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FORMULATION AND EVALUATION OF ANTIFUNGAL PAPER FILM

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2,3,4,5,6,7 .

ABSTRACT

Fungal infections pose a significant global health burden, affecting various body parts. Superficial and invasive infections caused by pathogens like dermatophytes, *Candida*, and *Aspergillus* require effective treatments. Traditional therapies face limitations, highlighting the need for innovative solutions. This review explores the potential of paper films with antifungal properties, incorporating essential oils, chitosan, and nanocellulose, as a promising alternative for preventing and treating fungal infections.

KEYWORDS

Fungal infections, antifungal properties, paper films, essential oils, chitosan, nanocellulose.

INTRODUCTION

- **Overview of Fungal Infections**

Fungal infections affect a wide range of body parts, with significant prevalence globally. Superficial fungal infections commonly involve the skin, nails, and mucous membranes, while invasive fungal infections can affect internal organs [1]

Mucosal infections like oral thrush and vaginal candidiasis are also prevalent, especially among those with compromised immune systems, including individuals with diabetes, HIV, or those on immunosuppressive therapies. [2] Traditional treatments for these infections include topical creams, ointments, and oral antifungals. However, these therapies often face significant limitations. Topical treatments, while effective for surface infections, may fail to penetrate deeper tissues such as nails, requiring systemic drugs for more severe conditions.[3] Oral antifungals, though effective, can cause systemic side effects such as gastrointestinal disturbances, Thus, novel delivery systems are needed to address these limitations and improve therapeutic outcomes.[4]

➢ **Advantages of Paper Film-based Dosage Forms**

Paper film-based drug delivery systems are gaining attention due to their unique advantages in topical drug delivery. One of the primary benefits is their ease of application. [5] Paper films are lightweight, easy to handle, and can be applied directly to the site of infection, making them a user-friendly alternative to traditional creams, ointments, or tablets.[6,7]

localized drug delivery, paper films have significant advantages in antifungal treatments which minimizes potential side effects. This targeted delivery system is particularly beneficial for treating superficial fungal infections, ensuring a higher concentration of the drug at the infection site with lower risks of adverse reactions.[8]

➢ **Purpose of the Study**: The growing prevalence of fungal infections, coupled with the limitations of conventional. These challenges can reduce the effectiveness of treatments and hinder patient compliance.[9,10]

THE LIMITATIONS OF CURRENT ANTIFUNGAL TREATMENTS:

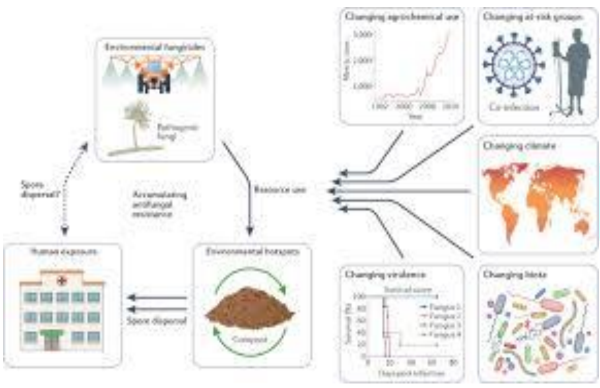

Fig no 1.: the limitations of current antifungal treatments

Conventional antifungal for many types of infections, have several limitations that can impact their success and patient adherence.[11]

- **Topical Antifungal Treatments-**Topical antifungals are commonly used for localized fungal infections like athlete's foot, ringworm, and vaginal candidiasis.. While they are effective for superficial skin infections, they come with several limitations:
- **Poor Penetration**: Topical treatments often struggle to penetrate deeper layers of the skin, nails, and

mucosal membranes.

- **Side Effects**: While generally mild, side effects like irritation, redness, or allergic reactions can occur. Prolonged use on sensitive skin areas can cause dermatitis or skin thinning.
- **Patient Compliance**: Many topical treatments require frequent applications, sometimes several times a day,[12]
- **Oral Antifungal Medications:** Oral antifungals such as fluconazole, itraconazole, terbinafine, and griseofulvin are used for more extensive or systemic infections.
- **Systemic Side Effects**: Oral antifungal medications can cause a range of side effects, including gastrointestinal distress, liver toxicity, and drug interactions
- **Bioavailability Issues**: Some oral antifungal agents suffer from poor bioavailability or variable absorption in the gastrointestinal tract
- **Long Treatment Duration**: Chronic fungal infections such as onychomycosis or systemic candidiasis often require prolonged treatment periods, sometimes lasting for months.
- **Antifungal Resistance**: With prolonged use, fungal pathogens like *Candida* species have developed resistance to common antifungal drugs, such as fluconazole, leading to treatment failure, especially in immunocompromised patients.

