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Review Article

Development of Bigel-Based Topical Drug Delivery of Amphotericin-B and Fluconazole in the Treatment of Fungal Infection: A Review

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Abstract

Fungal infections pose a significant health concern globally, with a rising incidence of resistance to conventional treatments. Topical drug delivery systems offer a promising approach to enhance the efficacy and safety of antifungal agents while minimizing systemic side effects. This review explores the design, development, and optimization of bigel-based topical drug delivery systems containing Amphotericin-B and Fluconazole for the treatment of fungal infections. It discusses the challenges associated with current treatment modalities, the rationale for utilizing bigel formulations, and recent advances in this field. Additionally, the review highlights the optimization strategies, including formulation variables, rheological properties, and in vitro/in vivo evaluation methods, aimed at enhancing the therapeutic outcomes of these novel formulations. **Keywords:** Bigel, Topical Drug Delivery, Amphotericin-B, Fluconazole, Fungal Infection, Optimization.

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Introduction

Fungal infections represent a significant burden on public health, affecting millions of individuals worldwide. Despite advancements in antifungal therapy, challenges such as resistance, poor drug penetration, and adverse effects associated with systemic administration persist. Topical drug delivery systems offer an attractive alternative for localized treatment, providing targeted therapy with reduced systemic exposure. Bigels, characterized by their dual gel and liquid phases, have emerged as promising carriers for delivering antifungal agents due to their enhanced stability, mucoadhesive properties, and controlled release capabilities. This review aims to provide a comprehensive overview of the design, development, and optimization of bigel-based topical formulations containing Amphotericin-B and Fluconazole for the management of fungal infections. Fungal infections pose a significant public health concern worldwide, with increasing incidence rates and challenges associated with treatment efficacy and patient compliance. Topical drug delivery systems have emerged as promising approaches to address these challenges by providing targeted therapy with reduced systemic side effects.

Among the various antifungal agents, Amphotericin-B and Fluconazole stand out for their broad-spectrum activity against a wide range of fungal pathogens. In recent years, bigel-based topical drug delivery systems have garnered

attention as novel formulations to enhance the therapeutic efficacy and safety of Amphotericin-B and Fluconazole for the treatment of fungal infections. Bigels, characterized by their dual-phase structure combining gel and liquid phases, offer advantages such as enhanced stability, controlled drug release, and improved skin permeation, making them ideal candidates for topical delivery. This review explores the design, development, and potential applications of bigel-based topical drug delivery systems containing Amphotericin-B and Fluconazole for the treatment of fungal infections. It discusses the rationale for utilizing bigel formulations, the challenges associated with conventional treatment modalities, and the recent advancements in this field. Additionally, it highlights the optimization strategies, formulation variables, and characterization techniques aimed at enhancing the therapeutic outcomes of these novel formulations. Understanding the multifaceted aspects of bigel-based topical drug delivery systems of Amphotericin-B and Fluconazole is crucial for advancing their clinical translation and addressing the unmet needs in the management of fungal infections. By harnessing the unique properties of bigels, researchers and clinicians can potentially improve treatment outcomes, reduce systemic side effects, and enhance patient adherence, ultimately contributing to the global efforts to combat fungal diseases.

Challenges in Fungal Infection Treatment

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Conventional treatment modalities for fungal infections include topical creams, oral medications, and intravenous administration of antifungal agents. However, these approaches are often associated with limitations such as poor drug penetration, low patient compliance, and systemic side effects. Moreover, the emergence of drugresistant fungal strains further complicates treatment outcomes, necessitating the exploration of novel delivery systems to overcome these challenges.

Amphotericin B (AmB) is a polyene antifungal drug known for its broad-spectrum activity against a wide range of fungal infections. Despite its long history of clinical use, AmB continues to be an essential component in the armamentarium against life-threatening fungal diseases. This review provides a comprehensive overview of the pharmacology, clinical applications, therapeutic challenges, and emerging trends related to Amphotericin B.Fluconazole is a broad-spectrum antifungal agent that has been widely used for the treatment of superficial fungal infections for decades. With its efficacy against various dermatophytes, yeasts, and molds, fluconazole has become a cornerstone therapy in the management of conditions such as tinea infections, candidiasis, and pitvriasis versicolor. This review provides an in-depth examination of the pharmacology, clinical applications, therapeutic challenges, and recent advancements related to fluconazole.

Rationale for Bigel-Based Topical Delivery

Bigels offer several advantages for topical drug delivery, including enhanced bioavailability, prolonged retention at the site of application, and improved patient acceptance. The dual-phase nature of bigels allows for the incorporation of hydrophilic and hydrophobic drugs, enabling synergistic therapeutic effects and enhanced efficacy against fungal pathogens. Additionally, the mucoadhesive properties of bigels promote intimate contact with the skin or mucosal surfaces, facilitating sustained drug release and prolonged therapeutic action. Bigel-based topical delivery systems have garnered significant attention in recent years due to their unique properties and potential applications in pharmaceutical and cosmetic formulations.

