REVIEW ARTICLE

Invasomes: A Novel Transdermal Approach for Antifungal Drug Delivery

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ABSTRACT

Management of fungal infections, for those affecting skin, has faced challenges in poor penetration and efficacy. Traditional topical antifungal therapies often show limited results due to the skin's barrier properties. Invasomes, has emerged as a greater tactic to improve drug penetration through skin, improving penetration and effectiveness of antifungal drugs. This review comprehensively analyzes invasomes as a transdermal drug delivery system specifically for antifungal therapies. It covers structure, composition, and mechanism of action of invasomes, Focusing on their advantages over conformist drug delivery systems. Key factors influencing invasome efficacy, such as the incorporation of phospholipids, ethanol, and terpenes, are discussed in detail. Invasomes significantly improve drug permeation through skin due to their flexible lipid bilayer structure and presence of ethanol and terpenes, which disrupt skin's lipid matrix. Various studies have demonstrated the potential of invasomes in delivering antifungal drugs more effectively than conventional topical formulations. The increased drug bioavailability and improved therapeutic outcomes underscore the utility of invasomes. Invasomes characterize a capable transdermal delivery system for antifungal drugs, offering improved drug permeation, stability, and therapeutic efficacy. Their ability to overcome the skin barrier makes them an alternative to traditional topical formulations.

Keywords: Invasomes, Transdermal drug delivery, Antifungal drug delivery, Vesicular systems, Skin penetration enhancers, Phospholipid-based vesicles, Terpenes in drug delivery.

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INTRODUCTION

Fungi are eukaryotic organisms characterized by membrane-bound organelles and defined nuclei, distinguishing them from plants. Fungi were formerly included in the kingdom of plants, but because they have distinct physiological and structural characteristics and no chlorophyll, they should be placed in their own kingdom. The realm There are about 144,000 species of fungi that are known to exist, including moulds, yeasts, rusts, smuts, mildews, and mushrooms. Even though they resemble fungi, other creatures that resemble fungus, including slime moulds and oomycetes (water moulds), really belong to separate taxonomic groupings.[1]

Fungal infections present with diverse signs and symptoms reliant on type and location of infection. For example, dermatophyte infections like Tinea pedis (athlete's foot) exhibit symptoms such as peeling, cracking, and scaling of feet, along with redness, blistering, or softening of skin, and burning or sweltering sensations. Tinea corporis (ringworm) appears as an itchy, red, ring-shaped patch with scaling. Yeast infections, such as vaginal candidiasis, manifest with itching, swelling around the vagina, burning pain during urination or intercourse, redness, soreness, and abnormal vaginal discharge. Onychomycosis, a fungal infection of the toenails, results in nail discoloration, flaking, and thickening. Tinea versicolor causes lighter or darker patches of skin with dry, itchy, scaly areas, while Tinea cruris (jock itch) presents as a red rash with a circular shape and rough edges in the groin or buttocks area.[2]

Fungal infections are categorized based on virulence into primary and opportunistic pathogens. Primary pathogens cause infections in healthy individuals, typically originating in lungs and potentially spreading to other organ systems. These fungi are inherently virulent and often exhibit dimorphic characteristics, capable of transitioning between yeast and mold forms. Opportunistic pathogens, on the other hand, infect individuals with compromised immune defenses, such as those with AIDS, undergoing immunosuppressive therapy, or experiencing alterations in normal flora due to antibiotics. Examples of opportunistic fungal infections include Candidiasis, Cryptococcosis, and Aspergillosis.[3]

Accurate diagnosis, treatment, and prevention strategies for fungal infections are crucial, particularly for vulnerable patient populations where these infections can lead to severe complications. Further research and clinical studies are necessary to enhance our understanding of fungal pathogenesis and improve therapeutic interventions against these diverse and often challenging pathogens.Fungal infections encompass a broad spectrum of diseases caused by various fungi, each with distinct clinical manifestations and treatment approaches. Candidiasis, primarily instigated by Candida albicans and other Candida species, is most common opportunistic fungal infection. It can manifest as superficial infections

