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Fighting Fungal Nail Infections: Transdermal Patches for Onychomycosis

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ABSTRACT :-
Onychomycosis, with prevalence of approximately 50% of the world population, has generated increased interest due to effective therapy such as terbinafine and ciclopirox. It is dominated by the presence of dermatophytes, most commonly by T. rubrum, involving nail brittleness, distortion, and discoloration. Issues involving drug solubility and poor compliance with itraconazole make traditional treatments challenging. This report undertakes the formulation of itraconazole incorporated polymeric nanoparticles with Eudragit RL100 using a solvent displacement technique to enhance percutaneous drug delivery via the nail. It explains the preparation process of the nanoparticles, focusing more on their better properties of being more reactive and stable. The application of transdermal patches would hence produce a controlled drug delivery system to allow the elimination of side effects encountered in the gastrointestinal tract, thus contributing to higher patient compliance rates. The findings indicate that nanoparticle-enhanced transdermal systems hold much promise in onychomycosis management, potentially overcoming the limitations of conventional therapies.
As a member of the triazole class of antifungals, itraconazole works by inhibiting the synthesis of ergosterol, a critical component of fungal cell membranes, thereby disrupting fungal growth. Standard treatment regimens often involve a pulse therapy approach or continuous daily dosing, with treatment duration typically extending from 6 to 12 weeks depending on the severity and type of onychomycosis.
Keywords:- Antifungal, Candidiasis, Aspergillosis, Histoplasmosis, Blastomycosis, Onychomycosis (fungal nail infection).

I. INTRODUCTION

Onychomycosis was n't regarded as a serious infection until relatively lately. It started gaining at pressure after the approbation of terbinafine for oral cure by the US Food and Drug Administration in 1996. This was succeeded by approbation of ciclopirox for topical cure in 1999[1]. It prevails among around 5 of the total world population and affects toe- nails much more than cutlet- nails[2]. substantially it's caused by dermatophytes, which belong to one of the three rubrics(Trichophyton, Epidermophyton, and Microsporum), with T. rubrum being the most current of all[3]. Physical instantiations include fineness of nails, deformation of nail structure and discoloration[4].

Varioustypes of onychomycosis infections are given in Fig.(2)

Nanoparticles are patches with one or further confines that range in size from 1 to 100nm. In the nanometric scale, nanoparticles are divided into organic, inorganic, and carbon- grounded patches, which have better characteristics than bigger sizes of separate materials. Because of their bitsy size, nanoparticles have bettered features similar as strong reactivity, strength, face area, perceptivity, stability, and so on. For exploration and marketable purposes, nanoparticles are synthesised using a variety of ways that are divided into three orders physical, chemical, and mechanical processes, all of which have witnessed significant advancements over time[5].

Generally, these ways involve applying topical formulations after cure to enhance saturation. The mechanical cure involves complete nail avulsion or nail bruise with filing the affected part of the nail. The physical treatment modalities include high-end ways like iontophoresis, phonophoresis, photodynamic cure or ray therapy[6].

Transdermal patches

A transdermal patch is used to deliver a specific cure of medication through the skin and into bloodstream. Transdermal patches products were first approved in 1981 by FDA. Transdermal delivery systems are presently available containing scopolamine(hyoscine) for stir sickness, clonidine and nitro- glycerine for cardiovascular condition, fentanyl for habitual pain, nicotine to prop smoking cessation. Transdermal delivery provides controlled, constant administration of the drug, and allows nonstop input of drugs with short natural

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half- lives and eliminates palpitated entry into systemic rotation. TDDS offers numerous advantages over conventional injection and oral methods. It reduces the load that the oral route generally places on the digestive tract and liver. It enhances patient compliance and minimizes dangerous side effects of a medicine caused from temporary overdose. It's accessible, especially notable in patches which bear only formerly daily application. Such a simple dosing authority aids in patient adherence to drug antidote. [7]

• Ancient Origins Beforehand topical therapies date back to ancient Egypt and Babylon, using plant, animal, or mineral excerpts.

• 20th Century Development The concept of transdermal delivery evolved significantly, with the first FDA- approved patch for scopolamine in 1979.

• ultramodern Innovations Advances include microneedle patches and active delivery systems, enhancing the range and effectiveness of transdermal drug delivery.