Challenges in Treating Mucosal Infections Recurrent Infections:

Both oral and vaginal candidiasis can be recurrent, requiring prolonged or repeated treatment. Chronic infections increase the risk of antifungal resistance, especially with drugs like fluconazole.

THE DRUG DELIVERY SYSTEM THAT IS BASED ON PAPER

Recent advances **in** paper-based drug delivery **systems** have gained significant attention due to their unique ability to offer localized drug release, ease of use, and cost-effectiveness. [14]

Advantages of Paper Films in Topical Drug Delivery

- **Bioadhesion**: Paper films naturally adhere well to the skin, eliminating the need for additional adhesives
- **Controlled Release**: Paper-based systems can be designed to release drugs at a controlled rate.
- **Ease of Use**: Paper films are lightweight, flexible, and non-invasive, making them easy for patients to apply and comfortable to wear.
- **Cost-Effectiveness**: Paper is a low-cost material, and paper-based drug delivery systems This makes them an attractive option, particularly for large-scale production or in resource-limited settings where affordable treatments are needed.[16]

Types of Polymers Used :The selection of appropriate polymers is critical in the formulation of antifungal paper films, as it influences drug release rates, physical properties, and patient comfort. Some of the most commonly used polymers in antifungal paper film formulations include: **Hydroxypropyl Methylcellulose (HPMC), Polyvinyl Alcohol (PVA)**, **Chitosan, Alginate[18]**

Incorporation Techniques : The incorporation of antifungal agents into paper films must ensure effective release and prolonged therapeutic action. Several techniques have been developed for this purpose:

- **Solvent Casting**: This is the most common technique for preparing drug-loaded films, where a polymer solution is prepared and mixed with the antifungal agent. The solution is then cast onto a substrate and dried to form a film. This method is cost-effective and allows for precise control over drug loading and release.
- **Spray Coating**: In spray coating, a solution of the antifungal agent is sprayed onto the paper matrix, and the solvent is evaporated to leave behind a film. This technique is used to ensure uniform distribution of the drug across the film, improving the release profile.[19]

Antifungal Agents Formulated into Films*:*

A range of **antifungal agents** has been successfully incorporated into paper films, improving their therapeutic efficacy against various fungal pathogens. Some commonly used antifungal agents include:

- **Clotrimazole**: This **azole antifungal** is widely used in treating dermatophyte infections,.
- **Miconazole**: Another **azole antifungal**, miconazole is often used in paper films for the treatment
- **Ketoconazole**: Known for its potent antifungal effects, ketoconazole is utilized in paper films for the treatment of both superficial and deep fungal infections.
- **Amphotericin B**: Although typically used for more severe fungal infections, amphotericin B has been incorporated into paper films for localized treatment,.[20][19]

I. Physical Properties Evaluation

Physical testing of paper films is crucial to determine the **mechanical strength**, **flexibility**, and **durability** of the films. The following tests are commonly used:

- **Thickness Measurement**: Thickness of the film is measured using a **micrometer or digital caliper**. Uniform thickness is important to ensure consistent drug release and film integrity. Variability in thickness can lead to uneven drug distribution or inconsistent performance.
- **Tensile Strength**: This test evaluates the force required to break the film, providing insight into the film's mechanical strength and resistance to rupture during application.
- **Folding Endurance**: This test assesses the flexibility of the film and its ability to withstand repeated bending without cracking or breaking.[22]

II. In Vitro Drug Release Evaluation

To ensure the efficacy of the paper films, it is essential to assess the **drug release profile** from the film. This is typically done through **in vitro release studies**, which simulate the conditions under which the film will be applied.

