Emerging Role of Microspheres in Topical Antifungal Therapy

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***Abstract*—Antifungal diseases represent a significant global health concern, particularly affecting the skin, hair, nails, and mucosal surfaces. The rising incidence of fungal infections, coupled with limitations of conventional topical antifungal formulations such as poor skin penetration, frequent dosing, drug instability, and reduced patient compliance, necessitates the development of advanced drug delivery systems. Microsphere-based topical drug delivery systems have emerged as a promising approach to overcome these challenges by providing controlled, sustained, and localized drug release at the site of infection. Microspheres are polymeric, spherical particulate systems capable of encapsulating antifungal agents, thereby enhancing drug stability, prolonging residence time, improving skin retention, and minimizing systemic absorption. This review highlights antifungal diseases, their conventional treatment strategies, and the limitations associated with traditional topical formulations. It further emphasizes the role of novel topical drug delivery systems, with a special focus on microspheres, including their composition, types, preparation techniques, mechanisms of drug release, and evaluation parameters. Overall, microsphere-based topical antifungal therapy offers an effective and patient-friendly alternative to conventional treatments, with potential to improve therapeutic outcomes and reduce recurrence of fungal infections.**

***Index Terms*—Antifungal diseases; Topical drug delivery; Microspheres; Controlled drug release; Polymer-based drug delivery; Skin retention; Novel drug delivery systems**

I. Introduction to Antifungal Diseases

Antifungal diseases, also known as fungal infections or mycoses, are a diverse group of infectious diseases caused by pathogenic fungi that invade and colonize human tissues. Fungi are eukaryotic microorganisms that exist in various forms, including yeasts, Molds, and dimorphic fungi. Under favourable conditions, these organisms can infect the skin, hair, nails, mucous membranes, and internal organs, leading to a wide spectrum of clinical manifestations ranging from mild superficial infections to severe, life-threatening systemic diseases. [1–3]

The incidence of fungal infections has increased markedly in recent years due to factors such as immunosuppression, diabetes mellitus, prolonged antibiotic therapy, aging population, poor hygiene, and climatic conditions favouring fungal growth.[2,3] Common topical fungal infections include dermatophytosis (tinea infections), candidiasis, and pityriasis versicolor, which significantly affect the quality of life and may lead to chronic or recurrent conditions if inadequately treated.

Conventional antifungal therapy involves the use of topical and systemic antifungal agents such as azoles, polyenes, and allylamines. Topical therapy is preferred for superficial fungal infections due to its localized action, reduced systemic side effects, and improved patient compliance. However, challenges such as poor drug penetration, frequent dosing, drug instability, and emergence of antifungal resistance limit the therapeutic efficacy of conventional topical formulations.

Therefore, there is a growing interest in the development of advanced drug delivery systems to enhance antifungal treatment outcomes.[21,23] Novel approaches aim to improve drug localization, sustain drug release, enhance skin retention, and reduce dosing frequency. Understanding the pathophysiology and therapeutic limitations of antifungal diseases is essential for designing effective topical antifungal delivery systems.

II. Treatment of Antifungal Diseases

The treatment of antifungal diseases depends on the type of fungal pathogen, site and severity of infection, and patient-related factors such as immune status and age. Antifungal therapy is broadly categorized into topical and systemic treatment, with topical therapy being the first-line approach for superficial and cutaneous fungal infections.

1. Topical Antifungal Therapy

Topical antifungal agents are primarily used for superficial and cutaneous mycoses as they provide localized drug action with minimal systemic side effects.[5,21] These agents are available in various dosage forms such as creams, gels, ointments, lotions, powders, sprays, and nail lacquers.

Common classes of topical antifungal drugs include:

- Azoles: Clotrimazole, Ketoconazole, Miconazole, Econazole
- Allylamines: Terbinafine, Naftifine
- Polyene antibiotics: Nystatin
- Others: Ciclopirox olamine, Amorolfine

Topical therapy is usually continued for 2–4 weeks, depending on the infection type, to prevent recurrence.

2. Systemic Antifungal Therapy

Systemic antifungal agents are indicated in severe, extensive, chronic, or refractory fungal infections, [3,4] and in immunocompromised patients. These drugs are administered orally or intravenously.

