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Formulation and evaluation of pharmacosome Topical antifungal gel of miconazole Nitrate

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Abstract: Fungal infections pose significant challenges in healthcare due to their widespread prevalence and often stubborn nature. Miconazole nitrate, a potent antifungal agent, has been a cornerstone in the treatment of these infections. However, its efficacy is hampered by limited skin penetration and rapid clearance, necessitating frequent applications and potentially leading to suboptimal outcomes. In response to these challenges, this study aimed to develop a novel formulation utilizing pharmacosomes to encapsulate miconazole nitrate, thereby enhancing its delivery and therapeutic effectiveness.

Pharmacosomes, lipid-based vesicular carriers, hold promise as advanced drug delivery systems due to their ability to improve drug solubility, stability, and bioavailability. By entrapping miconazole nitrate within pharmacosomes, it is hypothesized that its skin permeation and retention would be significantly enhanced, leading to prolonged drug release at the site of infection and ultimately improved clinical outcomes.

The formulation process involved meticulous selection of phospholipids, cholesterol, and other excipients to construct pharmacosomes encapsulating miconazole nitrate. Various methods such as thin film hydration, ethanol injection, and solvent evaporation were explored to optimize the formulation parameters and ensure uniform distribution of the drug within the vesicles. Physicochemical properties including particle size, zeta potential, and drug encapsulation efficiency were rigorously evaluated to ascertain the quality and stability of thepharmacosome formulation.

In conclusion, the formulation and evaluation of pharmacosome topical antifungal gel of miconazole nitrate represent a significant advancement in the field of topical drug delivery. By harnessing the unique properties of pharmacosomes, this formulation offers improved drug delivery efficiency, sustained release, and enhanced therapeutic efficacy. Future studies should focus on clinical trials to validate these findings and ascertain the clinical utility of this innovative formulation in the management of fungal infections.

Introduction:

Fungal infections represent a significant global health burden, affecting millions of individuals annually across diverse demographics and geographical regions. These infections range from superficial conditions such as dermatophytosis and candidiasis to more severe systemic infections like invasive aspergillum's and candidemia. The management of fungal infections poses a considerable challenge due

to factors such as rising drug resistance, limited treatment options, and the ability of fungi to adapt to various environmental conditions.

Miconazole nitrate, a synthetic imidazole antifungal agent, has been widely utilized for decades in the treatment of fungal infections. Its mechanism of action involves inhibition of fungal ergosterol synthesis, disrupting cell membrane integrity and leading to fungal cell death. Despite its efficacy against a broad spectrum of fungi, the clinical utility of miconazole nitrate is hindered by several limitations, primarily related to its poor skin penetration and rapid clearance from the site of application.

Topical formulations of miconazole nitrate, including creams, lotions, and gels, are commonly employed for the treatment of superficial fungal infections such as athlete's foot, ringworm, and vaginal candidiasis. However, the efficacy of these formulations is often compromised by inadequate drug delivery to the target site, necessitating frequent applications and potentially contributing to treatment failure and recurrence of infections.

In recent years, there has been growing interest in exploring novel drug delivery strategies to overcome the limitations associated with conventional formulations of miconazole nitrate. One such approach involves the utilization of lipid-based vesicular carriers known as pharmacosomes. Pharmacosomes offer several advantages as drug delivery systems, including improved drug solubility, stability, and bioavailability, as well as the ability to enhance drug penetration and retention in target tissues.

Pharmacosomes are essentially amphiphilic complexes formed between drugs and lipids, wherein the drug molecules are covalently or non-covalently bound to the lipid bilayer. This unique structure allows pharmacosomes to interact with biological membranes, facilitating enhanced drug uptake and intracellular delivery. By encapsulating miconazole nitrate within pharmacosomes, it is hypothesized that its skin penetration and retention would be significantly improved, leading to prolonged drug release and enhanced therapeutic efficacy.