III. Antifungal Efficacy Testing

The primary goal of antifungal paper films is to deliver a potent therapeutic effect at the site of infection. The following methods are commonly used to evaluate the **antifungal efficacy** of the films:

- **Agar Diffusion Assay**: This test is used to assess the antifungal activity of the paper films by placing the films on a solid agar plate inoculated with the fungal pathogen of different formulations or antifungal agents.
- **Minimum Inhibitory Concentration (MIC) Testing**: This method evaluates the minimum concentration of the drug (incorporated into the film) required to inhibit fungal growth. contact with fungal cultures and measuring growth inhibition, either visually or with spectrophotometric methods.
- **Time-Kill Assay**: This in vitro method is used to assess the bactericidal or fungicidal activity of the paper film by exposing fungal cultures to the film for a specific duration and measuring the reduction in fungal count over time [23]

IV. Stability Testing

Stability tests ensure that the paper films maintain their physical properties, drug release profile, and antifungal efficacy over time. This includes:

- **Storage Conditions**: Films are stored under different conditions (e.g., at room temperature, in a humid environment) and evaluated at regular intervals for **drug content**, **physical integrity**, and **release characteristics**.
- **Accelerated Stability Studies**: These studies simulate long-term storage conditions by exposing the films to higher temperatures and humidity to predict their shelf life and performance under real-world conditions.

❖ TESTING FOR BIOADHESION

Bioadhesion is a critical property for topical drug delivery, ensuring the film adheres to the skin or mucosal surfaces during treatment. Bioadhesion is typically tested using:

- **In Vitro Adhesion Testing**: The film is applied to a model substrate, such as porcine skin or a synthetic membrane, and the force required to detach the film is measured.[24]

DEVELOPING PAPER FILMS

The formulation of paper films for drug delivery is an emerging area of pharmaceutical research, particularly for topical and localized drug delivery systems.

1. **Drug Incorporation Techniques**:
   - **Solvent Casting**: A common method where the polymer solution is mixed with the drug, and the solvent is evaporated to form a thin film..
   - **Coating Techniques**: The drug is coated onto a paper substrate, followed by drying, to ensure a uniform distribution of the drug.
   - **Spray Drying and Electrospinning**: These advanced methods allow for the incorporation of drugs into nanofibrous films,
2. **Antifungal Agents**: Various antifungal agents are incorporated into paper films for localized treatment. These include:
   - **Clotrimazole**: A broad-spectrum antifungal often used in skin infections.
   - **Miconazole**: Another azole antifungal used in dermatological treatments.
   - **Ketoconazole**: Known for its potent antifungal action, ketoconazole is often used in more resistant infections.[30]

METHODOLOGY

- **ANTIFUNGAL PAPER FILMS: METHODOLOGY, MATERIALS, AND ACTIVE PHARMACEUTICAL INGREDIENTS (APIS):Antifungal paper films** are gaining attention in pharmaceutical research for their ability to provide localized, sustained-release drug delivery with minimal systemic side effects.[34]

- **Materials Used in Antifungal Paper Film Formulations**

- **Polymers:**
   - **Hydroxypropyl Methylcellulose (HPMC)**
   - **Polyvinyl Alcohol (PVA)**
   - **Chitosan**
   - **Alginate**

- **Plasticizers:**
   - **Glycerol** and **Triacetin**

- **Substrate:**

- **Paper:** Typically, a smooth, flexible, and absorbent paper is used as the primary substrate

- **Active Pharmaceutical Ingredients (APIs) Used in Antifungal Paper Films**

- **Azoles:**
  - **Clotrimazole:**
  - **Miconazole:**
  - **Ketoconazole**

- **Allylamines:**
  - **Terbinafine**

- **Polyenes:**
  - **Amphotericin B**
  - **Nystatin** [36]

- **Methodology for Preparing Antifungal Paper Films**

- **Solvent Casting Method:**
  - This is the most commonly used method for preparing drug-loaded paper films. In this process, the polymer(s) and antifungal APIs are dissolved in an appropriate solvent[37]
- **Coating Method:**
  - In this approach, a thin layer of the polymeric drug solution is applied to the paper substrate using spraying or dip-coating techniques.
- **Electrospinning:**
  - Electrospinning is a more advanced technique that uses an electric field to draw fine polymer fibers from a solution
  - .[38]
- **Spray Drying:**
  - Spray drying can be employed to load antifungal drugs into a polymeric solution. The drug-loaded solution is atomized into small droplets and rapidly dried to form a film. This technique provides a quick and uniform distribution of the antifungal agents in the film matrix.[39]

EVALUATION OF ANTIFUNGAL PAPER FILMS

- **Physical Characterization:** Includes tests for thickness, tensile strength, folding endurance, and surface morphology to evaluate the mechanical properties and durability of the films.[40]

- **In Vitro Drug Release Studies:** These studies assess how the antifungal drug is released from the paper film over time, helping to optimize release kinetics and achieve sustained drug delivery.[41]
- **Antifungal Efficacy Testing:** Standard microbiological methods, such as agar diffusion tests or minimum inhibitory concentration (MIC) assays, are used to evaluate the antifungal activity of the paper films against common fungal pathogens like *Candida albicans*,[42]