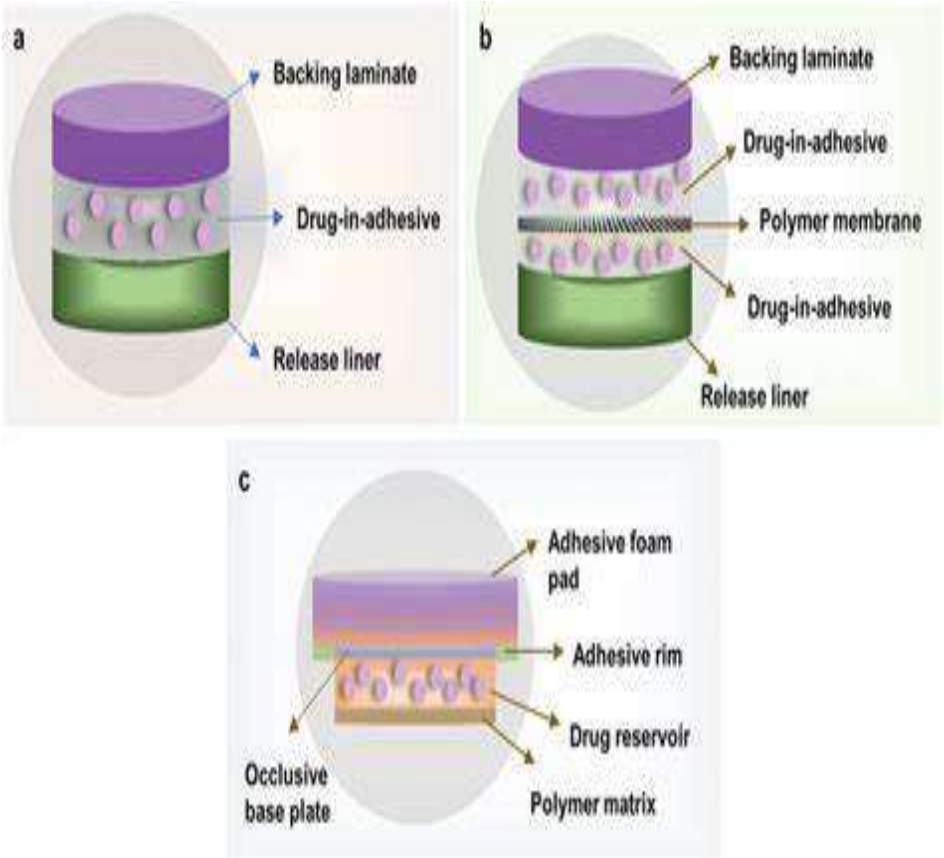

Fig. (1):- Transdermal Patch

BIOPHARMACEUTICAL PARAMETERS IN DRUG SELECTION FOR TRANSDERMAL PATCH[8]

1. Dose should be low i.e.<20mg/day.
2. Half-life should be 10 h or less.
3. Molecular weight should be <400.
4. Partition coefficient should be Log P(octanol-water) between 1.0 and 4.
5. Skin permeability coefficient should be <0.5 $X10^{-3}$cm/h.
6. Drug should be non-irritating and non-sensitizing to the skin.
7. Oral bioavailability should be low.
8. Therapeutic index should be low.

PRINCIPLES OF TRANSDERMAL PERMEATION-[9]

Earlier skin was considered as an impermeable defensive hedge, but latterly investigati- ons were carried out which proved the mileage of skin as a route for systemic administration. Skin is the most ferocious and readily accessible organ of the body as only a bit of

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millimeter of tissue separates its face from the underpinning capillary network.

The various way involved in transport of drug from patch to systemic rotation are as follows

1. Diffusion of drug from medicine reservoir to the rate controlling membrane.
2. Diffusion of drug from rate limiting membrane to stratum corneum.
3. Sorption by stratum corneum and penetration through feasible epidermis.
4. Uptake of drug by capillary network in the dermal papillary subcaste.
5. Effect on target organ.

Different transdermal patches are designed grounded on how the drug result deploys-

Transdermal results can come in a liquid, gel, or formed solid form. Choosing a type of transdermal patch revolves around the most effective skin transmission and the manufacturing feasibility.

At least six types of transdermal patches are available for different manufacturing and delivery methods. opting a type of patch to manufacture depends on the nature of your product set- up and the delivery conditions of your drug result. [10]

SINGLE- LAYER DRUG IN ADHESIVE PATCH-

The tenacious subcaste of this system contains the medicine. In this type of patch the tenacious subcaste not only serves to cleave the colorful layers together, along with the entire system to the skin, but is also responsible for the releasing of the medicine. The tenacious subcaste is girdled by a temporary liner and a backing.

MULTILAYER DRUG IN ADHESIVE PATCH-

1. Multilayer transdermal patches are analogous to the single- subcaste system in that tenacious layers release the drug, except BOTH tenacious layers contain drugs.
2. Typically, multilayer transdermal bonds emplace results over a longer period of time because the range of the layers determines how snappily the drug reaches the skin.

RESERVOIR PATCH-

1. Transdermal budgets are liquid layers containing the medicines which are gradationally delivered to the skin through a rate- controlling membrane.
2. These reservoir patches allow for further controlled delivery rates, but the original medicine release can come in a slight burst. In addition, if the membrane is damaged, there's a threat of unforeseen release in the skin.

MATRIX PATCH-

1. A transdermal matrix patch includes an tenacious polymer matrix containing the medicine, which is gradationally released into the skin.
2. Unlike the rate- controlling membrane in a force patch, the expression of its medicine and polymer matrix dictates the rate of medicine delivery. The active component is distributed unevenly throughout the patch, so there's lower threat of accidental release.

MICRONEEDLE PATCH-

Microneedle patches are transdermal patches with bitsy needles that access the epidermis deep enough to help medicines enter the bloodstream. [11]

Advantages-

1. It's accessible system and requires only formerly daily operation. Such a simple dosing authority can prop in patient adherence to medicine remedy.
2. Transdermal medicine delivery can be used as an indispensable route of administration to accommodate cases who cannot tolerate oral lozenge forms.
3. It's of great advantage in cases who are revolted or unconscious.
4. medicines that beget gastrointestinal derangement can be good campaigners for transdermal delivery because this system avoids direct effects on the stomach and intestine.
5. Drugs that are degraded by the enzymes and acids in the gastrointestinal system may also be good targets.
6. First pass metabolism, an fresh limitation to oral medicine delivery, can be avoided with transdermal administration.
7. Drugs that bear fairly harmonious tube situations are veritably good campaigners for transdermal medicine delivery.