Common systemic antifungal agents include:

- Azoles: Fluconazole, Itraconazole, Voriconazole
- Allylamines: Oral Terbinafine
- Polyenes: Amphotericin B
- Echinocandins: Caspofungin, Micafungin

Systemic therapy requires careful monitoring due to potential drug interactions, hepatotoxicity, and other adverse effects.

3. Combination Therapy

In certain cases, a combination of topical and systemic antifungal therapy is employed to enhance therapeutic efficacy, reduce treatment duration, and prevent resistance, especially in chronic or recurrent infections. [1,21]

4. **Supportive and Preventive Measures**

   Adjunctive measures play an important role in successful antifungal treatment, including:

   - Maintaining proper hygiene and dryness of affected areas
   - Avoiding occlusive clothing
   - Treating underlying conditions such as diabetes
   - Patient education to ensure treatment adherence [1,2]

5. **Emerging Treatment Approaches**

   Recent advances focus on novel drug delivery systems such as microspheres, nanoparticles, liposomes, and niosomes to overcome limitations of conventional therapy. These systems aim to improve drug penetration, sustain release, enhance local drug concentration, and minimize side effects, thereby improving overall treatment outcomes. [21–26]

III. Topical Drug Delivery System

A topical medication delivery system administers the medication directly to the site of skin damage. Creams, ointments, gels, lotions, powders, and sprays are examples of traditional formulations that are frequently used. However, a significant barrier that limits drug penetration is the stratum corneum, the skin's outermost layer.

Novel topical drug delivery systems, including microspheres, microsponges, liposomes, niosomes, and nanoparticles, have been developed to solve these issues. Drug permeation, retention, stability, and sustained release are all enhanced by these systems.

Advantages of Topical Drug Delivery :-

- Direct drug delivery to the site of infection
- Reduced systemic side effects
- Avoidance of first-pass metabolism
- Improved patient compliance
- Lower drug dose requirement
- Enhanced therapeutic efficacy

Conventional Topical Drug Delivery Systems :-

Traditional topical formulations are commonly used but often show limited efficacy due to short residence time and poor penetration.

- Creams
- Ointments
- Gels
- Lotions
- Powders
- Sprays

Novel Topical Drug Delivery Systems :-

To overcome the limitations of conventional formulations, advanced drug delivery systems have been developed to enhance skin penetration, drug retention, and sustained release.

- Microspheres
- Nanoparticles
- Liposomes
- Niosomes
- Transfersomes
- Ethosomes
- Solid lipid nanoparticles (SLNs)
- Nanostructured lipid carriers (NLCs)

Role of Topical Drug Delivery in Antifungal Therapy :-

Topical drug delivery plays a crucial role in antifungal treatment by:

- Enhancing drug concentration at the infected site
- Prolonging drug residence time on the skin
- Reducing dosing frequency
- Minimizing systemic toxicity

Advanced topical systems are particularly effective for antifungal drugs with poor aqueous solubility and limited skin permeability, thereby improving therapeutic efficacy and patient adherence.

IV. Drug Delivery System Based on Microspheres

Drug delivery systems based on microspheres represent an innovative and adaptable method for the targeted and controlled delivery of therapeutic agents. Microspheres are solid, spherical, free-flowing particulate systems made of synthetic or natural polymers that range in size from 1 to 1000 μm. By protecting medications in a polymeric matrix or shell, these systems allow for increased stability, extended drug release, and improved therapeutic efficacy.

Microsphere-based delivery systems have received a lot of attention in recent years, especially for topical applications, in the treatment of antifungal diseases. Microspheres are particularly useful for treating superficial and cutaneous fungal infections that need to be treated because of their capacity to localize the medication at the site of infection, decrease systemic absorption, and provide sustained drug release. [8–13,22]

Composition of Microspheres :-

One or more polymers that act as drug carriers form microspheres. Polymers that are frequently used include:

Chitosan, gelatin, alginate, starch, and albumin are examples of natural polymers.

Synthetic polymers include polycaprolactone, polymethacrylates, ethyl cellulose, and polylactic-co-glycolic acid (PLGA).

Drug encapsulation effectiveness, release kinetics, biodegradability, biocompatibility, and skin retention characteristics are all strongly influenced by the polymer selection. [9–13]

Types of Microspheres :-

Microspheres can be categorized according to their structure and functionality as:

The medication is evenly distributed throughout the polymer matrix in matrix microspheres.