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affecting the skin, mucosal surfaces (such as oral and vaginal candidiasis), and deeper infections involving organs like the kidneys, liver, and brain. Aspergillosis, another significant fungal infection, typically begins in the lungs and paranasal sinuses, potentially disseminating to affect the brain, kidneys, liver, heart, and bones. Respiratory tract injuries are common portals of entry for Aspergillus, though skin injuries can also introduce the fungus into susceptible hosts.[4]

Zygomycosis refers broadly to infections caused by fungi of the Zygomycota phylum. This group includes Mucormycosis, often referred to as 'black fungus,' which is rare but life-threatening, particularly for immunocompromised individuals such as those with diabetes or HIV/AIDS. Mucor mold, found in soil, plants, and decaying organic matter, can infect the sinuses, brain, and lungs. Cryptococcosis primarily affects individuals with compromised immune systems, causing pneumonia and meningitis. Defective cellular immunity, especially in those with AIDS, is a major risk factor for this opportunistic infection. Hyalohyphomycosis, caused by various hyaline hyphal fungi like Fusarium spp., predominantly affects immunocompromised patients. It can lead to severe systemic infections including pneumonia, fungemia, and skin lesions.[5]

The treatment of fungal infections often involves antifungal agents that selectively target fungal pathogens while minimizing toxicity to the host. Polyene antifungal drugs like amphotericin B and nystatin interact with fungal cell membrane sterols, disrupting membrane integrity. Azole antifungal drugs like fluconazole and itraconazole inhibit ergosterol biosynthesis, crucial for fungal membrane function. Allylamine (e.g., terbinafine) and morpholine (e.g., amorolfine) antifungal drugs target different steps in ergosterol biosynthesis, while 5-fluorocytosine is antimetabolite inhibiting DNA and RNA synthesis in fungi.[6]

Transdermal Drug Delivery System (TDDS)

TDDS can escape going through first-pass metabolism. It's also an intrusive technique. TDDS primary drawback is that it slows down the drug's rate of diffusion into the stratum corneum. In terms of structure, this stratum corneum resembles a brick wall and serves as a barrier. Within the intracellular lipid lamellae of the stratum corneum are keratin-rich coenocytes, which function as bricks. The stratum corneum's lipid lamella serves as a barrier. To disturb the stratum corneum, numerous techniques have been introduced. such as iontophoresis, microneedles, and vesicular drug carriers such liposomes, noisomes, transfersomes, ethosomes, flexosomes, vesosomes, and polymerosomes, among other chemical and mechanical techniques.

The ability to incorporate both hydrophilic and lipophilic medicines into liposomal vesicular systems facilitates penetration of incorporated agents. Because of their better ability to penetrate drugs and interact with the skin, novel elastic vesicles—which feature penetration enhancers—outperform conventional liposomes. This development could lead to better results in therapy and satisfaction for patients in a variety of medical applications by increasing the efficacy of drug delivery systems. Numerous scientists have developed novel types of lipid vesicles within the previous 20 years, all of which have advanced the field of drug delivery technology. In the most recent discoveries, scientists have concentrated on studying a brand-new class of vesicular system called invadesomes. With their distinctive qualities and prospective uses in improving therapeutic efficacy and penetration, these cutting-edge vesicles provide a promising new direction in drug delivery research. The investigation of invasive organisms highlights the continuous development and variety of lipid-based vesicular systems, opening the door to more effective medical treatments and pharmacological combinations. Out of all of these techniques, transdermal penetration is better with innovative vesicular carrier systems like invasomes than with traditional liposomes. These vesicles' structural components include phospholipids, ethanol, and terpenes.[7]

TDDS dose forms are made to spread a therapeutically effective dosage of medication throughout the skin of a patient. The FDA authorised Transderm SCOP, the first transdermal device, in 1979 to reduce travel-related nausea and vomiting. The majority of transdermal patches are made to release the active substance into the skin at a zero order rate for a few hours to many days after application. This is particularly beneficial for preventative treatment of long-term illnesses. The patient's clinical reactions to the prescribed medication therapy are all indicators of percutaneous drug absorption.[8]

Advantages of TDDS

TDDS offer some advantages over traditional routes of drug administration, making them increasingly valuable in pharmaceutical applications. Another key benefit is the ability of TDDS to maintain constant blood levels of drugs over an extended period. This sustained release characteristic not only improves patient convenience by reducing the frequency of dosing but also helps in achieving consistent therapeutic outcomes. This controlled release profile also contributes to improved bioavailability, ensuring a greater proportion of the administered drug reaches its target site in the body.