Disadvantages-

1. Possibility of original vexation at the point of operation.

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2. Erythema, itching, and original edema can be caused by the medicine, the adhesive, or other excipients in the patch expression.
3. May beget antipathetic responses.
4. A molecular weight lower than 500 Da is essential.
5. Sufficient waterless and lipid solubility, a log P(octanol/ water) between 1 and 3 is needed for percolate to transverse SC and underpinning waterless layers.[12]

Onychomycosis (fungal nail infection)

Onychomycosis, also known as tinea unguium, is a common fungal infection that affects the nails, causing abrasion, thickening, and fineness. It occurs when fungi, generally dermatophytes, incentive, or earth, infect the nail plate, nail bed, or girding tissue. Onychomycosis can affect both fingernails and toenails, but it's more common in toenails due to the warm, wettish terrain of shoes and socks.However, onychomycosis can lead to nail damage, pain, If left undressed. Treatment options range from topical creams and oral specifics like itraconazole, to ray remedy and surgical junking of the affected nail.

Onychomycosis, or fungal nail infection, is primarily caused by colorful types of fungi, including dermatophytes, provocations, and non-dermatophyte molds.

Then are some common causes and threat factors

1. **Dermatophytes:** These fungi are the most common cause and thrive in warm, wettish surroundings. They can infect the skin and nails, leading to conditions like athlete's bottom, which can spread to the nails.
2. **Yeasts**: Candida species can also beget nail infections, particularly in people who constantly immerse their hands in water.
3. **Non-dermatophytemolds**: These are less common but can still beget nail infections, especially in people with compromised vulnerable systems.

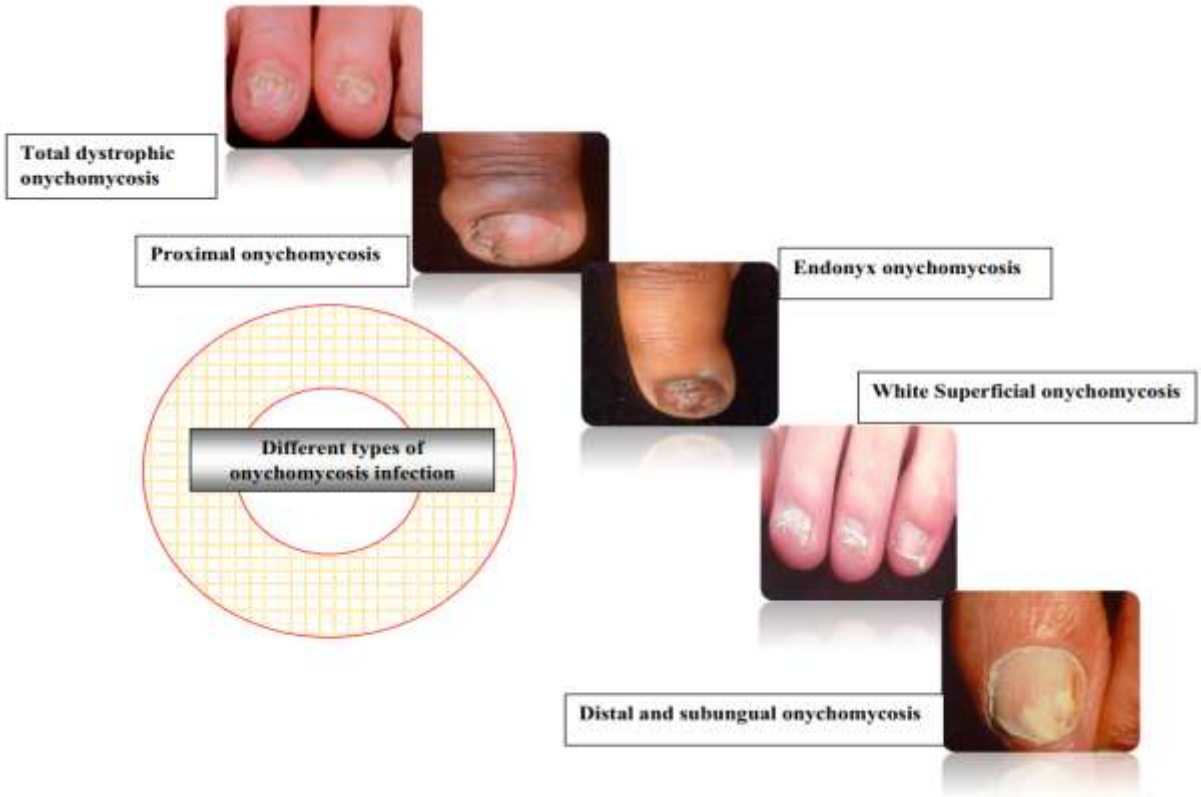

Fig. (2):- Various types of onychomycosis

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Threat factors:-

Factors that can increase your threat of developing nail fungus include

• Aged age
• Wearing shoes that make your bases sweat heavily
• Having had athlete's bottom in the once
• Having a minor skin or nail injury
• Having a skin condition that affects the nails, similar as psoriasis
• Having diabetes, blood inflow problems or a weakened vulnerable system

