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Review Article

Formulation and Evaluation of Herbal Antifungal Sprays: A Systematic Review

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ABSTRACT

In recent years, it has been found that fungal infections in humans have risen. Along with its growth rate, the kind of fungal species also increased considerably. An effective formulation is necessary to treat these fungal infections in a simple manner. The main aim of my research project was to develop a formulation of a topical antifungal spray. The formulation and development of tropical antifungal formulation have seen great results in the treatment of fungal infections. Over the conventional dosage forms, these topical drug delivery formulations have more benefits along with their extraordinary advantages. This spray formulation consists of natural as well as synthetic ingredients. Fungal infections, particularly those affecting large or difficult-to-reach areas, present significant challenges in treatment due to limited drug penetration, short duration of action, and issues with patient adherence. Traditional antifungal therapies, including creams and oral medications, often fail to meet these needs effectively. This study investigates the development of a novel antifungal spray designed to overcome these limitations by ensuring controlled drug release and enhanced therapeutic efficacy.

INTRODUCTION

Fungal infections, both superficial and systemic, are common and can be caused by various species such as Candida, Aspergillus, and Dermatophytes. The drawbacks of synthetic antifungal drugs such as side effects, resistance, and cost have driven interest in herbal alternatives. Medicinal plants have been traditionally used for treating skin infections and Offer potent antifungal compounds such as essential oils, tannins, alkaloids, and flavonoids.

Challenges in Treating Fungal Infections:

Despite advancements in antifungal therapy, managing fungal infections remains challenging. Key obstacles include:

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1. Inadequate Drug Penetration-

- Many antifungal drugs struggle to penetrate deeply into tissues, limiting their efficacy in infections that affect not only the skin's surface but also deeper layers or nail beds. This issue is particularly evident in subcutaneous or nail infections, where effective drug delivery is crucial for reaching the full extent of the infected site.

- Systemic fungal infections present even greater penetration challenges, often requiring high doses of antifungals to reach effective concentrations in deep tissues. These high doses can lead to increased side effects and toxicity.

2. Adverse Side Effects

- Antifungal drugs, especially systemic ones, can produce a range of side effects. These include gastrointestinal disturbances, liver toxicity, nephrotoxicity, and, in some cases, hematologic side effects. The risk of these adverse effects may discourage patients from adhering to their prescribed regimen, leading to incomplete or ineffective treatment.

Advantages of Spray-based Dosage Forms:

- Ease of Application: Sprays allow for quick, easy application over large or irregular areas, such as skin folds or the back, without requiring manual spreading like creams or ointments. This is particularly helpful for treating fungal infections, where extensive skin or nail coverage is needed, and reduces irritation on sensitive skin. It also facilitates sanitary, no-contact application, which is beneficial for caregivers.

- Even Distribution: Spray formulations deliver the active ingredient in fine, uniform droplets, ensuring even coverage of the affected area. This consistent distribution is vital in antifungal therapy to minimize the risk of under-treatment and to reduce the potential for resistant fungi development.

- Reduced Contact Contamination: Since sprays eliminate the need for direct hand-to-skin contact, they reduce the risk of contaminating the affected area or spreading pathogens, which is crucial for infectious skin conditions.

- Minimal Application Time: Sprays are quick to apply, reducing the time needed for reapplications, which enhances convenience and patient compliance. This is particularly beneficial for patients who need to apply treatment multiple times daily.

- Controlled and Consistent Dosage: Many spray systems offer metered dosing, ensuring consistent delivery of medication. This precision helps prevent under- or over-application, which can affect treatment efficacy and safety.

- Enhanced Drug Effectiveness and Comfort: Spray formulations, often with bio adhesive agents, improve drug retention and provide sustained release, reducing the need for frequent applications. They also dry quickly, leaving little residue, enhancing comfort and patient satisfaction.

Active Ingredients in Herbal Anti-Fungal Sprays:

- Commonly Used Plant Extracts:

Commonly used plant extracts, such as neem, turmeric, garlic, tea tree, and aloe vera, serve as potent sources of active ingredients in herbal anti-fungal sprays. Their diverse array of bioactive

compounds, multifaceted mechanisms of action, and established antifungal properties make them invaluable components in combating fungal infections. By synergistically harnessing the power of these plant-derived compounds, poly-herbal formulations offer promising therapeutic options for addressing fungal pathogens effectively and holistically.

- Bioactive Compounds and Mechanisms of Action:

Bioactive compounds within commonly used plant extracts contribute to the efficacy of herbal anti-fungal sprays through diverse mechanisms of action. The interplay of these compounds offers multifaceted attacks on fungal pathogens, reducing the risk of resistance development. The comprehensive understanding of these mechanisms enriches the development of potent and sustainable poly-herbal formulations for combating fungal infections.

Formulation and Development of Herbal Anti-Fungal Sprays:

1. Extraction Techniques and Solvents

Extraction techniques and solvents play a crucial role in the formulation and development of herbal anti-fungal sprays. Proper selection and optimization of these factors are essential for obtaining high-quality extracts rich in bioactive compounds, ensuring the efficacy and potency of the final formulation.

2. Excipients and Stabilizers

Excipients and stabilizers play a pivotal role in formulating herbal anti-fungal sprays. Their careful selection and incorporation contribute to the overall stability, bioavailability, and therapeutic effectiveness of the formulation. By optimizing these components, developers can create poly-herbal sprays that deliver enhanced antifungal activity while maintaining the desired physical and chemical attributes.