Reservoir (core-shell) microspheres, in which a polymeric shell encloses the medication

Bioadhesive microspheres are made to stick to biological surfaces and stay there longer.

Biodegradable microspheres that break down into harmless byproducts

Non-biodegradable microspheres that provide extended drug release but need to be carefully prepared [8,11,13]

Mechanism of Microsphere-Based Drug Delivery :-

By protecting the medication within a polymeric carrier, microsphere-based drug delivery systems are intended to deliver therapeutic agents in a controlled, sustained, and localized manner. The physicochemical characteristics of the drug, the features of the polymer, and the interaction of the microspheres with biological tissues all influence the mechanism of drug delivery from microspheres. This mechanism is essential for improving drug retention at the infection site and reducing systemic exposure in topical antifungal therapy.

1. Drug Encapsulation and Protection

The active pharmaceutical ingredient is incorporated into the microsphere either by uniform dispersion within the polymer matrix or by entrapment within a core surrounded by a polymeric shell. This encapsulation protects the drug from environmental degradation, oxidation, and photodegradation, thereby improving drug stability. In antifungal therapy, this is particularly important for drugs that are sensitive to moisture or light. [12,13]

2. Skin Adhesion and Localization

Upon topical application, microspheres adhere to the skin surface due to their small particle size and surface properties. Bioadhesive polymers further enhance attachment to the stratum corneum, resulting in prolonged residence time at the site of application. This localized delivery ensures that the antifungal drug remains concentrated in the infected area, reducing drug loss due to sweating, washing, or mechanical removal. [8,22]

3. Formation of a Drug Reservoir

Microspheres act as a drug reservoir on the skin surface. Instead of immediate release, the encapsulated drug is gradually released from the polymer matrix over an extended period. This reservoir effect maintains a consistent drug concentration in the skin layers, which is essential for effective antifungal activity and prevention of fungal regrowth.

4. Controlled Drug Diffusion

Drug molecules diffuse slowly from the microsphere through the polymer matrix into the surrounding skin layers. The rate of diffusion is influenced by factors such as:

Polymer molecular weight and porosity

Drug solubility and concentration gradient

Particle size and surface area

This controlled diffusion allows sustained therapeutic levels of the drug to be maintained in the epidermis and dermis. [12,13]

5. Polymer Swelling and Erosion

In the presence of skin moisture, hydrophilic polymers may swell, creating channels within the microsphere matrix that facilitate drug diffusion. Biodegradable polymers gradually undergo surface or bulk erosion, further contributing to sustained drug release. This dual mechanism of swelling and erosion ensures prolonged and predictable drug delivery.

6. Penetration into Skin Layers

While microspheres themselves generally remain on the skin surface due to their size, the released drug penetrates into the stratum corneum, epidermis, and superficial dermis, which are the primary sites of fungal infection. This localized penetration minimizes systemic absorption and associated side effects.

7. Reduction of Systemic Exposure

Because microsphere-based delivery systems primarily release the drug locally, systemic absorption is significantly reduced. This targeted approach lowers the risk of systemic toxicity and drug–drug interactions, making microspheres particularly suitable for long-term antifungal therapy.

8. Sustained Therapeutic Effect

The combined effects of controlled release, prolonged skin retention, and localized drug delivery result in a sustained therapeutic effect. This reduces the need for frequent application and enhances patient compliance, which is critical in the successful management of chronic fungal infections.

