, resulting in improved efficacy against drug-resistant fungal strains[13].

Overall, the mechanisms of antifungal action in nanoemulsion drug delivery systems are multifaceted and involve a combination of enhanced drug solubility, penetration, targeted delivery, membrane disruption, and synergistic effects. By harnessing these mechanisms, nanoemulsion-based formulations hold great promise for the treatment of fungal infections with improved efficacy and reduced side effects.

V. Applications of Nanoemulsions in Antifungal Therapy

Nanoemulsions have shown promising applications in antifungal therapy across various medical and pharmaceutical fields due to their unique properties and versatile formulations:

- Topical Antifungal Formulations: Nanoemulsions can be formulated into topical creams, gels, lotions, and sprays for the treatment of superficial fungal infections such as athlete's foot, ringworm, and candidiasis. Their small droplet size enables efficient skin penetration, delivering antifungal agents directly to the site of infection for rapid and targeted therapy.
- Oral Antifungal Delivery Systems: Nanoemulsions can encapsulate antifungal drugs for oral administration, improving drug solubility and bioavailability while minimizing gastrointestinal side effects. This approach is particularly beneficial for systemic fungal infections such as oral thrush and oesophageal candidiasis[14].
- Antifungal Nanoparticles: Nanoemulsions can serve as carriers for antifungal nanoparticles, enhancing their stability and dispersibility. These nanoparticulate systems can be functionalized with targeting ligands or surface modifications to improve their specificity and efficacy against fungal pathogens[15].
- Antifungal Coatings and Sprays: Nanoemulsions can be incorporated into coatings, paints, and sprays for antifungal protection of surfaces, textiles, and medical devices. By forming a thin, uniform film, nanoemulsions provide long-lasting antifungal activity, preventing the growth and colonization of fungal biofilms.
- Antifungal Nanocomposites: Nanoemulsions can be integrated into nanocomposite materials for the development of antifungal wound dressings, implants, and medical devices. These materials exhibit enhanced antimicrobial properties, promoting wound healing and preventing secondary fungal infections in clinical settings[16].

VI. Recent Advancements and Future Directions

Recent advancements in nanoemulsion-based antifungal therapy have led to significant progress in improving drug delivery, efficacy, and safety. Some notable advancements and future directions include:

- Enhanced Drug Loading and Stability: Researchers are developing novel strategies to improve the loading capacity and stability of antifungal drugs in nanoemulsions. This includes the use of advanced formulation techniques such as solid lipid nanoparticles, polymer-based nanoparticles, and lipid-drug conjugates to enhance drug solubility and encapsulation efficiency[17].
- Targeted Drug Delivery: Future nanoemulsion formulations aim to achieve targeted delivery of antifungal agents to specific sites of infection, minimizing systemic exposure and off-target effects. This involves the functionalization of nanoemulsion surfaces with targeting ligands, antibodies, or peptides that recognize and bind to fungal cell wall components, facilitating selective drug release and uptake.
- Combination Therapy: Researchers are exploring the potential of nanoemulsion-based combination therapy to combat fungal infections more effectively. By incorporating multiple antifungal agents or synergistic drug combinations into nanoemulsions, it is possible to overcome drug resistance mechanisms, broaden the spectrum of activity, and enhance therapeutic outcomes.
- Stimuli-Responsive Nanoemulsions: Stimuli-responsive nanoemulsions that undergo controlled drug release in response to specific triggers, such as pH, temperature, or enzymatic activity, are being investigated for antifungal therapy. These smart nanoemulsion systems enable site-specific drug delivery and can be tailored to respond to the unique microenvironment of fungal infections[18].
- Nanotechnology-Based Diagnostics: Advances in nanotechnology-based diagnostics, such as biosensors and imaging techniques, are complementing nanoemulsion-based antifungal therapy. These diagnostic tools enable rapid and accurate detection of fungal pathogens, guiding personalized treatment decisions and monitoring therapeutic responses in real-time[19].