❖ ANTIFUNGAL PAPER FILMS: EXCIPIENTS AND THEIR ROLE

In the formulation of **antifungal paper films**, excipients play a crucial role in enhancing the stability, bioavailability, release characteristics, and adhesion properties of the films. Excipients used in these formulations include **polymers**, **plasticizers**, **stabilizers**, **solvents**, and **other additives**. 43]

Common Excipients in Antifungal Paper Films:

- ✓ **Polymers**:
  - **Hydroxypropyl Methylcellulose (HPMC)**: Often used as a film-forming agent due to its water-solubility, biocompatibility
  - **Polyvinyl Alcohol (PVA)**: A highly flexible polymer used for its good adhesion to mucosal surfaces, enhancing the delivery of antifungal agents like **clotrimazole** and **miconazole**.
  - **Chitosan**: A natural polymer with antimicrobial properties, ideal for enhancing antifungal efficacy and promoting wound healing.
  - **Alginate**: A polysaccharide used for controlled release formulations, providing a gel matrix for sustained drug delivery.
- ✓ **Plasticizers**:
  - **Glycerin** and **propylene glycol** are commonly used to enhance the flexibility and mechanical properties of the paper films, ensuring they do not become brittle.
- ✓ **Stabilizers**:
  - **Tocopherol (Vitamin E)** and other antioxidants can be incorporated to prevent degradation of sensitive antifungal agents, such as **fluconazole** and **ketoconazole**.
- ✓ **Solvents**:
  - **Water** is typically used as a solvent for hydrophilic polymers, whereas **ethanol** or **acetone** may be employed for dissolving hydrophobic agents.
- ✓ **Antifungal Agents (Active Pharmaceutical Ingredients, APIs)**:
  - **Clotrimazole**, **miconazole**, **ketoconazole**, and **terbinafine** are commonly used antifungal agents incorporated into paper films for their broad-spectrum activity against dermatophytes.[44]

Role of Excipients in the Performance of Antifungal Paper Films:

- **Controlled Release**: The choice of excipient affects the release rate of the antifungal agent, ensuring a sustained effect at the site of infection.
- **Bioadhesion**: Polymers like PVA and chitosan enhance the adhesive properties, allowing the film to stay in place for prolonged periods, thus improving the therapeutic efficacy.
- **Stability and Bioavailability**: The use of stabilizers, antioxidants, and plasticizers ensures that the antifungal agent remains
- **Patient Compliance**: The ease of application and comfort offered by these films, owing to their flexible nature and minimal to treatment.[45]

❖ ANTIFUNGAL PAPER FILMS: FORMULATION METHODS, API ADDITION, AND MATRIX FORMATION

The formulation of antifungal paper films involves several critical steps, including the preparation of the polymer matrix,including methods of preparation, API incorporation, and matrix formation.[46]

Formulation Methods:

- **Polymer Selection and Matrix Formation:** The first step in preparing antifungal paper films is the selection of suitable polymers. Commonly used polymers for paper film formulations include:
    - **Hydroxypropyl Methylcellulose (HPMC)**: Known for its excellent film-forming properties, it provides good **controlled release** and **biocompatibility**.
    - **Polyvinyl Alcohol (PVA)**: Often selected for its **water solubility**, **flexibility**, and **adhesion to mucosal surfaces**.
    - **Chitosan**: A natural biopolymer that adds **antimicrobial** properties and helps in **wound healing**.
    - **Alginate**: Provides **controlled release** and **gelation properties** for sustained drug delivery.[46]
- **Incorporation of Active Pharmaceutical Ingredients (APIs):** The antifungal agent, such as **clotrimazole**, **miconazole**, **fluconazole**, or **amphotericin B**, is incorporated into the polymer matrix either during the preparation of the solution or post-casting using different methods, including:

Solvent Casting: The API is dissolved in a solvent along with the polymer, and the solution is then cast to form a film. This method ensures uniform distribution of the API throughout the film matrix.

Spray Drying: The drug is sprayed onto a pre-formed polymer film in a **fine mist** and dried to form a thin layer that encapsulates the drug.

Electrospinning: For nanofiber-based films, APIs can be incorporated into the polymer solution and electrospun to form a nano-structured film for **enhanced release** profiles.