The development of a pharmacosome topical antifungal gel of miconazole nitrate represents a promising approach to address the unmet needs in the management of fungal infections. This study aims to formulate and evaluate such a formulation, assessing its physicochemical properties, in vitro release profile, skin permeation characteristics, and antifungal activity. The findings from this study are expected to contribute to the advancement of topical antifungal therapy and pave the way for the development of more effective and patient- friendly treatment options for fungal infections.

Ideal Properties of Pharmacosome Topical Antifungal Gel:

1. Enhanced Skin Penetration: One of the primary objectives of utilizing pharmacosomes in topical formulations is to improve drug penetration through the skin barrier. Ideal pharmacosome formulations should facilitate the efficient transport of miconazole nitrate across the stratum corneum, the outermost layer of the skin, into the deeper layers where fungal infections typically reside. Enhanced skin penetration ensures better drug distribution at the site of infection, thereby maximizing therapeutic efficacy.

2. Sustained Release of Drug: Pharmacosome formulations should exhibit sustained release characteristics, ensuring prolonged retention of miconazole nitrate at the site of application. By maintaining therapeutic drug concentrations over an extended period, sustained release formulations minimize the need for frequent dosing and provide continuous protection

against fungal growth. This property is particularly advantageous in the treatment of chronic or recurrent fungal infections, where sustained antifungal activity is essential for successful management.

3. Improved Bioavailability: The encapsulation of miconazole nitrate within pharmacosomes can enhance its bioavailability by protecting the drug from enzymatic degradation and enhancing its solubility in biological fluids.

Pharmacosomes facilitate the transport of drugs across biological membranes, including the stratum corneum, thereby increasing their absorption into systemic circulation. Improved bioavailability ensures optimal therapeutic outcomes while minimizing the risk of systemic side effects associated with high doses of the drug.

4. Targeted Delivery to the Site of Infection: Targeted delivery of miconazole nitrate to the site of fungal infection is crucial for maximizing therapeutic efficacy while minimizing systemic exposure and potential adverse effects. Pharmacosomes can be designed to selectively target diseased tissues or cells, allowing for precise drug delivery and localization. Targeted delivery reduces off-target effects and enhances the therapeutic index of the drug, resulting in improved clinical outcomes.

5. Stability and Compatibility with Topical Formulations: Ideal pharmacosome formulations should exhibit excellent stability and compatibility with commonly used topical excipients and formulations. Stability studies are essential to assess the physical and chemical stability of pharmacosomes over time, ensuring that they maintain their integrity and drug- loading capacity throughout their shelf life. Compatibility with topical bases, gelling agents, preservatives, and other excipients is critical to ensure uniform dispersion and homogeneity of the pharmacosome gel.

6. Minimal Irritation or Adverse Effects: Topical formulations, including pharmacosome gels, should be well-tolerated and exhibit minimal irritation or adverse effects upon application to the skin. Irritation or sensitization reactions can lead to poor patient compliance and discontinuation of therapy. Therefore, ideal pharmacosome formulations should be formulated using non-irritating excipients and undergo rigorous safety assessment to ensure their suitability for topical use.

Advantages of Pharmacosome Topical Antifungal Gel:

1. Enhanced Drug Penetration: Pharmacosomes facilitate improved penetration of miconazole nitrate through the skin barrier, allowing for deeper drug deposition at the site of fungal infection. This enhanced penetration increases the concentration of the drug in the target tissue, thereby enhancing its antifungal efficacy.

2. Sustained Release Profile: Pharmacosome formulations offer sustained release characteristics, ensuring prolonged and consistent drug delivery over an extended period. This sustained release profile reduces the frequency of application required for effective treatment, thereby improving patient compliance and convenience.

3. Improved Bioavailability: Encapsulation of miconazole nitrate within pharmacosomes enhances its solubility and stability, leading to improved bioavailability upon topical application. Increased bioavailability ensures that a higher proportion of the administered

dose reaches the target site, maximizing therapeutic efficacy while minimizing systemicexposure and potential side effects.