Furthermore, TDDS can lead to a reduction in the total dose required compared to other routes of administration. This is particularly advantageous as it can minimize the potential for side effects and unwanted reactions associated with higher drug concentrations. Moreover, by delivering drugs directly through the skin, TDDS can circumvent gastrointestinal side effects, which are common with oral medications.

An additional advantage of TDDS is its ease of discontinuation in cases where toxic effects or adverse reactions occur. Unlike orally administered drugs that are absorbed and distributed systemically, transdermally delivered drugs can be promptly removed by discontinuing the patch or system, offering a rapid response to adverse events.[9]

Disadvantages of TDDS

TDDS offer distinct advantages, but they also come with limitations that must be considered in their application and development. One significant disadvantage is the

relatively high cost associated with developing and manufacturing transdermal patches or systems compared to conventional oral medications or simple topical formulations. The complex technology involved in ensuring controlled release and skin permeation adds to production expenses, which can limit widespread accessibility and affordability.

Another limitation of TDDS is their inability to effectively deliver ionic drugs. Transdermal delivery relies on the drug being able to penetrate the skin barrier, which is challenging for drugs that are ionized in physiological conditions. Since ions have difficulty crossing biological membranes, TDDS cannot deliver these types of drugs efficiently, restricting their applicability.

When contrasted with alternative delivery methods, including intravenous injection, TDDS may also have difficulty reaching high plasma or blood medication levels. While transdermal delivery provides sustained release over time, it may not achieve rapid or high peak concentrations of drugs in the bloodstream, which are sometimes necessary for acute treatment scenarios.

Another practical limitation is the inability of TDDS to accommodate drugs with large molecular sizes. Large molecules may not penetrate the skin barrier effectively, thereby limiting the feasibility of developing transdermal formulations for these drugs.

Furthermore, TDDS are unable to deliver drugs in a pulsatile manner, which is required for certain therapeutic applications that demand precise timing and dosage intervals. The continuous release nature of transdermal patches or systems may not be suitable for treatments that require periodic, fluctuating drug delivery patterns.

Lastly, the development of TDDS can be hindered if the drug or formulation causes irritation or allergic reactions on the skin. Skin irritation can affect patient compliance and comfort, potentially leading to discontinuation of treatment or adverse events.[10]

Various Methods for Preparation TDDS

Mercury Substrate Method

The medication and plasticiser are dissolved in a polymer solution in this process. To make sure the solvent doesn't evaporate too quickly, swirl the mixture for 10–15 minutes until it's completely mixed. Then, pour it onto a levelled surface of mercury and cover it with an inverted funnel.

By using IPM Membranes Method

A magnetic stirrer is used to agitate a solution of water and propylene glycol containing carbomer 940 polymer for 12 hours in order to disseminate the medication. Triethanolamine is to be added to the mixture in order to neutralise it and make it thicker. If the drug's solubility in water is low, solution gel can be prepared using a buffer with a pH of 7.4. Incorporating the gel into the IPM membrane is the plan.

Asymmetric TPX Membrane Method

The backing membrane for the prototype patch can be a 3m length of heat sealable polyester film (type 1009) with a concave diameter of 1 cm. The concave membrane is used to dispense the drug sample, followed by an asymmetric TPX poly (4-methyl-1-pentene) membrane and an adhesive sealant.

By using EVAC Membranes Method

The target transdermal treatment system can be prepared using rate control membranes made of ethylene vinyl acetate copolymer (EVAC) or polyethylene (PE) and 1% carbopol reservoir gel. A gel can be prepared using propylene glycol if the medicine is insoluble in water. A 5% w/w sodium hydroxide solution will be used to neutralise the carbopol resin before adding it to the drug-dissolved propylene glycol solution. The medication, which is in the form of a gel, is applied to the designated location by means of a backing layer. To create a watertight seal, we'll place a rate-controlling membrane over the gel and then use heat to seal the edges.