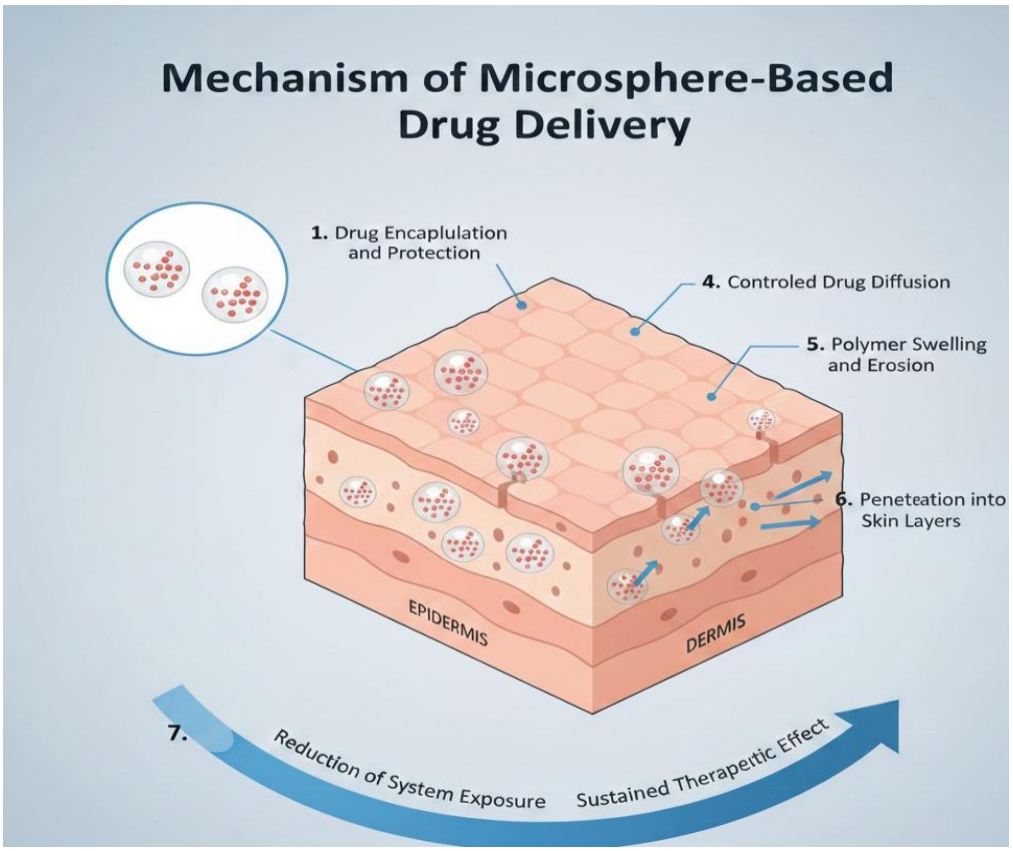

Figure 1. Overview of microsphere-mediated drug encapsulation, release, and penetration into skin layers.

Mechanism of Drug Release from Microspheres :-

A critical aspect of microspheres' effectiveness as regulated drug delivery systems is their drug release mechanism. The microsphere structure, polymer properties, drug physicochemical properties, and environmental factors all influence drug release. Controlled drug release from microspheres in topical antifungal therapy ensures longer drug availability at the infection site, improves therapeutic efficacy, and lowers dosage frequency.

Diffusion, polymer erosion or degradation, swelling, dissolution, and initial burst release are some of the mechanisms that typically cause drug release from microspheres.

1. Diffusion-Controlled Drug Release

Diffusion is the most common mechanism of drug release from microspheres. In this process, the drug diffuses from the interior of the microsphere through the polymer matrix into the surrounding medium. The driving force for diffusion is the concentration gradient between the microsphere and the external environment. The diffusion rate depends on polymer porosity, drug solubility, particle size, and thickness of the polymer matrix. In matrix-type microspheres, the drug is uniformly dispersed throughout the polymer, resulting in a gradual and sustained release. Diffusion-controlled release is particularly beneficial for topical antifungal therapy as it maintains a constant therapeutic drug level in the skin layers over an extended period. [12,18]

2. Polymer Erosion or Degradation-Controlled Release

In biodegradable microspheres, drug release occurs as the polymer undergoes surface erosion or bulk degradation. Surface erosion involves gradual degradation of the outer polymer layer, leading to controlled drug release. Bulk degradation occurs throughout the polymer matrix, allowing drug release from within the microsphere. Polymers such as PLGA, chitosan, gelatin, and alginate degrade into non-toxic by-products, making them suitable for pharmaceutical applications. The degradation rate influences the duration and pattern of drug release. [13]

3. Swelling-Controlled Drug Release

Hydrophilic polymers absorb moisture from the surrounding environment, causing the microspheres to swell. Swelling creates aqueous channels within the polymer matrix, facilitating drug diffusion. The extent of swelling depends on polymer composition, cross-linking density, and environmental pH. Swelling-controlled release is particularly relevant in topical formulations, where skin moisture activates drug release from the microspheres. [19]