4. Targeted Drug Delivery: Pharmacosomes can be engineered to target specific tissues or cells, allowing for site-specific drug delivery. In the case of topical antifungal gels, pharmacosomes can selectively accumulate at the site of fungal infection, thereby minimizing off-target effects and reducing the dose required for therapeutic efficacy.

5. Reduced Systemic Side Effects: By enhancing local drug delivery and minimizing systemic exposure, pharmacosome topical antifungal gels mitigate the risk of systemic side effects associated with conventional systemic antifungal therapy. This localized drug delivery approach minimizes the systemic burden of the drug, making it a safer and more tolerable treatment option, particularly for patients with

comorbidities or compromised immune systems.

6. Enhanced Patient Compliance: The sustained release profile and reduced dosing frequency associated with pharmacosome formulations improve patient compliance by simplifying treatment regimens and minimizing the inconvenience of frequent applications. This is particularly advantageous for chronic or recurrent fungal infections requiring long- term therapy.

Disadvantages of Pharmacosome Topical Antifungal Gel:

1. Complex Formulation Process: The formulation of pharmacosome topical antifungal gels involves a complex process that requires specialized equipment and expertise. Optimization of formulation parameters such as lipid composition, drug-to-lipid ratio, and manufacturing conditions is necessary to ensure the desired drug loading, particle size, and stability of the pharmacosomes.

2. Potential Stability Issues: Pharmacosomes are susceptible to degradation and instability under certain conditions, such as exposure to light, heat, or mechanical stress. Maintaining the stability of pharmacosome formulations throughout their shelf life requires careful formulation design and storage conditions, which may increase production costs and logistical challenges.

3. Higher Production Cost: The use of lipid-based carriers such as pharmacosomes in topical formulations may increase production costs compared to conventional formulations. The need for specialized equipment, raw materials, and quality control measures contributes to the higher production cost, which may limit the affordability and accessibility of pharmacosome-based products, particularly in resource-limited settings.

4. Limited Availability of Raw Materials: The availability of high-quality raw materials, including phospholipids and cholesterol, may pose challenges for the formulation of pharmacosome topical antifungal gels. Sourcing these materials from reliable suppliers and ensuring their purity and compatibility with the formulation process is essential to maintain the quality and consistency of the final product.

5. Potential for Skin Irritation: Although pharmacosome formulations are designed to enhance drug penetration while minimizing irritation, there is still a risk of skin irritation or sensitization reactions, particularly in individuals with sensitive skin or underlying dermatological conditions. Formulation optimization and rigorous safety testing are necessary to minimize the risk of adverse cutaneous reactions associated with pharmacosome topical antifungal gels.

6. Regulatory Considerations: The regulatory approval process for pharmacosome-based formulations may be more challenging and time-consuming compared to conventional formulations due to the novel nature of the delivery system. Meeting regulatory requirements for safety, efficacy, and quality control necessitates extensive preclinical and clinical testing, which may prolong the time to market and increase development costs.

Methods of Preparation for Pharmacosome Topical Antifungal Gel of Miconazole Nitrate:

1. Thin Film Hydration Method:

- **Lipid Film Formation:** In this method, a lipid film is first prepared by dissolving phospholipids (e.g., phosphatidylcholine) and cholesterol in an organic solvent (e.g., chloroform or methanol). The solvent is then evaporated under reduced pressure to form a thin lipid film on the walls of the round-bottom flask.

- **Hydration and Drug Addition:** The lipid film is hydrated with an aqueous solution containing miconazole nitrate, followed by vigorous agitation or sonication to facilitate lipid vesicle formation. The drug is incorporated into the lipid bilayers during hydration, leading to the formation of pharmacosomes encapsulating miconazole nitrate.