By using Free Film Method

The process of casting cellulose acetate onto a mercury surface produces a free film. The purpose of employing chloroform is to create a 2% w/w polymer solution. The specified amount of plasticisers to be added is 40% by weight of polymer. Over the surface of the mercury in a glass petri dish, five millilitres of polymer solution was poured into a glass ring. By positioning an inverted funnel on the Petri dish, one may regulate the pace at which the solvent evaporates.

Simple Method of Preparing Transdermal Patches

By making small adjustments to the previously described procedures, the process of preparing TDDS was summarised. The solvent casting procedure was used to prepare the patches. A beaker containing the polymer (e.g., PVP/HPMC) and a little amount of solvent was used. After that, the additional polymers (such PVA) were combined with two thirds of the solvent and added while stirring at low rpm at first, and then at increasing speed. Following the addition and thorough mixing of the plasticiser, the medicine was added with continuous stirring, and the volume was adjusted to the desired level. The films were placed into a glass mould that had been appropriately developed and made, and then they were dried in an oven set at 400C. A sharp blade was inserted along the film's edges to remove the films. The films that had dried were placed in an airtight container, protected from light and kept in a cool, dark area, and wrapped in butter paper.

Evaluation or Characterization of TDDS

To increase the medicine's therapeutic efficacy, transdermal drug delivery methods have been created. Patches, on the other hand, increase patient compliance by administering a smaller, longer-lasting dose of the drug at a predetermined rate.

Physical Appearance

Colour, transparency, opacity, clarity, smoothness, and flexibility were all evaluated visually for each of the developed patches.

Thickness of Patch

To determine thickness of formulated patches, various points on each patch were measured using digital micrometers, micrometer screw gauges, traveling microscopes, or vernier calipers.

Weight Uniformity

The created patches were dried at 60°C for four hours before the weight uniformity test was run. The test was

conducted by dividing each patch into its component pieces and then weighing each part using a digital scale.

Folding Endurance

A small section of the patch is uniformly sliced and then folded repeatedly in the same spot until it snaps. Before the patch breaks, its number of folds is recorded. Folding abidance will be provided by it.

Percentage Moisture Loss

Each of the prepared patches is given a weight before being left at room temperature for 24 hours in desiccators with anhydrous calcium chloride. The patches are weighed at regular intervals after the first 24 hours until a steady weight is achieved.

Percentage Moisture Uptake

Each patch that has been prepared is carefully weighed and stored in a desiccator that has saturated potassium chloride or ammonium chloride. We keep the relative humidity at 84%. A steady weight is achieved by reweighing the patches at certain intervals after 24 hours.

Water Vapor Permeability Evaluation (WVP)

It is resolute by natural air circulation.

Drug Content Analysis

The formulated patches are carefully weighed and added to a solvent that can dissolve the drug effectively. This mixture is then subjected to continuous shaking for a duration of 24 hours using a shaker incubator. Subsequently, the solution undergoes sonication to ensure proper mixing, followed by filtration to remove any impurities.

Percentage Elongation Break Test

The length of the patch immediately preceding the break point is used to determine it.

Flatness

A medication transdermal patch should have a smooth, non-constricting surface area. An examination for flatness can be conducted on it. One strip is cut in the middle, and two strips are cut on either side, for this test. We measure the length of every single strip. Percentage constriction is used to measure the difference in length. When the proportion of constriction is 0, it means that there is complete flatness.

$$\%\, construction = \frac{(initial\ length - final\ length)}{initial\ length}\ x\ 100$$

Thumb Tack Test

To find out how sticky an adhesive is, it's one of the qualitative tests used. Finding the relative tack property is as easy as pressing the thumb over the adhesive layer.

Rolling Ball Tack Test

Stainless steel balls are tested by tracking their distance along an upward-facing adhesive. A less sticky adhesive membrane will be indicated by a rolling ball that is travelling forward.

Quick Stick (Peel Tack) Test

This device measures the amount of force needed to separate the adhesive layer from the stainless steel plate by pulling the tape (the adhesive layer) away from the plate at a pace of 12 inches per minute.