- **Shaping and Cutting of Films**
- **Evaluation of Film Properties**

❖ PHYSIOCHEMICAL PROPERTIES

I. **pH of Paper Films:**The **pH** of paper is a critical property that affects its durability, stability, and how it reacts to environmental factors (like moisture and pollutants).Typical paper pH ranges between **4.5 to 8.5**.[50]

II. **Weight of Paper (Basis Weight):**The **weight** of paper is usually measured by **basis weight**, which refers to the weight of a ream (500 sheets) of paper cut to a standard size (typically 17 x 22 inches, or 43 x 56 cm for U.S. letter-size paper).

III. **Size (Dimensions) of Paper Films:Size** refers to the **area** of the paper film. This could mean the dimensions of individual sheets (like A4, letter, legal, or custom sizes) or the overall size in terms of a continuous sheet of paper (e.g., rolls of paper used in packaging).

IV. **Thickness (Caliper or Grammage):Thickness** of paper is often referred to as **caliper**, which is the measurement of the paper's thickness in micrometers (µm) or mils (thousandths of an inch).[51]

Typically, the physicochemical properties of paper films include:

i. **Mechanical properties**: These are related to the paper’s strength, including tensile strength, tear strength, burst strength, and elongation.

ii. **Surface properties**: This involves surface roughness, smoothness, porosity, and absorptivity, which affect the paper's interaction with ink, coatings, or other materials.

iii. **Moisture absorption**: Paper is hygroscopic, meaning it absorbs moisture from the air, which affects its dimensional stability and mechanical properties.

iv. **Chemical composition**: This could include the cellulose content, lignin, hemicellulose, and the presence of any additives or treatments like fillers, sizing agents, or coatings.

v. **Optical properties**: These include brightness, opacity, and whiteness, which are influenced by both the chemical composition and surface finish.

vi. **Thermal properties**: The thermal stability of paper films, including melting or decomposition points and heat resistance.

vii. **Barrier properties**: Some paper films are treated to improve their barrier properties (e.g., moisture or gas permeability), which is important for packaging applications.[52]

❖ IN VITRO AND MICROBIAL TESTING OF PAPER FILMS

In vitro antimicrobial testing is used to assess the efficacy of materials, like paper films, in inhibiting the growth of microorganisms (bacteria, fungi, etc.) under controlled laboratory conditions. The two most common methods for **microbial testing** of paper films are **Agar Well Diffusion** and **Minimum Inhibitory Concentration (MIC)** testing. Below is a detailed explanation of these methods, with their relevance to antimicrobial paper films.

1. Agar Well Diffusion Method

The **Agar Well Diffusion** method is a classic approach to assess the antimicrobial activity of paper films. It is simple to perform and widely used for testing antimicrobial agents, including those incorporated into materials like paper films.

Applications:

- The **agar well diffusion method** is commonly used to assess antimicrobial coatings or treatments on paper films for food packaging, wound dressings, and other medical applications.[53]

2. Minimum Inhibitory Concentration (MIC)

MIC is the lowest concentration of an antimicrobial agent that will inhibit the growth of a microorganism. This method helps determine the **potency** of the antimicrobial substances used in paper films.

Applications:

- MIC testing is especially useful in assessing the **effectiveness of antimicrobial coatings** or treatments on paper films used in sensitive applications like **food packaging** or **medical dressings**, where it is critical to know the exact amount of antimicrobial agent required to prevent microbial contamination.[54]

❖ STABILITY OF ANTIFUNGAL PAPER FILMS: EFFECTS OF TEMPERATURE, HUMIDITY, AND RETENTION OF ACTIVITY

The **stability** of **antifungal paper films** (which are typically treated with antimicrobial agents such as silver nanoparticles, essential oils, or chitosan) is crucial for their **long-term effectiveness**, especially in applications like **food packaging**, **medical dressings**, and **environmental hygiene**. Environmental factors like **temperature**, **humidity**, and **storage conditions** can significantly influence the **physical properties** and **antifungal activity** of these films.[56]

1. Stability of Antifungal Paper Films Under Temperature and Humidity Conditions

Effect of Temperature:

- At elevated temperatures, the **volatility** of antimicrobial agents increases, leading to the **loss of activity** over time. For example, the **antifungal activity** of silver nanoparticles or chitosan-coated paper films may decline at **temperatures above 40°C**.