3. Nano formulations for Enhanced Efficacy

Integration of nano formulations into herbal anti-fungal sprays holds great promise for enhancing their efficacy, bioavailability, and targeted delivery. While challenges exist, the potential benefits of improved treatment outcomes, reduced dosing frequency and enhanced patient compliance make nanoformulations a compelling avenue for advancing poly-herbal spray development and optimizing antifungal therapy.

Mechanisms of Action:

1. Disruption of Fungal Cell Membranes-

Disruption of fungal cell membranes is a key mechanism through which herbal anti-fungal sprays exert their antifungal activity. By targeting this essential component of fungal cells, these sprays effectively inhibit growth, prevent colonization, and contribute to the overall management of fungal infections.

2. Inhibition of Fungal Enzymes-

Inhibition of fungal enzymes is a pivotal mechanism through which herbal anti-fungal sprays exert their antifungal effects. By disrupting key cellular processes and metabolic pathways, these sprays effectively target fungal growth and proliferation. The combination of enzyme inhibition with other mechanisms of action enhances their overall antifungal efficacy, offering a multifaceted approach to combatting fungal infections.

3. Modulation of Host Immune Response-

The modulation of host immune responses is a crucial mechanism through which herbal anti-fungal sprays combat fungal infections. By enhancing immune cell activation, signaling pathways, and overall immune defence, these sprays contribute to a comprehensive and effective approach to managing fungal pathogens.

Evaluation Parameter of antifungal spray

1. pH - Using the digital pH meter, the pH of the optimized spray solution was calculated. The pH meter was adjusted using phosphate buffer of different pH values (4.0, 7.0, and 9.0) before calculating the pH of the optimized formulation. The pH was determined for the spray solution. Each formulation was measured in triplicate and calculated.

2. Viscosity: then the mean values were Viscosity was calculated at 25±1°C using a Brookfield viscometer (digital viscometer model). The rotation of the ULA spindle was kept as 1 rpm. The solution equivalent of 10ml was taken into a volumetric flask (100ml) and diluted using methanol.

3. Drying Time: Evaporation time is the time needed to dry the spray film. It was measured by spraying the formulation on a glass slide and noting down the drying time.

4. Stickiness of the spray after evaporating the solvent: Low pressure cotton wool is used to press the dry film to determine the stickiness of it. The stickiness is rated depending on how much of the cotton fibresis retained by the film. The stickiness is rated high if there is a thick accumulation of fibres on the film, medium if there is a thin fibre layer on the film and poor if fibre adherence occurs rarely or never. This parameter of assessment is important.

Container related evaluations

5. Spray angle: First, the distance from nozzle between papers was fixed. After that, one actuation was sprayed onto paper and the circle size was measured. Spray angle is calculated as: Spray angle (Ɵ) =tan-1 (h/r) Where, l and r are the paper ‘s distance from the nozzle and average circle radius, resp.

6. Solution volume delivered at each actuation: The following equation was used to measure how much solution is delivered at each actuation. AL=WO-Wt/D Where, VL — Solution volume supplied at each Actuation, Wt — Formulation weight after Actuation, Wo — Formulation initial weight before Actuation, and D — Formulation density (Measured using a pycnometer

7. Spray patterns: A pH-sensitive paper was prepared by dipping the Whatman filter paper in a methyl red solution. The formulation (one actuation) was sprayed onto this paper. The distance between the container and the destination was kept constant at 5 cm. Then, the pattern of spray was assessed by spraying the concentrates vertically and horizontally.

9. Leakage test: Leakage of canisters was verified by passing the canisters at 55°C and variability in weight in the water bath. Testing was done on selected samples. This examination was passed in batches.

In vitro Evaluation:

1 . Minimum Inhibitory Concentration (MIC) Assays-

Minimum Inhibitory Concentration (MIC) assays play a pivotal role in evaluating the antifungal activity of -herbal sprays. By providing quantitative data on the concentration required to inhibit fungal growth, MIC assays guide

formulation optimization, clinical relevance assessment, and the development of effective antifungal therapies.

2 Disk Diffusion and Agar Well Diffusion Tests-

Disk diffusion and agar well diffusion tests are valuable tools for evaluating the antifungal activity of poly-herbal sprays. While they offer a qualitative assessment of inhibitory potential, these tests provide rapid and informative insights into the formulation's effectiveness against fungal pathogens. When combined with other in vitro and in vivo evaluations, these methods contribute to a comprehensive understanding of the antifungal properties of herbal anti-fungal sprays.

In vivo Studies:

1 Animal Models for Fungal Infections –

Animal models provide a crucial platform for evaluating the safety and efficacy of herbal anti-fungal sprays in a biologically relevant context. By mimicking various aspects of human fungal infections, these models contribute to our understanding of the formulation's potential clinical utility and guide further research and development efforts.

2 Efficacy and Safety Evaluation -

In vivo, efficacy and safety evaluation of poly-herbal anti-fungal sprays in animal models is crucial for determining their potential clinical utility. By assessing the formulation's impact on fungal infections and the host's health, these studies contribute to our understanding of the formulation's overall effectiveness and safety profile. When combined with in vitro and other preclinical evaluations, in vivo studies guide further development and optimization efforts of poly-herbal sprays as antifungal therapies.

CONCLUSION:

herbal anti-fungal sprays present a promising avenue in the fight against fungal infections. Their multi-faceted approach, combining the therapeutic potential of various plant-derived compounds, holds great potential for enhanced efficacy and reduced side effects. By drawing insights from a multitude of studies, this review contributes to the understanding of poly-herbal anti-fungal sprays as a viable and versatile treatment option.

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