Overall, the future of nanoemulsion-based antifungal therapy holds great promise for addressing the challenges of fungal infections, including drug resistance, limited efficacy, and adverse effects. By leveraging innovative nanotechnology approaches, researchers aim to develop safer, more effective, and patient-friendly antifungal treatments for improved clinical outcomes.

VII. Conclusion

In conclusion, nanoemulsion-based antifungal therapy represents a promising avenue for addressing the challenges associated with fungal infections. The unique characteristics of nanoemulsions, including their small particle size, high stability, and enhanced drug solubility, make them ideal candidates for delivering antifungal agents to target sites of infection. Through recent advancements in formulation techniques, drug loading strategies, and targeted delivery approaches, nanoemulsions offer improved efficacy, safety, and patient compliance compared to conventional antifungal treatments.

The development of stimuli-responsive nanoemulsions, combination therapy approaches, and nanotechnology-based diagnostics further expands the therapeutic potential of nanoemulsion-based antifungal therapy, enabling personalized treatment strategies and precise monitoring of therapeutic responses. Additionally, the integration of nanotechnology with traditional antifungal agents holds promise for overcoming drug resistance mechanisms, broadening the spectrum of activity, and mitigating off-target effects.

References

[1] M. Hakemi-Vala, H. Rafati, A. Aliahmadi, and A. Ardalan, "Nanoemulsions: A Novel Antimicrobial Delivery System," in Nano- and Microscale Drug Delivery Systems: Design and Fabrication, Elsevier, 2017, pp. 245–266. doi: 10.1016/B978-0-323-52727-9.00013-3.

[2] P. Sahu, D. Das, V. K. Mishra, V. Kashaw, and S. K. Kashaw, "Nanoemulsion: A Novel Eon in Cancer Chemotherapy," Mini-Reviews in Medicinal Chemistry, vol. 17, no. 18, Nov. 2017, doi: 10.2174/1389557516666160219122755.

[3] M. Jaiswal, R. Dudhe, and P. K. Sharma, "Nanoemulsion: an advanced mode of drug delivery system," 3 Biotech, vol. 5, no. 2. Springer Verlag, pp. 123–127, Apr. 01, 2015. doi: 10.1007/s13205-014-0214-0.

[4] H. Cui, W. Li, C. Li, S. Vittayapadung, and L. Lin, "Liposome containing cinnamon oil with antibacterial activity against methicillin-resistant Staphylococcus aureus biofilm," Biofouling, vol. 32, no. 2, pp. 215–225, Feb. 2016, doi: 10.1080/08927014.2015.1134516.

[5] N. Shams and M. A. Sahari, "Nanoemulsions: Preparation, Structure, Functional Properties and their Antimicrobial Effects," Review Article APPLIED FOOD BIOTECHNOLOGY, vol. 3, no. 3, pp. 138–149, 2016, [Online]. Available: www.journals.sbmu.ac.ir/afb

[6] H. H. Tayeb, R. Felimban, S. Almaghrabi, and N. Hasaballah, "Nanoemulsions: Formulation, characterization, biological fate, and potential role against COVID-19 and other viral outbreaks," Colloid Interface Sci Commun, vol. 45, p. 100533, Nov. 2021, doi: 10.1016/j.colcom.2021.100533.

[7] Z. A. A. Aziz et al., "Essential Oils: Extraction Techniques, Pharmaceutical And Therapeutic Potential - A Review," Curr Drug Metab, vol. 19, no. 13, pp. 1100–1110, Nov. 2018, doi: 10.2174/1389200219666180723144850.

[8] M. Dávila-Rodríguez, A. López-Malo, E. Palou, N. Ramírez-Corona, and M. T. Jiménez-Munguía, "Antimicrobial activity of nanoemulsions of cinnamon, rosemary, and oregano essential oils on fresh celery," LWT, vol. 112, p. 108247, Sep. 2019, doi: 10.1016/j.lwt.2019.06.014.