Probe Tack Test

There is a constant rate of reduction in the measured force needed to remove the probe from the glue. The unit of measurement is grammes.

Peel Adhesion Properties

For various substrates, the force needed to peel the adhesive film off is referred to as peel adhesion. This test determines the amount of force needed to pull a single-coated tape. At 180 degrees Celsius, the coating must be applied to the substrate.

Skin Irritation Test

Rabbits in good health are used for skin penetration and sensitisation testing. Carefully applying the prepared patches to the dorsal surface of rabbits' skin is the recommended method of administration. The rabbits' fur is plucked out before the patch is fastened. Careful monitoring and evaluation of the skin for symptoms of irritation or adverse responses is carried out after a 24-hour period.

In vitro release studies

In vitro evaluations of transdermal patches can be conducted using the Franz diffusion cell model, which consists of a donor and a receptor compartment. There is an effective surface area of 1–5 cm2 and a volume of 5–12 ml in the receptor compartment. A magnetic bar is used to continuously stir the diffusion buffer at 600 rpm. A water jacket encircling the receptor compartment circulates thermostated water to keep the bulk of the solution at a constant temperature. It is crucial to maintain the sink state while analysing the drug content using the appropriate procedure.

In vivo Studies

In vivo evaluations of transdermal patches might be conducted according to The actual picture of the drug's efficacy is shown by in vivo studies. While in vitro studies can only account for some factors, in vivo investigations allow researchers to examine all relevant variables. The in vivo assessment of TDDS can be accomplished through the utilisation of animal models and human volunteers.[11]

Application of TDDS

TDDS have found diverse applications across various therapeutic areas, offering convenient and effective alternatives to traditional routes of drug administration. One prominent example is the nicotine patch, widely used for smoking cessation. Approved as a vapor patch in 2007, it delivers nicotine through the skin, helping individuals reduce their dependence on tobacco without the need for frequent dosing or inhalation, thereby supporting smoking cessation efforts effectively.

Hormonal applications of TDDS include estrogen patches used to alleviate menopausal symptoms such as hot flashes and vaginal dryness. These patches provide a controlled release of estrogen through the skin, maintaining stable hormone levels in the body. Additionally, contraceptive patches like Ortho Evra or Evra offer a convenient option for birth control, delivering hormones transdermally to prevent pregnancy.

Scopolamine patches are another notable application of TDDS, primarily used to manage motion sickness. By delivering scopolamine through the skin, these patches provide sustained relief from nausea and vomiting associated with motion sickness, making them particularly beneficial for travelers and individuals prone to seasickness.

In the treatment of angina, nitroglycerin patches are employed to alleviate chest pain by delivering nitroglycerin directly through the skin into the bloodstream. This controlled delivery helps maintain stable blood levels of the drug, effectively dilating blood vessels and improving blood flow to the heart muscle, thereby reducing angina symptoms.

For patients with Alzheimer's disease, the Exelon patch is utilized to administer rivastigmine, a medication that helps improve cognitive function and manage symptoms associated with the condition. The patch provides continuous delivery of rivastigmine, offering a consistent therapeutic effect and potentially enhancing patient compliance with treatment regimens.

In conclusion, transdermal drug delivery systems have revolutionized the way medications are administered, offering benefits such as controlled release, enhanced patient compliance, and reduced systemic side effects. Applications highlighted, from smoking cessation to hormonal therapy and motion sickness management, underscore the versatility and efficacy of TDDS in modern pharmacotherapy.[12]

Invasomes

It was determined whether vesicular systems such as traditional liposomes or newer vesicular carriers such as niosomes, transferosomes, ethosomes, invasomes, fexosomes, vesosomes, ufasomes, polymerosomes, etc., were suitable for transdermal drug administration. Liposomes that have been traditionally used for transdermal drug administration have a low penetration power and can only reach the outer dermal layers. As a result, their therapeutic effects are limited to the outer dermal layers. To improve medication permeability, new vesicular systems with the right amount of flexibility were created. These new vesicular systems improve skin permeation by including a penetration enhancer in their formulation. It was found that niosomes, which are elastic vesicular carriers made from a mix of cholesterol and nonionic surfactants, might be used for transdermal medication administration. Using phospholipids, alcohol (ethanol and isopropyl alcohol), and water, vesicular structures called ethosomes are created. When compared to traditional liposomes, their transdermal penetration is significantly faster and more pronounced. Phospholipids (phosphatidylcholine) and an edge activator (polysorbate or sodium cholate) make up transferosomes, which are elastic vesicular drug transporters (Figure 1).