4. Dissolution-Controlled Drug Release

In this mechanism, drug release is governed by the dissolution rate of the drug from the microsphere surface or matrix. Poorly water-soluble drugs exhibit slower dissolution and prolonged release. The dissolution rate can be modified by drug particle size, polymer–drug interaction, and presence of solubilizing agents. This mechanism is advantageous for antifungal drugs with low aqueous solubility. [12,18]

5. Initial Burst Release

An initial burst release often occurs due to the presence of drug molecules located on or near the surface of the microspheres. Burst release provides a rapid onset of therapeutic action, which is beneficial in controlling acute symptoms such as itching and inflammation. Excessive burst release, however, may cause local irritation and must be carefully controlled during formulation development. [12,18]

6. Combined Release Mechanisms

In most microsphere formulations, drug release occurs through a combination of mechanisms rather than a single process. For example, an initial burst release may be followed by diffusion-controlled and erosion-controlled release, resulting in a biphasic or triphasic release profile.

7. Factors Affecting Drug Release from Microspheres

Several formulation and processing parameters influence drug release kinetics: [17–19]

Type and molecular weight of polymer

Drug loading and solubility

Particle size and surface morphology

Degree of cross-linking

Preparation method

Environmental conditions such as pH and temperature

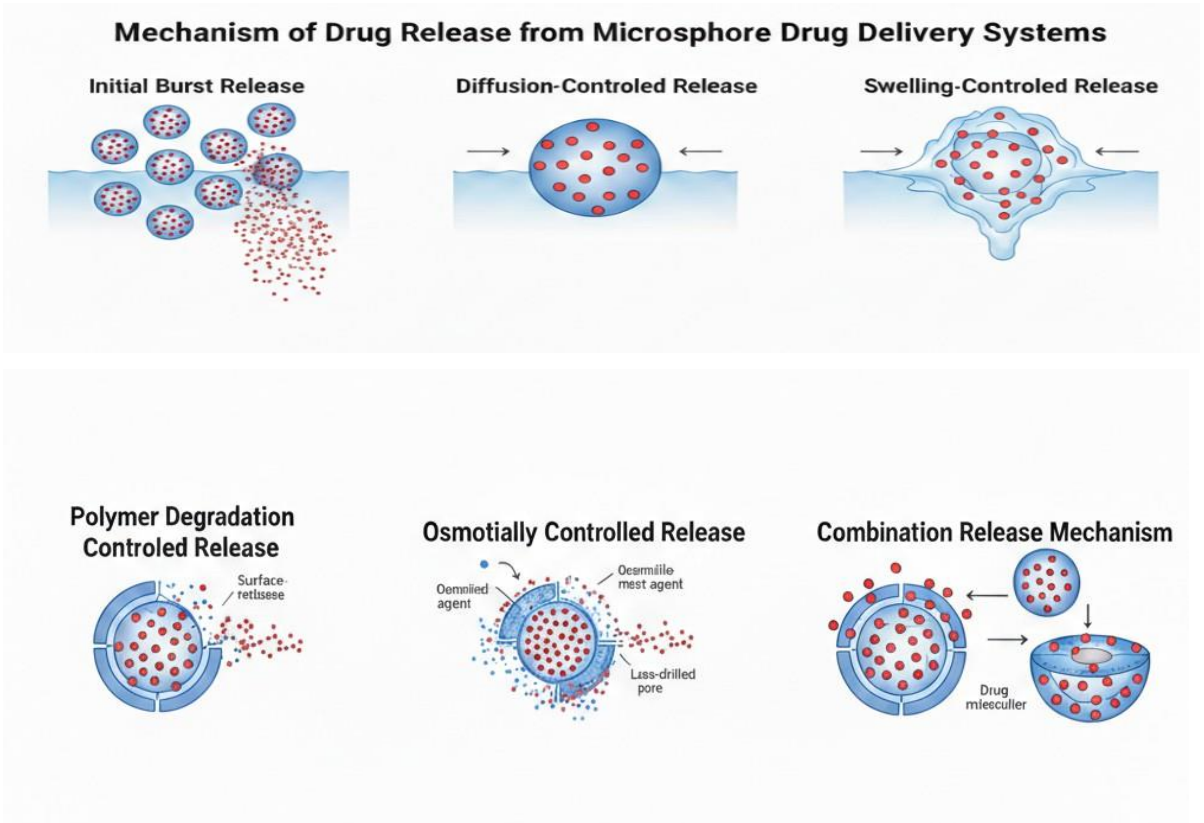

Figure 2. Overview of initial burst, diffusion-controlled, swelling-controlled, degradation-controlled, osmotically controlled, and combination drug release mechanisms in microspheres.