These systems, characterized by a combination of both gel and liquid phases, offer advantages such as stability, controlled release, enhanced and improved skin permeation compared to conventional formulations. Additionally. it discusses recent advancements, challenges, and future perspectives in this field, highlighting the potential of bigels to revolutionize topical drug delivery and skincare products. Topical drug delivery systems play a crucial role in the treatment

of dermatological conditions and cosmetic formulations by providing localized therapy with reduced systemic side effects. Bigel-based formulations, characterized by their dual-phase nature, offer unique advantages over traditional dosage forms, making them promising candidates for various applications. This review aims to explore the formulation aspects, characterization methods, and diverse applications of bigel-based topical delivery systems, shedding light on their potential in pharmaceutical and cosmetic industries.

Design and Development of Bigel Formulations

The formulation of bigel-based topical delivery systems involves the selection of suitable gelling agents, surfactants, and rheological modifiers to achieve the desired physicochemical properties. Various techniques such as phase inversion, cold processing, and solvent evaporation are employed to prepare stable and homogeneous bigel formulations. Optimization strategies focus on controlling drug release kinetics, enhancing skin permeation, and improving patient comfort.

Advantages of Bigel Formulations

Enhanced Stability

Bigel formulations exhibit improved stability compared to conventional gels or emulsions due to their unique dual-phase structure, which helps prevent phase separation and degradation of active ingredients.

Controlled Drug Release

Bigels offer controlled release of active ingredients, allowing for sustained and prolonged drug release at the site of application. This controlled release profile can enhance therapeutic efficacy and patient compliance.

Versatile Formulation Platform

Bigels can accommodate both hydrophilic and hydrophobic drugs, making them suitable for a wide range of active pharmaceutical ingredients (APIs) with different physicochemical properties.

Improved Skin Permeation

The dual-phase nature of bigels enhances skin permeation by promoting intimate contact with the skin and facilitating drug penetration through the stratum corneum, leading to improved therapeutic outcomes.

Enhanced Mucoadhesive Properties

Bigel formulations possess mucoadhesive properties, allowing them to adhere to mucosal surfaces for prolonged periods, thereby increasing residence time and bioavailability of drugs at the application site. Ease of Application: Bigel formulations are typically easy to apply and spread over the skin or mucosal surfaces, providing uniform coverage and ensuring efficient drug delivery.

Potential for Combination Therapy

Bigels can incorporate multiple drugs or therapeutic agents, enabling combination therapy to target different aspects of a disease or achieve synergistic effects.

Optimization Strategies

Optimization of bigel formulations involves the systematic investigation of formulation variables, including polymer concentration, drug-to-polymer ratio, and lipid composition, to optimize drug release kinetics and rheological properties. Advanced characterization techniques such as rheology, microscopy, and spectroscopy are utilized to evaluate the physicochemical attributes of bigels. In vitro and in vivo studies assess the efficacy, safety, and pharmacokinetic profile of optimized formulations, guiding further refinement and clinical translation.

Conclusion

Bigel-based topical drug delivery systems represent a promising approach for the treatment of fungal infections, offering enhanced efficacy, improved patient compliance, and reduced systemic toxicity. The design, development, and optimization of bigel formulations containing Amphotericin-B and Fluconazole hold significant potential in addressing the unmet needs of current antifungal therapy. Further research focusing on clinical validation and commercialization of these novel formulations is warranted to translate these advancements into clinical practice.

References

- 1. SmitaKumbhar, Vinod Matole, Yogesh Thorat, SailiMadur, SmeetaPatil, Anita Shegaonkar. Formulation and Evaluation of Lignocaine Hydrochloride Topical gel. Research J. Pharm. and Tech. 2021; 14(2):908-910.
- Agrawal D, Goyal R, Bansal M, Sharma AK, Khandelwal M, Development And Evaluation Of EconazoleOrganogel; International Journal of Current Pharmaceutical Review and Research., 13(2), Pages: 15-23.
- Garima Gupta and Ajit Kiran Kaur., Formulation And Standardization of Topical Polyherbal Gel, International Journal of Recent Scientific Research Vol. 12, Issue, 08 (B), pp. 42735-42739, August, 2021.
- Goudanavar, P., Ali, M., Din Wani, S. U., &Sreeharsha, N. (2021). Formulation and evaluation of in-situ gel containing linezolid in the treatment of periodontitis. International Journal of Applied Pharmaceutics, 13(3), 79– 86.