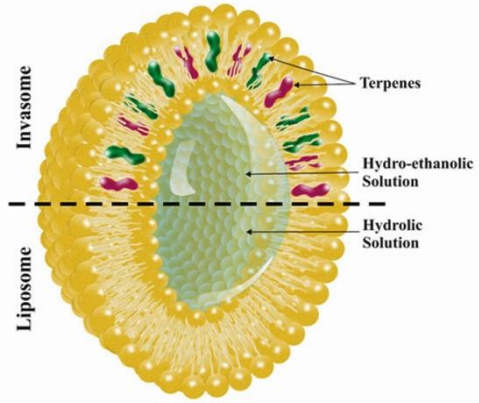

Figure 1: Invasome versus liposome

Improving the transdermal penetration of active pharmacological chemicals is being facilitated by a novel family of vesicles known as Invasomes. Within these vesicles, you can find a combination of ethanol, phospholipids, and terpenes. These components had great transdermal penetration properties.[13]

Composition

Phospholipids

The alcohol is linked to hydrophobic acyl chains in phospholipids, which are water-loving. A wide variety of phospholipids were able to endure because of variations in head groups, aliphatic chains, and alcohols. Consequently, the phospholipid classes gain from the modified phospholipid sources. A wide range of formulations incorporate phospholipids, both natural and synthetic, including PEGylated Phospholipids. Skin care products are no exception. A method for creating nanovesicles has even been proposed using hydrogenated phosphatidylcholine.

Ethanol

Using ethanol can increase permeability. The zeta potential, entrapment efficacy, skin permeability, and specific size of vesicles play a significant role in nano-vascular systems. Multiple investigations have shown that vesicle size and entrapment efficacy are negatively correlated with increasing ethanol concentration. Membrane thickness and, by extension, vesicular volume, are both decreased by increasing ethanol concentrations. Ether reduces the average size of vesicles by penetrating hydrocarbon chains and altering their net charge. Additionally, nanovesicles can have their fluidity enhanced by ethanol. Ethanol causes SC lipids to break because it disturbs their densely packed structure. Lipid transition temperatures can be lowered by ethanol due to its effects on keratinise or lipophilic domain structures.

Terpenes

In transdermal drug administration systems, terpenes or terpene combinations at extremely low dosages have also been demonstrated to be penetration enhancers, sorption boosters, or accelerants, enabling the drugs to pass through the skin and decrease resistance. The solubility of terpenes, the hydrolysis of lipid and protein layers, and the micro-ingredient loss in the skin all play a role in their ability to penetrate the skin.[14]

Advantages of Invasomes

Invasomes represent an innovative approach to drug delivery that offers several distinct advantages, making them promising candidates in pharmaceutical applications. One of the primary advantages of invasomes is their non-invasive nature, which means they do not require invasive procedures like injections or surgeries. Instead, they deliver drugs through the skin, providing a convenient and patient-friendly alternate to traditional routes of administration.

Enhancing medication penetration through the skin for transdermal distribution is a significant property of invasomes. They are able to accomplish this by interacting with the epidermal barrier and facilitating the entry of

hydrophilic and lipophilic medicines, thanks to their particular lipid composition and structure. Because of this feature, invasomes are able to administer a wider variety of medications, increasing their versatility in pharmaceutical compositions.

Invasomes are formulated using non-toxic raw materials, ensuring safety for use in drug delivery applications. This characteristic is crucial for minimizing adverse effects and ensuring patient safety during treatment.

Furthermore, the administration of drugs via invasomes is typically in the form of semisolid preparations such as gels or creams. This formulation allows for easy application and ensures patient compliance, as it is familiar and convenient for users. The semisolid nature also facilitates controlled release and absorption of drug into skin, contributing to consistent therapeutic outcomes.