V. Microsphere Preparation Techniques

Microspheres are spherical, free-flowing particulate systems ranging from 1–1000 µm, designed to encapsulate drugs for controlled, sustained, targeted, or localized drug delivery. Various preparation techniques are employed depending on drug nature, polymer type, desired particle size, entrapment efficiency, and release profile.

1. Solvent Evaporation Technique

Principle :-Microspheres are formed by emulsifying a polymer–drug solution in an immiscible continuous phase, followed by evaporation of the solvent, leading to polymer precipitation and microsphere formation.

Procedure:-

1. Drug and polymer are dissolved in a volatile organic solvent (e.g., dichloromethane, chloroform).
2. This solution is emulsified into an aqueous phase containing a stabilizer (e.g., PVA).
3. Continuous stirring allows evaporation of the solvent.
4. Solidified microspheres are collected by filtration.
5. Washed and dried. [11,14]

Types :-

- O/W emulsion – for hydrophobic drugs
- W/O/W emulsion – for hydrophilic drugs

Advantages :-

- Simple and reproducible
- Suitable for controlled drug release
- Use of organic solvents
- Not ideal for heat-sensitive drug

2. Solvent Extraction Technique

Principle :- Instead of evaporation, the solvent is removed by diffusion into an external aqueous phase, causing polymer precipitation.

Procedure :-

1. Drug–polymer solution prepared in organic solvent.
2. Emulsified into aqueous phase containing surfactant.
3. Solvent diffuses out into water.
4. Microspheres harden and are recovered.

Advantages:-

- Faster than solvent evaporation
- Lower thermal stress
- Possible drug loss into aqueous phase
- Limited polymer choice

3. Emulsion Cross-Linking Technique

Principle :- Natural polymers are cross-linked within an emulsion system using chemical cross-linking agents.

Procedure :-

1. Polymer solution containing drug is emulsified in oil phase.
2. Cross-linking agent (e.g., glutaraldehyde) added.
3. Cross-linking stabilizes microspheres.
4. Microspheres are filtered, washed, and dried.
5. Polymers Used : Gelatin, Albumin, Chitosan

Advantages :-

- Suitable for hydrophilic drugs
- Good mechanical strength
- Toxic cross-linking agents

4. Spray Drying Technique

Principle :- A drug–polymer solution is atomized into a hot air chamber, causing rapid solvent evaporation and microsphere formation.

Procedure :-

1. Drug and polymer dissolved in solvent.
2. Solution sprayed through nozzle.
3. Solvent evaporates instantly.
4. Dry microspheres collected. [11]

Advantages :-

- One-step, rapid process
- Scalable for industrial use
- Suitable for heat-stable drugs
- Low yield for some polymers
- Thermal degradation risk

5. Ionic Gelation Technique :-

Principle :-Microspheres are formed by ionic cross-linking between oppositely charged polymers and ions.

Procedure :-

1. Polymer (e.g., sodium alginate) dissolved in water.
2. Drug incorporated into polymer solution.
3. Dropped into solution containing cross-linking ions (e.g., Ca^{2+}).
4. Microspheres instantly formed and hardened. [13]

Advantages :-

- No organic solvents
- Mild preparation conditions
- Suitable for proteins and peptides
- Poor mechanical strength
- Burst release possible

6. **Coacervation–Phase Separation Technique**

Principle :- Microspheres are formed by phase separation of polymer from solution, followed by deposition around drug particles.

Procedure :-

1. Drug dispersed in polymer solution.
2. Phase separation induced by temperature change or nonsolvent addition.
3. Polymer coats drug particles.

4. Hardening by cross-linking or solvent removal. [11]

Advantages :-

- High drug loading
- Uniform coating
- Process complexity
- Sensitive to process variables

7. Interfacial Polymerization Technique

Principle :- Polymerization occurs at the interface of two immiscible liquids, forming microspheres.