- R. R. Baghwan, A. W. Ambekar, S. S. Tamboli. Formulation, Development and Evaluation of in-situ Periodontal Gel Containing Ofloxacin. Research Journal of Pharmacy and Technology. 2021; 14(9):4609-4.
- C. Kumaresan. Thumb arthritis treatment with diclofenac sodium Gel Formulation. Asian J. Res. Pharm. Sci. 2020; 10(4):239-240.
- Hoang Nhan Ho, ThienGiap Le, Thi Thanh Tuyen Dao, Thi Ha Le, Thi Thanh Hai Dinh, Dang Hoa Nguyen, Trinh Cong Tran, Chien Ngoc Nguyen, Development of Itraconazole-Loaded Polymeric Nanoparticle Dermal Gel for Enhanced Antifungal Efficacy, Journal of Nanomaterials, December 2020.
- 8. Patil M.V, Formulation and Evaluation Thermoreversible Gel of Antifungal Agent for Treatment of Vaginal Infection, Journal of Pharmaceutical Research International, March 2020.
- Mukherjee, S., Majee, S. B., & Biswas, G. R. (2019). Formulation and In Vitro Characterisation of Soybean Oil-Hpmck4m Based Bigel Matrix for Topical Drug Delivery. International Journal of Applied Pharmaceutics, 11(5), 33-38.
- Lilian Sosa, Anna, C. C., et al. (2019) Thermoreversible Gel-Loaded Amphotericin B for the Treatment of Dermal and Vaginal Candidiasis. MDPI journal Pharmaceutics. 11,312 (2019) 2-18.
- Agnemazurkeviciute, kristinaramanauskiene, marijaivaskiene, aidasgrigonis, vitalisbriedis, (2018) Topical antifungal bigels: Formulation, characterization and evaluation. Acta Pharm. 68 (2018) 223-233.
- 12. Lopez L, Velez I, Asela C, Cruz C, Alves F, Robledo S, et al. (2018) A phase II study to evaluate the safety and efficacy of topical 3% amphotericin B cream (Anfoleish) for the treatment of uncomplicated cutaneous leishmaniasis in Colombia. PLoSNegl Trop Dis 12(7).
- Lakhvir Kaur, Subheet Kumar Jain, Rajesh Kumari Manhas & Deepika Sharma (2018) Nanoethosomal formulation for skin targeting of amphotericin B: an in vitro and in vivo assessment, Journal of Liposome Research, 25:4, 294-307.
- Lopez-Castillo, C.; Rodríguez-Fernández, C.; Córdoba, M.; Torrado, J.J.(2018) Permeability Characteristics of a New Antifungal Topical Amphotericin B Formulation with γ-Cyclodextrins. Molecules 2018, 23, 3349.
- Sharma AK el al. Pharmaceutical gel: A review, International Journal of Pharmacy & Technology, Dec. 2020. 12(4), 7223-7233.
- 16. Muneer S, Masood Z, Butt S, Anjum S, Zainab H, et al. (2017) Proliposomes as

Pharmaceutical Drug Delivery System: A Brief Review. J NanomedNanotechnol 8: 448.

- Rishpa K, (2017) A Review on Cipla Liposomes (Dsoxorubicin and Amphotericin B), Rishpa, J FormulSciBioavailab, Journal of Formulation Science & Bioavailability2017, 1:1.
- Jill P Adler-Moore, Jean-Pierre Gangneux and Peter G Pappas, (2016) Comparison between liposomal formulations of amphotericin B. Medical Mycology, 2016, 54, 223–231.
- Yucel C. et at Development of Cisplatinloaded Liposome and Evaluation of Transport Properties Through Caco-2 Cell Line, Turk J Pharm Sci, 2016, 13(1), 69-80.
- David Cipolla, Jim Blanchard and Igor Gonda (2016) "Development of Liposomal Ciprofloxacin to Treat Lung Infections". Pharmaceutics MDPI, 2016 Mar; 8(1): 6.
- 21. Mistry A and Padmini RK, (2016) "Development and Evaluation of Azelaic Acid

Based Ethosomes for Topical Delivery for the Treatment of Acne". Indian Journal of Pharmaceutical Education and Research, Vol 50, Issue 3, Jul-Sep (Suppl.), 2016.

- 22. Agrawal D, Goyal R, Bansal M, Sharma AK, Khandelwal M, Development And Evaluation Of Econazole Organogel; International Journal of Current Pharmaceutical Review and Research., 13(2), Pages: 15-23.
- 23. Sharma A K, Naruka P S, Soni S, Khandelwal M, Shaneza A, Sharma M, Development And Evaluation Of Hydrogel of Kitoconazole; International Journal of Current Pharmaceutical Review and Research., Aug. 2019, 11(3), Pages: 01-11.
- Sharma A K, Naruka P S, Soni S, Sarangdewot YS, Khandelwal M, Shaneza A, Formulation, Development And Evaluation of Luliconazole Hydrogel; International Journal of Current Pharmaceutical Review and Research, Nov. 2018, 10(4), Pages: 01-06.