Symptoms:-

Symptoms of nail fungus include a nail or nails that are

• Thickened
• Discoloured
• Brittle, crispy or ragged
• monstrous
• Separated from the nail bed

Prevention:-

The following habits can help nail fungus or reinfections and athlete's bottom, which can lead to nail fungus

• Keep your nails clean and dry. Wash your hands and bases regularly. Wash your hands after touching an infected nail. Dry well, apply an antifungal bottom greasepaint and moisturize your nails. Consider applying a nail hardener, which might help strengthen nails and cuticles.
• Wear spongy socks or change your socks throughout the day.
• Discard old shoes or treat them with detergents or antifungal maquillages.
• Wear footwear in pool areas and locker apartments.
• Choose a nail salon that uses castrated manicure tools for each client. Or disinfect tools you use for home pedicures.
• Give up nail polish and artificial nails.
• If you have athlete's bottom, treat it with an antifungal product.

Diagnosis:-

Your health care provider will examine your nails and maybe take some nail parings or scrape debris from under your nail. These samples are transferred to a lab to identify the cause of your symptoms.

Other conditions, similar as psoriasis, can mimic a fungal infection of the nail. Microorganisms similar as incentive and bacteria also can infect nails. Knowing the cause of your infection helps determine the stylish treatment.

Treatment:-

Treatment for toenail fungus is not always demanded. And occasionally tone- care and nonprescription products clear up the infection. Talk with your health care provider if your condition does not ameliorate. Treatment depends on the inflexibility of your condition and the type of fungus causing it. It can take months to see results. And indeed if your nail condition improves, repeat infections are common.

Literature Survey

- **Laxman Subedi 2021:-** Lists the chemicals and reagents used, including itraconazole (ITZ), solvents, and other components. Describes the use of female BALB/c mice for in vivo studies, including housing conditions and ethical approval. Details the preparation of ITZ formulations, including solubility tests and the incorporation of various agents to enhance stability and permeability. Explains the methods for testing ITZ permeability, deposition in human skin and nails, and antifungal efficacy using both in vitro and in vivo models[13].**(**Laxman Subedi et. al. 2021**)**

- **Rupinder K.Dhamoon2019:-** Onychomycosis is a persistent fungal nail infection, primarily caused by dermatophytes, affecting around 5% of the global population. Oral antifungal agents are effective but have side effects like hepatotoxicity. Topical treatments are safer but struggle with nail penetration. Recent research focuses on nanoparticles, microemulsions, polymeric films, and nail lacquers to enhance drug permeation and localized therapy. The rigid nail barrier and high relapse rates make treatment difficult, necessitating innovative approaches for better patient compliance and efficacy[14.]

(Rupinder K. Dhamoon et.al.2019)

- **Kamal Kumar 2023:-**Clotrimazole, Eudragit RL100, Liquid paraffin, white soft paraffin, methanol, HPMC, PEG 400, and other analytical grade chemicals**.** Preparation of Nanoparticles Clotrimazole nanoparticles were created using the solvent displacement approach with Eudragit RL100 and PVA as a stabilizer. Parameters like particle size, drug content, and entrapment efficiency were

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measured using various techniques. Nanoparticles were incorporated into a transdermal patch using HPMC and PVP, followed by evaluation of thickness, tensile strength, and drug release[15]. (Kamal Kumar et.al. 2023)

- **Gamal Osman Elhassan 2022**:-Materials**:** Itraconazole (ITZ), Carbopol 934, Polyethylene glycol (PG), Eudragit, Carboxy methyl cellulose (CMC), Triethanolamine, Methyl Paraben, Glutaraldehyde, Dichloromethane, and surfactants were used. Preparation of ITZ Emulgel Carbopol 934 was mixed with distilled water and stirred to make a gel. Triethanolamine was used to neutralize the dispersion, and the pH was adjusted to 6.5. The emulsion was prepared by heating span 20 in liquid paraffin and mixing it with ITZ dissolved in ethanol. Preparation of Release Liner Layer Evaluation parameters the formulations were evaluated for consistency, homogeneity, colour, phase, separation, pH, viscosity, spread-ability, Hydrophobic polymer Eudragit was used, dissolved in a Methanol: Dichloromethane mixture, and stirred with PG to form the release liner layer and drug content. In vitro drug permeation studies were conducted using a Franz diffusion cell[16.] (Gamal Osman Elhassan et.al 2022)

- **Swapnil Nazarkar2014:-**Miconazole Nitrate, Eudragit RL 100, Eudragit RS 100, Polyethylene Glycol 400, Acetone, Ethanol. Polymer Composition: Eudragit RL 100 and Eudragit RS 100 were selected based on their solubility, film-forming capacity, and drug release rate. The drug was incorporated into a polymeric solution, mixed with a plasticizer, and poured onto a mercury surface to form films. The patches were assessed for weight variation, thickness, moisture absorption and loss, water vapor transmission, tensile strength, drug content, and in vitro drug release[17]. (Swapnil Nazarkaret.al. 2014)