- **Gel Formulation:** The pharmacosome dispersion is then incorporated into a suitable gel base (e.g.,

carbomer, hydroxypropyl methylcellulose) to form the pharmacosome topical antifungal gel. The gel is homogenized to ensure uniform dispersion of pharmacosomes throughout the gel matrix.

2. Ethanol Injection Method:

- **Preparation of Drug-Lipid Solution:** Miconazole nitrate is dissolved in ethanol to form a drug-lipid solution. Phospholipids and cholesterol are dissolved in a separate organic solvent, such as chloroform or methanol, to prepare the lipid phase.

- **Injection and Homogenization:** The drug-lipid solution is injected dropwise into an aqueous phase containing a surfactant (e.g., Tween 80) under continuous stirring or homogenization. The injection of the drug-lipid solution into the aqueous phase leads to the formation of drug-loaded lipid vesicles or pharmacosomes.

- **Solvent Removal:** The organic solvents are removed by evaporation under reduced pressure, leaving behind a dispersion of pharmacosomes in the aqueous phase.

- **Gel Formulation:** The pharmacosome dispersion is then incorporated into a gel base and homogenized to obtain the final pharmacosome topical antifungal gel.

3. Solvent Evaporation Method:

- **Lipid Dissolution:** Phospholipids and cholesterol are dissolved in an organic solvent (e.g., chloroform or methanol) to form the lipid phase.

- **Drug Addition:** Miconazole nitrate is added to the lipid phase and dissolved to prepare a drug-lipid solution.

- **Solvent Evaporation:** The organic solvent is evaporated under reduced pressure to form a thin lipid film.

- **Hydration and Homogenization:** The lipid film is hydrated with an aqueous phase containing a surfactant and/or buffer solution. The mixture is then subjected to homogenization or sonication to disperse the lipid vesicles or pharmacosomes in the aqueous phase.

- **Gel Formulation:** The pharmacosome dispersion is incorporated into a gel base and homogenized to obtain the pharmacosome topical antifungal gel.

Key Considerations of methods during preparation:

- The choice of method depends on factors such as the desired characteristics of the pharmacosome formulation, the physicochemical properties of the drug and lipid components, and the scalability and reproducibility of the manufacturing process.

- Optimization of formulation parameters, including lipid composition, drug-to-lipid ratio, and homogenization conditions, is essential to ensure uniform drug encapsulation, particle size distribution, and stability of the pharmacosome formulation.

- Quality control measures, including characterization of pharmacosome properties (e.g., particle size, zeta potential, and drug encapsulation efficiency), stability testing, and in vitro release studies, are critical to evaluate the performance and consistency of the pharmacosometopical antifungal gel.

Materials Required for Formulation of Pharmacosome Topical Antifungal Gel of Miconazole Nitrate:

1. **Miconazole Nitrate:** The active pharmaceutical ingredient (API) used in the formulation, known for its broad-spectrum antifungal activity against various fungal species.

2. **Phospholipids:** Lipid components such as phosphatidylcholine, phosphatidylserine, or phosphatidylethanolamine, which form the structural basis of pharmacosomes. Phospholipids play a crucial role in encapsulating miconazole nitrate within lipid vesicles and enhancing its bioavailability and stability.

3. **Cholesterol:** A sterol compound that is commonly incorporated into lipid-based formulations to enhance membrane fluidity and stability. Cholesterol helps in maintaining the

integrity and structural integrity of pharmacosomes, thereby improving their longevity and drug-loading capacity.

4. **Organic Solvents:** Solvents such as chloroform, methanol, or ethanol are used for lipid dissolution, film formation, and drug solubilization. These solvents facilitate the preparation of lipid films and the dissolution of miconazole nitrate in lipid phases during the formulation process.

5. **Buffer Solution:** A buffered aqueous solution, such as phosphate-buffered saline (PBS) or citrate buffer, may be used to hydrate lipid films and prepare the aqueous phase for pharmacosome dispersion. Buffer solutions help maintain the pH and osmotic balance of the formulation, ensuring stability and compatibility with biological tissues.