[9] F. Branco Filippin Liliete Canes Souza and R. Cavalcante Maranhão, "AMPHOTERICIN B ASSOCIATED WITH TRIGLYCERIDE-RICH NANOEMULSION: STABILITY STUDIES AND IN VITRO ANTIFUNGAL ACTIVITY," 2008.

[10] F. Branco Filippin Liliete Canes Souza and R. Cavalcante Maranhão, "AMPHOTERICIN B ASSOCIATED WITH TRIGLYCERIDE-RICH NANOEMULSION: STABILITY STUDIES AND IN VITRO ANTIFUNGAL ACTIVITY," 2008.

[11] P. Pongsumpun, S. Iwamoto, and U. Siripatrawan, "Response surface methodology for optimization of cinnamon essential oil nanoemulsion with improved stability and antifungal activity," Ultrason Sonochem, vol. 60, Jan. 2020, doi: 10.1016/j.ultsonch.2019.05.021.

[12] R. Pathania, H. Khan, R. Kaushik, and M. A. Khan, "Essential oil nanoemulsions and their antimicrobial and food applications," Current Research in Nutrition and Food Science, vol. 6, no. 3. Enviro Research Publishers, pp. 626–643, Dec. 01, 2018. doi: 10.12944/CRNFSJ.6.3.05.

[13] R. Santamaría et al., "Systems biology of infectious diseases: A focus on fungal infections," Immunobiology, vol. 216, no. 11. Elsevier GmbH, pp. 1212–1227, 2011. doi: 10.1016/j.imbio.2011.08.004.

[14] E. O. Ajaiyeoba, "PHYTOCHEMICAL AND ANTIMICROBIAL STUDIES OF GYNANDROPSIS GYNANDRA AND BUCHHOLZIA CORIACEAE EXTRACTS," 2000. [Online]. Available: http://www.ajbr98.com

[15] I. de A. Freires et al., "Coriandrum sativum L. (Coriander) Essential Oil: Antifungal Activity and Mode of Action on Candida spp., and Molecular Targets Affected in Human Whole-Genome Expression," PLoS One, vol. 9, no. 6, p. e99086, Jun. 2014, doi: 10.1371/journal.pone.0099086.

[16] N. Kumar Verma, A. P. Singh, G. Alam, S. Bali, S. Chaudhary, and P. Panda, "NANOEMULSION BASED DRUG DELIVERY-A REVIEW European Journal of Pharmaceutical and Medical Research NANOEMULSION BASED DRUG DELIVERY-A REVIEW," 2023. [Online]. Available: www.ejpmr.com

[17] R. Krishnamoorthy, M. A. Gassem, J. Athinarayanan, V. S. Periyasamy, S. Prasad, and A. A. Alshatwi, "Antifungal activity of nanoemulsion from Cleome viscosa essential oil against food-borne pathogenic Candida albicans," Saudi J Biol Sci, vol. 28, no. 1, pp. 286–293, Jan. 2021, doi: 10.1016/j.sjbs.2020.10.001.

[18] C. M. Bedoya-Serna, G. C. Dacanal, A. M. Fernandes, and S. C. Pinho, "Antifungal activity of nanoemulsions encapsulating oregano (Origanum vulgare) essential oil: in vitro study and application in Minas Padrão cheese," Brazilian Journal of Microbiology, vol. 49, no. 4, pp. 929–935, Oct. 2018, doi: 10.1016/j.bjm.2018.05.004.

[19] Y. Hu, J. Zhang, W. Kong, G. Zhao, and M. Yang, "Mechanisms of antifungal and anti-aflatoxigenic properties of essential oil derived from turmeric (Curcuma longa L.) on Aspergillus flavus," Food Chem, vol. 220, pp. 1–8, Apr. 2017, doi: 10.1016/j.foodchem.2016.09.179.