- **M. T. Rao 2020:-** The study focuses on developing and evaluating nanoparticle-incorporated transdermal patches of itraconazole to enhance drug absorption and bioavailability. Itraconazole nanoparticles were prepared using Eudragit RL 100 and incorporated into transdermal patches. Various formulations were tested for drug content, release, entrapment efficiency, and particle size. The optimized formulation showed high drug entrapment efficiency and a biphasic release pattern. The transdermal patch demonstrated significantly higher drug permeability compared to pure drug forms. The nanoparticle-loaded transdermal patch of itraconazole can effectively enhance transdermal drug delivery, offering improved patient compliance and sustained drug release[18]. (M. T. Rao et.al. 2020)

II. AIM & OBJECTIVES

Aim:-

To provide a localized and targeted treatment for fungal infections, such as athlete's foot, ringworm, and nail fungus.

Objectives:-

- To inhibit the growth and spread of fungal cells.
- To reduce symptoms such as itching, redness, and inflammation.
- To prevent further infection and promote healthy skin.
- To provide a convenient and easy-to-use treatment option.
- To minimize the risk of side effects and interactions associated with oral antifungal medications.

Need Of Study

The need for this study on Itraconazole Transdermal Patches for Onychomycosis:

- Oral Itraconazole has many side effects, including liver and kidney damage. A topical gel formulation aims to reduce these side effects and improve patient compliance.
- There are no commercially available Itraconazole topical gel preparations, creating a need for such a product.
- Topical application of Itraconazole can provide targeted therapy for local fungal infections, avoiding the first-pass effect and gastrointestinal irritation associated with oral administration.
- The study aimed to develop a gel with optimal drug release, viscosity, and other rheological properties to ensure effective treatment.
- Onychomycosis is a stubborn infection with high relapse rates, making it difficult to treat effectively.

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- Oral antifungal agents can be hepatotoxic and cause drug-drug interactions, while topical treatments struggle with nail penetration.
- Prolonged treatment durations and high costs are significant barriers to effective management.

Developing transdermal patches aims to improve drug absorption, reduce side effects, and enhance patient compliance.

III. MATERIAL & METHODS

Material:-

Sr. No.	Material
1.	Itraconazole
2.	Liquid Paraffin
3.	White Soft Paraffin
4.	Methanol
5.	Hydroxyl Propyl Methyl Cellulose (HPMC)
6.	Polyethylene Glycol 400

All other chemicals were analytical grades.

Method:-

1. Polymeric nanoparticles of itraconazole were prepared with Eudragit RL100 by solvent displacement technique.
2. The polymer (100 mg) along with itraconazole (100 mg) was dissolved in 20 ml acetone and methanol (3:1), which formed the organic phase.
3. This organic phase was poured through an orifice of size 0.22 µm, at the rate of 1 ml/min under atmospheric pressure into an aqueous medium (40 ml) containing 1 % polyvinyl alcohol (PVA) (hydrophilic surfactant) as a stabilizer under moderate magnetic stirring (1000 rpm).
4. After the addition of the organic phase, stirring was continued for 1 h at the same speed.
5. After 1 h, it was sonicated for 2 min to obtain desired particle size.
6. Later the colloidal dispersion was subjected to heating under reduced pressure at 580° to remove acetone & methanol (solvents) and the solution concentrated depends on the solvent: non-solvent ratio. [18]

IV. DRUG PROFILES

1. Itraconazole:-

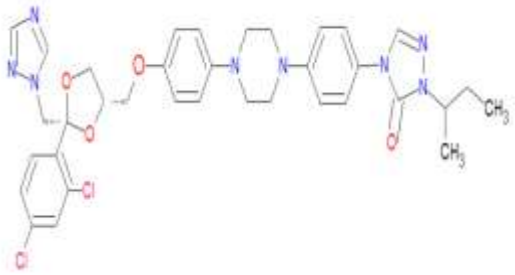

Fig. (3):-Chemical structure of Itraconazole

- **Molar mass:-** 705.64 g·mol⁻¹
- **Chemical Formula:-** $C_{35}H_{38}Cl_2N_8O_4$
- **IUPAC Name**:- (±)-1-[(RS)-sec-butyl]-4-[p-[4-[p-[[(2R,4S)-rel-2-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-1-piperazinyl]phenyl]-Δ²-1,2,4-triazolin-5-one
- **Melting Point:-**166.2 ^{0}C (359 ^{0}F)
- **Boiling Point:-**850^{0}C
- **Ionization Constants :-** pK_avalue:-3.7
- **Partition Coefficients :-** n-Octanol/ aqueous buffer of pH 8.1= 5.66
- **Solubility:-**Itraconazole is weakly basic (pKa =3.7) and highly hydrophobic (log P= 6.2). It shows pH dependent solubility and can be solubilized only under extremely acidic condition (4 µg/ml). ITZ is practically insoluble in water.
- **Mechanism of Action:-**Itraconazole is a broad-spectrum antifungal agent; it has an active metabolite; hydroxyitraconazole. Itraconazole inhibits ergosterol synthesis, which helps maintain the cell membrane in fungi. Lanosterol must undergo a 14 alpha-demethylation reaction to become ergosterol, which is catalysed by fungal 14 alpha-demethylase. Itraconazole blocks this reaction by interacting with the fungal 14 alpha-demethylase substrate-binding site. This impaired ergosterol synthesis leads to fungal membrane abnormalities that increase permeability and disrupt fungal cell membrane integrity, changing membrane-bound enzyme activity. The drug is metabolized extensively via the CYP450 system; specifically, itraconazole is a CYP3A4 substrate. It has a half-life of 34 to 42 hours. The drug is excreted in the urine (35%) feces (between 3 and 18%)[19]
- **Adverse Effects:-**While itraconazole is a