Compared to other advanced transdermal delivery methods like iontophoresis and phonophoresis, invasomes offer a simpler and straightforward approach. They do not require complex equipment or specialized training, making them more accessible and cost-effective for drug delivery applications.[15]

Penetration Mechanism of Invasomes

The presence of terpenes and ethanol in invasomes makes them more permeable by making the vesicles more malleable, which in turn disrupts the skeleton of the SC bilayer. In order to facilitate invasome penetration and fluidisation of SC lipids, terpenes, phospholipid segments, and individual phospholipid molecules are released when a portion of the vesicle breaks down, as reported by Dragicevic-Curic et al. The SC is unharmed by smaller invasome vesicles because they do not break down. The intact invasomes may be able to penetrate the SC and reach its inner portions through the follicular transport pathway or the thin hydrophilic channels found in the intercellular region. A study demonstrated that smaller invasomes, while intact, are able to access the deeper regions of the SC via the sections that resemble channels (Figure 2).

Mechanical Dispersion Method

An ethanolic phospholipid solution is prepared by dissolving the drug and terpene, or terpene combinations. To achieve a transparent solution, the mixture is vortexed for 5 minutes and then subjected to sonication for 5 minutes. The solution is continuously mixed with phosphate buffer saline (PBS) through syringe, maintaining a pH of 7.4. Final invasomal preparation is achieved by continuing the vortexing for a further 5 minutes (Figure 3).

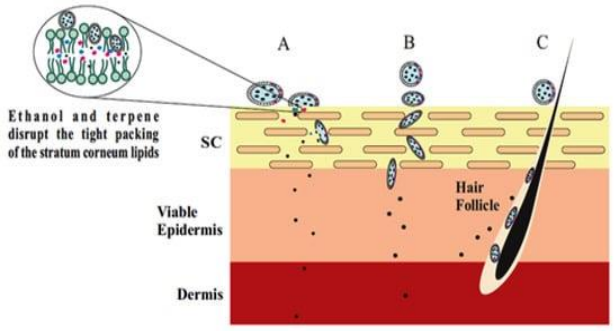

Figure 2: Penetration mechanism of invasomes through the stratum corneum (SC). (A) Enhanced penetration, (B) Intact penetration and (C) Trans-appendageal penetration

Thin Film Hydration Method

The traditional film process is another option for preparing invasomes. In a ratio of 2:1 (volume/volume), methanol and chloroform dissolve phospholipids in ethanol. The rotating flash evaporator is used to gradually lower the pressure from 500 to 1 mbar at 50°C, drying the mixture to a thin film (Figure 4).[16]

Characterization of Invasomes

Entrapment Efficiency

The efficiency of entrapment was investigated using the ultracentrifugation technique. In two cycles, 1 ml of the invasomal formulation was spun at 15,000 rpm at 4°C for 15 minutes in Eppendorf tubes in order to extract the free drug. To find the amount of free medication, the transparent fraction was utilised. The amount of free drug from the formula is used to indirectly compute the percentage entrapped.

$$\text{Entrapment Efficiency (\%)} = \frac{\text{total drug} - \text{free drug}}{\text{total drug}} \times 100$$

Surface Morphology

The procedure involved applying a small amount of the preparation on a transparent glass slide, letting it air dry, and then coating it with gold using a sputter coater (Polaron E5100, Watford, UK). SEM images were then taken to examine the results. Analyses of Stability A 10-milliliter glass vial containing the optimised intravenous formulation was either in a refrigerator (between 4 and 8 degrees Celsius) or left at room temperature for a month. At regular periods, we measured entrapment efficiency