Procedure :-

1. Drug dissolved in one phase.
2. Monomers added to both phases.
3. Polymerization at interface forms microspheres.
4. Microspheres separated and purified.

Advantages :-

Strong, stable microspheres

Controlled size

Toxic monomers

Not suitable for biological drugs

8. Hot Melt Encapsulation Technique

Principle :- Polymer is melted and mixed with drug, then dispersed into a non-miscible phase and solidified.

Procedure :-

Polymer melted above melting point.

Drug added and mixed.

Dispersion into oil phase.

Cooling leads to microsphere formation. [15]

Advantages :-

Solvent-free

Environment-friendly

Not suitable for heat-sensitive drugs.

VI. Evaluation Parameters of Microspheres

1. Particle Size Analysis (Optical Microscopy Method)

Procedure :-

1. Place a small quantity of microspheres on a clean glass slide.
2. Disperse uniformly using a drop of liquid paraffin.
3. Cover with a cover slip.
4. Measure diameter of at least 100 microspheres using calibrated eyepiece micrometer.
5. Calculate mean particle size. [11]

2. Surface Morphology (SEM Analysis)

Procedure :-

1. Mount dried microspheres on aluminum stubs using double-sided adhesive tape.
2. Coat with gold using sputter coater.
3. Observe under scanning electron microscope.
4. Record images at different magnifications.

3. Percentage Yield

Procedure :-

1. Accurately weigh dried microspheres.
2. Record total weight of drug and polymer used.
3. Calculate percentage yield using formula.

Formula :-

$$\text{Percentage Yield (\%)} = \frac{\text{Theoretical Yield}}{\text{Practical Yield}} \times 100$$

4. Drug Entrapment Efficiency (DEE)

Procedure :-

1. Accurately weigh 10–50 mg of prepared microspheres.
2. Crush the microspheres using a mortar and pestle.
3. Dissolve the crushed powder in a suitable solvent.
4. Sonicate the solution for 15–30 minutes to ensure complete drug extraction.
5. Filter the solution to remove particulate matter.
6. Analyze the filtrate using UV–Visible spectrophotometer or HPLC.
7. Calculate the Drug Entrapment Efficiency (DEE) using the above formula.

Drug Entrapment Efficiency (DEE, %) = $\frac{\text{Amount of drug entrapped in microspheres}}{\text{Total amount of drug added initially}} \times 100$

5. Drug Loading Capacity :-

Procedure :-

1. Determine the drug content of the microspheres using the same method described for Drug Entrapment Efficiency (DEE).
2. Accurately weigh a known quantity of microspheres.
3. Analyze the extracted drug using UV–Visible spectrophotometer or HPLC.
4. Calculate the drug loading capacity using the formula given below.

Formula :-

$$Drug\ Loading\ (\%) = \frac{Weight\ of\ drug\ present\ in\ microspheres}{Total\ weight\ of\ microspheres} \times 100$$

6. Micromeritic Properties :-

Bulk Density :-

1. Pour microspheres into measuring cylinder.
2. Record untapped volume.
3. Calculate bulk density.

Tapped Density :-

1. Tap cylinder 100 times.
2. Record tapped volume.
3. Calculate tapped density.

Derived Parameters :-

Carr's Index

Hausner's Ratio

Angle of Repose

7. Swelling Index

Procedure :-

1. Weigh dried microspheres (W_0).
2. Immerse in swelling medium.
3. Remove at fixed intervals.
4. Blot surface moisture.
5. Weigh swollen microspheres (Wt).
6. Calculate swelling index.

Swelling Index (%)= $\frac{Wt - W0}{} \times 100$

W0

Where:

- W_0 = Initial weight of dried microspheres
- W_t = Weight of swollen microspheres at time t

8. In-Vitro Drug Release Study

Procedure :-

1. Place microspheres equivalent to required drug dose in dissolution apparatus.
2. Use suitable dissolution medium.
3. Maintain temperature at 37 ± 0.5°C.
4. Stir at specified RPM.
5. Withdraw samples at predetermined intervals.
6. Replace with fresh medium.
7. Analyze samples spectrophotometrically. [16]