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relatively safe medication, there are some adverse side effects with itraconazole use. Cardiotoxicity is a rare adverse effect. Itraconazole can decrease heart contractility and left ventricular ejection fraction. The risk of cardiotoxicity increases with a dose greater than 400 mg/day. While most patients' heart function improves after discontinuing itraconazole, some require a transplant. In patients already being treated for hypertension, itraconazole can cause resistant hypertension. The most common Adverse Effects are gastrointestinal disturbances, such as nausea, mild diarrhoea, vomiting, and abdominal pain. When itraconazole administration is via the intravenous formulation, there is also a risk of injection site reactions, headache, and rash.[20]

2. Liquid Paraffin:-

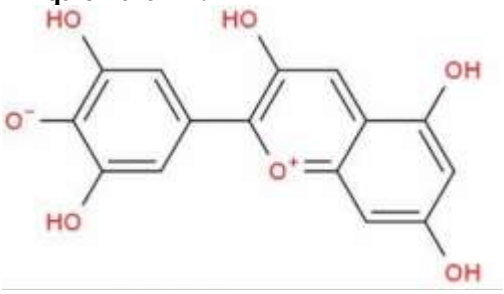

Fig. (4):- Chemical structure of liquid paraffin

- **Molar Mass:-** 635.96927 ± 0.00025 g/mo
- **IUPAC Name:-**3,5,7-trihydroxy-2- (3,4,5-trihydroxyphenyl)-1λ^4 -chromen-1-ylium chloride.
- **Melting point :-** The melting point of liquid paraffin is approximately **-24°C** or **-9°C**.
- **Boiling point:-**310°C
- **Solubility**:- Colourless, transparent, unctuous liquid, free from luminescence in daylight, virtually undoable in water, slightly answerable in ethanol(96 percent), miscible with hydrocarbons.
- **Mechanism of Action:-** It acts primarily as a coprolite lubricant, and is therefore not associated with abdominal cramps, diarrhoea, flatulence, disturbances in electrolytes, or forbearance over long ages of operation, side goods that bibulous and goadlaxatives frequentlyengender(still, some literature suggests that these may still do). The medicine acts by softening the feces and fleeces the intestine with an unctuous film.
- **Adverse Effects:-**

➢ Diarrhoea
➢ Stomach pain
➢ Nausea and vomiting
➢ Itching and skin rash
➢ Anal leakage of paraffin with anal irritation after using this product for a long time

3. **White SoftParaffin:-**

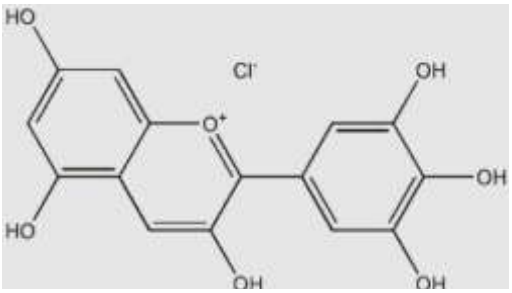

Fig. (5):- Chemical structure of white soft paraffin

- **Molar Mass :-** 341.44398
- **IUPAC:-**Petrolatum
- **Solubility:-** Colourless, transparent, unctuous liquid, free from luminescence in daylight, virtually undoable in water, slightly answerable in ethanol(96 percent), miscible with hydrocarbons.
- **Mechanism of Action:-** It acts primarily as a coprolite lubricant, and is therefore not associated with abdominal cramps, diarrhoea, flatulence, disturbances in electrolytes, or forbearance over long ages of operation, side goods that bibulous and goadlaxatives frequentlyengender(still, some literature suggests that these may still do). The medicine acts by softening the feces and fleeces the intestine with an unctuous film.
- **Adverse Effects :-**

➢ Anal irritation (excessive dose) and seepage
➢ Foreign-body granulomatous reactions
➢ Vasospasm
➢ Lipoid pneumonia
➢ Interference with absorption of fat-soluble vitamins[21]

4. Methanol:-

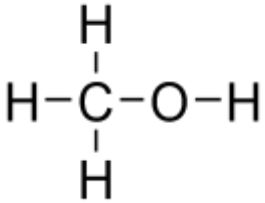

Fig. (6):- Chemical structure of Methanol

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- **Molar Mass:-** 32.042 g·mol−¹
- **Chemical Formula:-**CH_3OH
- **IUPAC Name:-**Methyl alcohol
- **Boiling Point:-**64.7 °C
- **Solubility:-**The lowest and lightest alcohols(methanol, ethanol, propanol) are completely answerable in water in all proportions. In a result, the hydroxyl groups of alcohol motes and the water motes form hydrogen bonds with each other, performing in complete miscibility. still, as the length of the carbon chain increases, the solubility decreases.
- **Mechanism of Action:-** A CNS depressant, methanol is potentially poisonousin quantities as small as a single nibble When metabolized by hepatic alcohol and aldehyde dehydrogenase, methanol forms formaldehyde and formic acid, both of which are poisonousThe eyes, CNS, and GI tract are affected.
- **Adverse Effects:-**