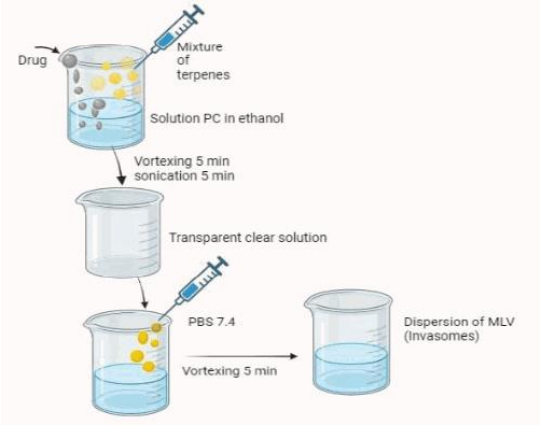

Figure 3: Mechanical dispersion method

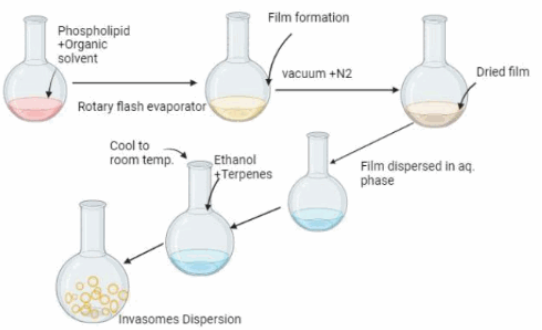

Figure 4: Film hydration method

and physical appearance.[17]

Drug Content

A UV spectrophotometer can be used to find out how much drug is in the invasomes. One way to measure this is using a modified HPLC technique.

Vesicular Size and Shape

Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) are two methods that can be used to visualise invasomes. Photon correlation spectroscopy and Dynamic Light Scattering (DLS) can measure the invasomes' vesicles and zeta potential particles.[18]

Applications

Anticancer Drug Delivery

For postmenopausal women battling breast cancer, there is some indication that invasomes can improve the skin deposition property of anastrozole to reduce the difficulty of taking the active ingredient orally. Breast cancer treatment in postmenopausal women using anastrozole invasomal gel can thus pave the road.[19]

Treatment of Erectile Dysfunction

In ex vivo permeation testing, the optimised AVA invasomal film performed better than the raw AVA invasomal film, with an enhancement factor of 2.514 on excised abdominal Wistar rat skin. The invasome had a bioavailability that was more than four times higher than the raw film containing avanafil. These results suggest that medication-loaded invasomal transdermal film may be an effective alternative to oral drug absorption in cases when the drug has low water solubility or significant pre-systemic metabolism. The invasomal formulation of avanafil can thereby enhance its skin penetration and absorption. This allows for novel drug administration strategies for erectile dysfunction treatment.[20]

CONCLUSION

Antifungal drugs are commonly used in treatment to target fungal diseases in a safe and effective manner. The transdermal drug delivery systems (TDDS) are individual dose containers that, when placed on healthy skin, slowly release their contents into the bloodstream. TDDS have several benefits over conventional drug delivery systems, including the ability to circumvent the liver's first-pass metabolism, keep blood levels stable, decrease the overall dosage needed, and lessen the likelihood of side effects. But TDDS has its limits, like expensive prices, trouble distributing ionic medications, and not being able to handle pharmaceuticals with big molecular sizes. You can prepare TDDS in a number of ways, and each has its own set of pros and cons. The goal of developing transdermal drug delivery systems (TDDS) was to increase the medicine's clinical effectiveness and patient compliance by the controlled release of a lesser dose of medication over an extended period of time. The development of these systems involves solvent casting, which involves mixing polymers with plasticiser, adding the medication, and then continuing to agitate the mixture. A number of tests are used to assess the outward appearance of TDDS, such as colour, transparency, clarity, opacity, smoothness, and flexibility. The manufactured patches are dissolved in a solution that allows for drug content analysis. Tests for skin irritation are carried out on rabbits that are in good health. Animal models and human volunteers can be used for in vivo investigations, while Franz diffusion cell cells can be used for in vitro release experiments.Pharmaceutical companies have created many vesicular systems, including niosomes, transferosomes, ethosomes, invasomes, fexosomes, vesosomes, ufasomes, and polymerosomes, to facilitate transdermal drug administration. The non-invasive, safe, and convenient character of invasomes makes them an attractive medication delivery method. They could be used to treat erectile dysfunction, increase the bioavailability of antifungal medications, and improve the penetration of skin for cancer therapy delivery. Improving invasome formulations, increasing their clinical use, and learning more about their function in drug delivery should be the goals of future studies.

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