Effect of Humidity:

- **Humidity** plays a critical role in the **plasticity** and **mechanical stability** of paper films. High humidity can cause paper to **absorb moisture**, which can **affect the integrity** of the film, making it more **brittle** or causing it to **lose rigidity**.
- In the case of **antifungal coatings**, excess moisture may lead to the **dissolution** or **leaching out** of active agents, reducing the retention of **antifungal activity**.[57]

2. Retention of Antifungal Activity

The **retention of antifungal activity** over time is essential for evaluating the **long-term viability** of antimicrobial paper films. The **stability of the antimicrobial agent** incorporated into the paper film directly influences how long the paper film can retain its **antifungal properties**.

- **Retention of antifungal activity** is typically tested through **periodic re-testing** of the paper film, using methods such as **agar diffusion** or **MIC (Minimum Inhibitory Concentration) testing**.
- During accelerated aging tests, the paper films are subjected to specific **temperature** and **humidity** conditions for a period of time (e.g.30/60 days). After this period, the **antifungal activity** is re-assessed, and the **zone of inhibition** or MIC values are compared to those obtained at the start of the test to determine the **loss of activity**.[58]

❖ RELEASE PROFILE OF ANTIFUNGAL PAPER FILMS

➢ Franz Diffusion Cell for Release Studies:

The **Franz diffusion cell** is an **in vitro** method commonly used to evaluate the **release of antifungal agents** from **paper films** or similar materials. This method involves two compartments: a **donor chamber** where the paper film is placed, and a **receptor chamber** filled with a medium (e.g., **simulated skin fluid** or **phosphate-buffered saline (PBS)**) to mimic the environment the material will come into contact with.

➢ Simulated Skin Fluid (SSF):

In many antifungal paper film studies, simulated skin fluid (SSF) or artificial sweat is used to mimic the physiological conditions under which the paper films would be used (e.g., in wound care or skin-related applications). SSF typically contains ions like sodium chloride, calcium chloride, and potassium chloride, as well as buffers like phosphate or acetate, to simulate the composition of human sweat.

❖ TOPICAL FORMULATION OF PAPER FILMS: SENSORY EVALUATION, TEXTURE, EASE OF USE, AND FOAMING ABILITY

Topical formulations of paper films typically refer to thin films used for topical delivery of active ingredients, such as antifungal agents, medicinal compounds, or cosmetic substances. These films are designed to adhere to the skin or mucous membranes, providing a controlled release of the active substance while ensuring ease of use and comfort for the user. The performance of these films is evaluated based on several sensory and mechanical characteristics, such as texture, ease of use, sensory feel, and foaming ability (if applicable to the active ingredient).[60]

A. Sensory Evaluation of Topical Paper Films

The **sensory evaluation** of paper films.The **sensory properties** assessed typically include:

- **Feel** on the skin (smooth, sticky, or greasy)
- **Transparency** and **appearance**
- **Comfort** during wear (non-irritating, non-itching)
- **Adhesion** to skin (whether it stays in place or easily detaches)
- **Drying time** (how long the film takes to dry after application)

B. Texture and Mechanical Properties

The **texture** of the paper films is typically assessed through **rheological tests** or **texture analysis** to determine:

- **Flexibility**: How well the film conforms to body contours.
- **Elasticity**: The ability of the paper film to return to its original shape after deformation.
- **Tensile strength**: How much force the film can withstand before breaking.
- **Peelability**: The ease with which the film can be removed from the skin.

C. Ease of Use

The **ease of use** of a **topical paper film** formulation depends on factors like:

- **Application process**: The ease with which users can apply the film to their skin
- **Size and shape**: Films are typically made in **pre-cut sizes** ,**face**, **wounds**, or **small** The **shape** and **size** of the film can affect ease of use.

- **Adhesion**: The film should be **adhesive enough** to stay in place but not so sticky that it causes discomfort or is difficult to remove.

D. Foaming Ability (for Active Ingredients that Create Foam)

In some formulations, such as those containing **antifungal agents** there may be a desire for the paper film to **foam** upon contact with water or skin, particularly for **cleansing** or **antimicrobial applications**.

- **Foaming ability** is important when the film is designed to release **foaming agents** or **cleansing agents**
- **Foaming tests** can be conducted to determine:
    - **Foam volume**: How much foam the film generates when activated
    - **Foam stability**: How long the foam lasts after generation.

CONCLUSION

In conclusion, paper films demonstrate significant potential as an innovative antifungal delivery system, offering advantages such as localized drug release, ease of use, and cost-effectiveness. The formulation and evaluation techniques discussed provide a foundation for further research and development. Future studies should focus on optimizing paper film properties, exploring novel antifungal agents, and conducting in vivo trials to establish clinical efficacy.

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