➢ Drowsiness, confusion, headache, dizziness, and poor coordination
➢ Nausea, vomiting, abdominal pain, and gastric disturbances
➢ Heart and respiratory failure
➢ Visual disturbances, blurred vision, and blindness
➢ Insomnia, conjunctivitis, and a specific smell on the breath[22]

5. Hydroxyl Propyl Methyl Cellulose (HPMC):-

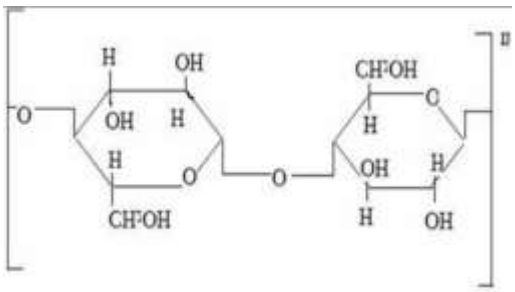

Fig. (7):- Chemical structure of (HPMC)

- **Molar Mass:-**1261.4 g/mol
- **Chemical Formula:-**C56H108O30
- **IUPAC Name:-**Cellulose, 2-hydroxypropyl methyl ether
- **Melting Point:-**225-230 °C
- **Boiling Point:-**1101.5°C
- **Mechanism of Action**:- By reducing the molar negotiation of hydroxyl propyl group, the glass transition temperature of HPMC can be reduced to 40 o C. HPMC forms flexible and transparent flicks from waterless result.
- **Adverse Effects:-**Hydroxypropyl Methylcellulose(HPMC) is generally safe for consumption and is approved by food safety authorities like the FDA and EFSA. As a factory- grounded cumulative, it's salutary for insectivores and those with salutary restrictions. still, inordinate consumption may lead to gastrointestinal discomfort, and rare antipathetic responses may do.[23]

6. Polyethylene Glycol 400:-

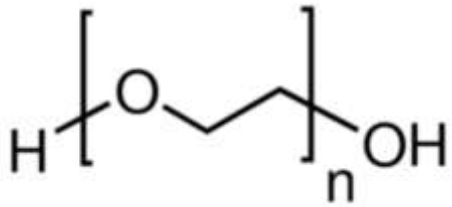

Fig. (8):- Chemical structure of Polyethylene Glycol 400

- **Molar Mass:-**380-420 g/mol
- **Chemical Formula:-** $C_2\ nH_4\ n+_2\ On+_1\ ,n=_8\ .2\ to_9\ .1$
- **IUPAC Name:-**ethane-1,2-diol
- **Melting Point:-**4-8°C
- **Boiling Point:-**200°C
- **Solubility:-** Completely answerable in water Molecularly stable andnon-volatile Excellent hygroscopicity Low toxin High lubricity and solvency.
- **Mechanism of action:-** cut forms hydrogen bonds with water motes. For this reason, it can help the reabsorption of water, which causes water retention in the coprolite and increases the bibulous pressure.
- **Adverse effects:-**numerous people using this drug do n't have serious side goods. Eye pain, change in vision, continued eye greenishness/ vexation. A veritably serious antipathetic response to this medicine is rare.[24]

Future Perspective

Antifungal patches are an emerging area in the treatment of fungal infections, offering several advantages over traditional oral or topical treatments. Here are some perspectives on their development and future potential:

1. Enhanced Drug Delivery

Antifungal patches can provide a

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controlled and sustained release of medication directly to the affected area. This targeted approach can improve the efficacy of the treatment and reduce systemic side effects.

2. Improved Patient Compliance

Patches are generally easier to use and more convenient than oral medications or creams, which require frequent application. This can lead to better adherence to the treatment regimen, especially for chronic conditions like onychomycosis (fungal nail infections).

3. Innovative Formulations

Recent advancements in drug delivery systems have led to the development of patches that incorporate various antifungal agents, including natural products, essential oils, and synthetic compounds. These formulations can be tailored to combat specific fungal strains and reduce the risk of resistance.

4. Combination Therapies

Patches can be designed to deliver multiple antifungal agents simultaneously, enhancing their effectiveness. This approach can be particularly useful in treating infections caused by resistant strains of fungi.

5. Research and Clinical Trials

Ongoing research and clinical trials are crucial for validating the efficacy and safety of antifungal patches. Studies are exploring various materials and technologies, such as microneedles and nanotechnology, to improve drug penetration and effectiveness.

6. Potential Challenges

Despite their promise, antifungal patches face challenges such as ensuring consistent drug release, avoiding skin irritation, and maintaining stability under different environmental conditions. Addressing these issues will be key to their successful adoption.

Overall, antifungal patches represent a promising direction in the treatment of fungal infections, with the potential to improve outcomes and patient experience significantly.