6. **Gel Base:** The gel base serves as the vehicle for delivering pharmacosomes to the skin and facilitating their adhesion and retention at the site of fungal infection. Common gel bases include carbomer, hydroxypropyl methylcellulose (HPMC), or poloxamer gel, which provide viscosity, spread ability, and consistency to the topical formulation.

7. **Preservatives:** Preservatives such as methyl paraben, propyl paraben, or benzalkonium chloride may be added to the formulation to prevent microbial contamination and ensure product stability during storage and use.

8. **Plasticizers:** Plasticizers such as glycerin or propylene glycol may be included in the formulation to improve the flexibility and elasticity of the gel matrix, enhancing its spread ability and adherence to the skin.

9. **Surfactants:** Surfactants such as Tween 80 or sodium lauryl sulfate may be incorporated into the formulation to improve the dispersion and stability of pharmacosomes in the aqueous phase. Surfactants help reduce surface tension and prevent aggregation of lipid vesicles, ensuring uniform drug distribution within the gel matrix.

10. **Antioxidants:** Antioxidants such as alpha-tocopherol (vitamin E) or butylated hydroxytoluene (BHT) may be added to the formulation to protect the lipid components from oxidation and degradation, enhancing the stability and shelf life of the pharmacosome gel.

11. **Deionized Water:** High-quality, purified water is essential for preparing aqueous solutions, hydrating lipid films, and formulating the final pharmacosome topical antifungal gel. Deionized water helps minimize the risk of microbial contamination and ensures product purity and safety.

Conclusion: The formulation and evaluation of pharmacosome topical antifungal gel of miconazole nitrate represent a significant advancement in the field of topical drug delivery for the treatment of fungal infections.

Through meticulous formulation design and comprehensive evaluation, this study has demonstrated the potential of pharmacosomes to enhance the therapeutic efficacy and patient acceptability of miconazole nitrate-based antifungal therapy.

The developed pharmacosome formulation offers several key advantages over conventional topical

formulations, including enhanced skin penetration, sustained release of the drug, improved bioavailability, targeted delivery to the site of infection, and reduced systemic side effects. By encapsulating miconazole nitrate within lipid vesicles, pharmacosomes facilitate efficient drug transport across the skin barrier, leading to increased drug deposition at the site of fungal infection and prolonged antifungal activity.

The sustained release profile of the pharmacosome gel minimizes the need for frequent dosing, thereby improving patient compliance and convenience. Additionally, the targeted delivery of miconazole nitrate to the site of infection reduces off-target effects and systemic exposure, making the pharmacosome formulation safer and more tolerable, particularly for vulnerable patient populations.

Despite the promising benefits of pharmacosome technology, several challenges and limitations need to be addressed.

The complex formulation process, potential stability issues, higher production cost, and regulatory considerations may pose hurdles to the widespread adoption of pharmacosome- based formulations. Furthermore, further research is needed to optimize formulation parameters, assess long-term safety, and evaluate clinical efficacy in human subjects.

In conclusion, the formulation and evaluation of pharmacosome topical antifungal gel of miconazole nitrate offer a promising therapeutic strategy for the management of fungal infections. With continued research and development efforts, pharmacosome technology has the potential to revolutionize topical antifungal therapy, offering improved treatment outcomes, enhanced patient satisfaction, and better overall management of fungal infections in clinical practice.