9. Release Kinetics Study

Procedure :-

1. Obtain cumulative in vitro drug release data (%**)** at predetermined time intervals.
2. Fit the release data into the following kinetic models:
    - **Zero-order model**
    - **First-order model**
    - **Higuchi model**
    - **Korsmeyer–Peppas model**
3. Plot the corresponding graphs for each model.
4. Calculate the regression coefficient (R^2) for each plot.
5. The model showing the highest R^2 value is considered the best-fit release kinetic model. [17–19]

10. FTIR Compatibility Study

Procedure :-

1. Accurately weigh the pure drug, polymer, and drug-loaded microspheres separately.
2. Mix each sample with potassium bromide (KBr) in an appropriate ratio.
3. Compress the mixtures into transparent pellets using a pellet press.
4. Scan the pellets using an FTIR spectrophotometer over a wavelength range of 4000–400 cm^{-1}.
5. Record and compare the spectra of:

- Pure drug
- Polymer
- Drug-loaded microspheres

11. Differential Scanning Calorimetry (DSC)

Procedure

1. Accurately weigh 5–10 mg of the sample (pure drug, polymer, and drug-loaded microspheres).
2. Seal the sample in an aluminum pan using a pan crimper.
3. Use an empty sealed aluminum pan as a reference.
4. Heat the samples at a constant heating rate of 10°C/min under an inert atmosphere (usually nitrogen).
5. Record the DSC thermogram over an appropriate temperature range.

12. X-Ray Diffraction (XRD)

Procedure

1. Place an adequate quantity of microspheres uniformly on the sample holder.
2. Mount the sample in the X-ray diffractometer.
3. Scan the sample over an appropriate 2θ range (commonly 5°–60° or as required).
4. Record the diffraction pattern at a suitable scanning rate.

13. Zeta Potential Measurement

Procedure :-

1. Disperse an appropriate quantity of microspheres in distilled water to obtain a dilute suspension.
2. Sonicate the dispersion briefly to ensure uniform distribution and to break agglomerates.
3. Measure the zeta potential using a zeta potential analyzer at room temperature.

14. Mucoadhesion Study (Wash-Off Method)

Procedure :-

1. Excise suitable mucosal tissue (e.g., buccal or intestinal mucosa) and wash gently with physiological saline.
2. Apply a known quantity of microspheres uniformly onto the mucosal surface.
3. Mount the mucosal tissue on a glass slide using thread or adhesive.
4. Place the slide in a disintegration test apparatus or similar setup containing simulated physiological fluid maintained at 37 ± 0.5 °C.

5. Operate the apparatus at a predetermined speed.
6. At specific time intervals, record the number of microspheres remaining adhered to the mucosal tissue.

15. Stability Studies

Procedure :-

1. Accurately pack the prepared microspheres in suitable, well-closed containers.
2. Store the samples in a stability chamber maintained at specified temperature and relative humidity conditions.
3. Withdraw samples at predetermined time intervals (e.g., 0, 1, 3, and 6 months).
4. Evaluate the samples for:
    - Physical appearance (color, aggregation, flow)
    - Drug content
    - In vitro drug release profile
5. Compare the results with initial values to assess stability. [20]

Storage Conditions

- Long term stability :-
  25°C ± 2°C / 60% ± 5% RH
- Accelerated stability :-

  40°C ± 2°C / 75% ± 5% RH

VII. Conclusion

Topical antifungal therapy remains the preferred approach for the management of superficial and cutaneous fungal infections due to its localized action and reduced systemic side effects. However, conventional topical formulations often suffer from drawbacks such as inadequate drug penetration, short residence time, frequent application, and poor patient compliance. Microsphere-based drug delivery systems have emerged as an advanced and effective strategy to address these limitations. By encapsulating antifungal drugs within biocompatible and biodegradable polymers, microspheres enable sustained and controlled drug release, improved skin retention, enhanced stability, and reduced systemic exposure. The ability of microspheres to act as a drug reservoir at the site of infection significantly improves therapeutic efficacy and minimizes recurrence. Various preparation techniques and evaluation parameters allow optimization of microsphere formulations for topical antifungal applications. Based on the reviewed literature, microsphere-based topical drug delivery systems represent a promising and innovative platform for antifungal therapy. Future research focusing on clinical translation, large-scale manufacturing, and long-term stability studies may

further establish microspheres as a valuable tool in the effective management of antifungal diseases.

[21,22,26]

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