V. CONCLUSION

Onychomycosis is a persistent fungal nail infection that is difficult to treat and prone to relapses. Itraconazole is effective in treating onychomycosis but has limitations like poor solubility and gastrointestinal irritation. The development of itraconazole-loaded transdermal patches aims to improve drug absorption and patient compliance. Using nanoparticles in transdermal patches enhances drug permeation through the nail, offering a promising alternative to conventional treatments. With negligible side effects, better and deeper drug release and drug retention, these systems have a lot to offer to the antifungal therapy. Coupled with a novel dosage form which can act as an excellent delivery vehicle, novel delivery systems have the potential to replace the conventional therapy in coming years. More attention is being focused on eradicating the long-standing issues associated with onychomycosis and it will not be surprising to assume the solution may well be on its way.

REFERENCE

[1]. Thapa RK, Choi JY, Go TG, et al. Development of ciclopirox nail lacquer with enhanced permeation and retention. Arch Pharm Res 2016; 39(7): 953-9.

[2]. McAuley WJ, Jones SA, Traynor MJ, Guesné S, Murdan S, Brown MB. An investigation of how fungal infection influences drug penetration through onychomycosis patient's nail plates. Eur J Pharm Biopharm 2016; 102: 178-84.

[3]. Ghannoum M, Isham N. Fungal nail infections [onychomycosis]: a never-ending story? PLoSPathog 2014; 10(6): e1004105.

[4]. Kushwaha A, Murthy RN, Murthy SN, Elkeeb R, Hui X, Maibach HI. Emerging therapies for the treatment of ungual onychomycosis. Drug Dev Ind Pharm 2015; 41(10): 1-7.

[5]. Bseiso EA, Nasr M, Sammour OA, Abd El Gawad NA. Novel nail penetration enhancer containing vesicles "nPEVs" for treatment of onychomycosis. Drug Deliv 2015; 23: 1-7.

[6]. Rocha KAD, Krawczyk-Santos AP, Andrade LM, et al. Voriconazole-loaded nanostructured lipid carriers [NLC] for drug delivery in deeper regions of the nail plate. Int J Pharm 2017; 531(1): 292-8.

[7]. Gaur PK, Mishra S, Purohit S, Dave K. Transdermal drug delivery system- A review. Asian Journal of Pharmaceutical and Clinical Research. 2009; 2:14-20.

[8]. Aggarwal G. Development, Fabrication an d Evaluation of Transdermal Drug Deliver

y A Review. Pharmainfo.net.2009.
[9]. Chandrashekhar-
N S, Shobha Rani R H. Physicochemical a nd
Pharmacokinetic Parameters in Drug Selec tion and Loading of Transdermal Drug De livery. Indian Journal of Pharmaceutical Sciences. 2008; 70[1]: 94-96
[10]. Heather AE. Transdermal Drug Delivery: Penetration Enhancement Techniques. Current Drug Delivery. 2005; 2:23-33.
[11]. Lee WR, Shen SC, Lai HH, Hu CH, Fang JY. Transdermal drug delivery enhanced and controlled by erbium:YAG laser. J controlled release. 2001; 75:155-166.
[12]. Sonia Dhiman, Thakur Gurjeet Singh and Ashish Kumar Rehni, International Journal of Pharmacy and Pharmaceutical Sciences, Vol 3, 2011:(5), 26-34.
[13]. Subedi, L.; Song, S.-Y.; Jha, S.K.; Lee, S.-H.; Pangeni, R.; Koo, K.-T.; Kim, B.J.; Cho, S.-S.; Park, J.W. Preparation of Topical Itraconazole with Enhanced Skin/Nail Permeability and In Vivo Antifungal Efficacy against Superficial Mycosis. Pharmaceutics 2021, 13, 622.
[14]. Rupinder K. Dhamoon, Harvinder Popli and Madhu Gupta, Pharmaceutical Nanotechnology, 2019, 7, 24-38.
[15]. Kamal Kumar, Nida Parveen, Research J. Pharm. and Tech. 16(5): May 2023
[16]. Gamal Osman Elhassamn, International Journal of Applied Pharmaceutics, Thematic Special Issue 2022, 195-200
[17]. Swapnil Nazarkar, Manish Kondawar, Prasad Vedpathak, Samrat Khedkar, Dharmesh Dayama, Int J Curr Pharm Res, Vol 6, Issue 4, 2014; 32-36.
[18]. M. T. Rao, Y. S. Rao, Vijaya Ratna J1 AND Kamala Kumari PV, Indian Journal of Pharmaceutical Sciences,2020;82(5):809-818.
[19]. Boogaerts M, Maertens J. Clinical experience with itraconazole in systemic fungal infections. Drugs. 2001;61 Suppl 1:39-47.
[20]. Pierard GE, Arrese JE, Pierard-Franchimont C. Itraconazole. Expert OpinPharmacother. 2000 Jan;1(2):287-304.
[21]. Patel et al. Formulation and evaluation of t ransdermal patch of Aceclofenac.
International Journal of Drug Delivery.
2009;1:41-51.
[22]. Anissimov YG, Roberts MS (2011). Modelling dermal drug distribution after topical application in human. Pharm Res 28: 2119–2129.
[23]. Busse KL, Maibach HI (2011). Transdermal estradiol and testosterone transfer in man: existence, models, and strategies for prevention. Skin PharmacolPhysiol 24: 57–66.
[24]. Brown EW, Scott WO (1934). The absorption of methyl salicylate by the human skin. J Pharmacol Exp Ther 50: 32–50.