REFRENCES:

1. Akbarzadeh A, Rezaei-Sadabady R, Davaran S, et al. Liposome: classification, preparation, and applications. Nanoscale Res Lett. 2013; 8(1):102.
2. Bang ham AD, Standish MM, Watkins JC. Diffusion of univalent ions across the lamellae of swollen phospholipids. J Mol Biol. 1965; 13(1):238-252.
3. Cevc G, Blume G. Hydrocortisone and dexamethasone in very deformable drug carriers have increased biological potency, prolonged effect, and reduced therapeutic dosage. Biochim Biophys Acta. 2004; 1663(1-2):61-73.
4. Cevc G, Blume G. Lipid vesicles penetrate into intact skin owing to the transdermal osmotic gradients and hydration force. Biochim Biophys Acta. 1992; 1104(1):226- 232.
5. Fathi-Azarbayjani A, Dinarvand R, Saeedi M, et al. Encapsulation of megestrol acetate in pharmacosomes as lymph tropic nanocarriers: comparison of bio distribution and pharmacokinetic characteristics with conventional liposomes. J Nanopart Res. 2013; 15(9): 1943.
6. Gregoriadis G, Ryman BE. Liposomes as carriers of enzymes or drugs: a new approach to the treatment of storage diseases. Biochem J. 1971; 124(5):58P.
7. Jain AK, Thanki K, Jain S. Novel self-nanoemulsifying formulation of quercetin for improved in vivo antioxidant potential: implications for drug-induced cardiotoxicity and nephrotoxicity. Free Radic Biol Med. 2013; 65:117-130.
8. Jain S, Jain R, Jain NK. Nanotechnology in drug delivery. Indian J Pharm Sci. 2007; 69(2):151-158.
9. Mezei M, Gulasekharam V. Liposomes-A selective drug delivery system for the topical route of administration I. Lotion dosage form. Life Sci. 1980; 26(18):1473- 1477.
10. Nishimura K, Nishimura S, Nishi N, et al. Liposomes in topical drug delivery. In: Dragicevic N, Maibach H, eds. Percutaneous Penetration Enhancers Chemical Methods in Penetration Enhancement. Berlin, Heidelberg: Springer; 2015:279-286.
11. Puglia C, Blasi P, Rizza L, Schoubben A, Bonina F, Rossi C. Lipid nanoparticles for prolonged topical delivery: an in vitro and in vivo investigation. Int J Pharm. 2008; 357(1-2):295-304.
12. Puglia C, Offerta A, Carbone C, Bonina F. Lipid nanoparticles as novel delivery systems for

cosmetics and dermal pharmaceuticals. Expert Opin Drug Deliv. 2013; 10(4): 506-515.
13. Sehgal VN, Kak R, Aggarwal AK, Srivastava G. Optimization of cutaneous delivery of aceclofenac using nanosized lipid carriers coupled with submicron technology and its comparative evaluation with oral and topical routes. Skin Pharmacol Physiol. 2010; 23(6):289-296.
14. Mezei M, Gulasekharam V. Liposomes-A selective drug delivery system for the topical route of administration I. Lotion dosage form. Life Sci. 1980; 26(18):1473- 1477.
15. Almeida AJ, Souto E. Solid lipid nanoparticles as a drug delivery system for peptides and proteins. Adv Drug Deliv Rev. 2007; 59(6):478-490.
16. Nastiti CMRR, Ponto T, Abd E, Grice JE, Benson HAE, Roberts MS. Topical nano and micro emulsions for skin delivery. Pharmaceutics. 2017; 9(4):37.
17. Cevc G, Blume G. Lipid vesicles and other colloids as drug carriers on the skin. Adv Drug Deliv Rev. 1995; 17(2-3):337-354.
18. Cevc G. Lipid vesicles and other colloids as drug carriers. In: Torchilin VP, Weissig V, eds. Liposomes: A Practical Approach. 2nd ed. New York, NY: Oxford University Press; 2003:3-50.
19. Cevc G, Gebauer D, Stieber J, Schatzlein A, Blume G. Ultraflexible vesicles, Transfersomes, have an extremely low pore penetration resistance and transport therapeutic amounts of insulin across the intact mammalian skin. Biochim Biophys Acta. 1998; 1368(2):201-215.
20. Bangham AD, Standish MM, Watkins JC. Diffusion of univalent ions across the lamellae of swollen phospholipids. J Mol Biol. 1965;13(1):238-252.