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Transungual Drug Delivery System: A Newer Approach

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ABSTRACT

This review aims to investigate the challenges associated with drug penetration through nail plates and the ways in which antifungal drug bioavailability can be improved. Based on available clinical information, efficiently breaking through the nail barrier is crucial for the effective treatment of fungal illnesses with topical antifungal products. The reason for the low therapeutic efficiency of current topical treatments may be that they are unable to effectively penetrate the nail plate to deliver an antifungal agent in a therapeutically sufficient quantity to the target locations in order to destroy the protection. It's also challenging to analyze the drug's permeation. This comprehensive analysis includes the human nail's structure, nail plate-related illnesses, nail application formulations, and methods for improving the topical bioavailability of the medication distribution throughout the nail, including current developments in this area.

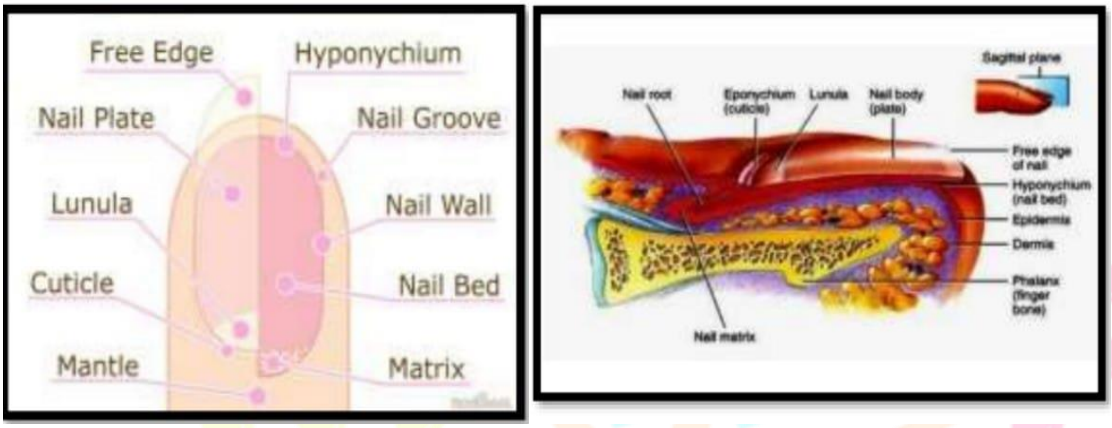
Keyword: Nail penetration, bioavailability, antifungal, nail barrier.

The kind of drug administration pathway is known as the tantsungual drug delivery system. "Trans" denotes "through," while "ungual" denotes "the nail." This is known as the transungual drug delivery system, and it deals with the distribution of medication through the nail, where it passes through and has a specific effect on the nail's infected area. The nail plates that allow drugs to pass through them.[2] The structure of the nail is horny. A nail plate is what allows the medication to pass through.[1] However, the structure of the nail is so hard that very few medications can pass through it and take action. Because of this, topical drug delivery is far more effective than oral drug delivery and has far fewer side effects on body or the nail's affected area. [2] The dorsal and intermediate layers, which come from the matrix, and the ventral layer, which comes from the nail bed, make up the human nail plate. The soft keratin makes up the intermediate layer, which makes up three-quarters of the nail's total thickness. The dorsal layer, which makes up 94% of the nail's weight, is the top layer. It is only a few cell layers thick and is made of strong keratin with a comparatively high sulfur concentration, mostly in the form of amino acid cysteine. The nail plate serves as the primary conduit for the top layer of the nail. The soft hyponychial layer that makes up the ventral layer is where numerous pathological alterations take place. Therefore, an effective medication concentration in the ventral nail plate is necessary for the treatment of various nail illnesses. The soft hyponychial layer that makes up the ventral layer is where numerous pathological alterations take place. Therefore, it would be crucial to have an effective drug concentration in the

ventral nail plate while treating these nail illnesses. [3] Iontophoresis, acid etching, carbon dioxide laser, hydration and occlusion, electroporation, UV light, photodynamic therapy, sonophoresis, and phonophoresis are the physical techniques for improving penetration.Chemicals such as sulphites, mercaptans, hydrogen peroxides, urea, water, keratolytic agents, keratinolytic enzymes, etc., increase the drug's penetration potential. Furthermore, nail abrasion and nail avulsion contribute to the mechanical improvement of penetration. [2]

2) THE NAIL ANATOMY:

The nail plate, the nail matrix, the nail bed beneath it, and the grooves that encircle it make up the nail.



The human nail's structure consists of:

Matrix (onychostroma, keratogenous membrane, nail matrix, and matrix unguis):

It is the portion of the nail bed that extends beneath the nail root and contains blood, lymph, and nerve vessels. It is also known as the germinal matrix. This tissue is where the nail rests. The cells that eventually form the nail plate are produced by the matrix. The size, length, and thickness of the matrix dictate the breadth and thickness of the nail plate. [4]

Lunula

Lunula sometimes known as "the moon," is the visible portion of the matrix and the pale, crescent-shaped base of the visible nail. The thumb has the largest lunula, whereas the little finger frequently has none at all. [6]

Nail Bed

The nail bed Underneath the nail plate is the skin. It consists of two different types of tissues, just like all skin.

a) The deeper dermis- which is the living tissue that is attached to the bone and has glands and capillaries in it.

b) The Superficial epidermis-

The layer directly below the nail plate, which advances along with the plate, is known as the superficial epidermis. Little longitudinal "grooves" called matrix crests or crests of nail matrix (cristae matricis unguis) hold the epidermis to the dermis. [6]

Nail Sinus

The deep furrow is known as the nail sinus (sinus unguis) into which the nail root is inserted. [6]

Nail root (radix unguis):

This is the portion of the nail that is embedded beneath the skin and is located in the nail sinus. It comes from the tissue that is actively growing beneath the matrix. [6]

Nail plate (corpus unguis):

The nail is composed of the transparent protein keratin, which is derived from amino acids. It takes the form of many layers of dead, flattened cells to form a strong, flexible material in the nail. The capillaries underneath give the plate its pink appearance. Its transverse shape is dictated by the shape of the bone underneath.

Hyponychium

The free margin is the nail plate's anterior margin that lines up with the nail's cutting or abrasive edge. [5] 2.8. Hyponychium: The layer of epithelium underneath the nail plate where the skin of the fingertip meets the free edge. It creates a barrier to keep the nail bed safe. [6]

Onychodermal band:

This is the membrane that separates the hyponychium from the nail plate. It can be identified by its glassy, greyish color, which is situated right under the free edge in the area of the nail where the nail bed stops (infair-skinned persons). In some people, it is barely noticeable, but in others, it is rather noticeable. [7]

Eponychium

It is the thin layer of epithelium that connects the base of the nail to the posterior nail wall. 5. The eponychium, the extremity of the proximal fold that folds back over itself to shed an epidermal layer of skin onto the freshly formed nail plate, is mistakenly and frequently referred to as the "proximal fold" or "cuticle". This nearly undetectable, non-living skin layer is the cuticle that "rides out" across the nail plate's surface. The cuticle and eponychium work together to create a protective seal. While the eponychium is made of live cells and shouldn't be handled, the cuticle on the nail plate is made of dead cells and is frequently removed during manicures. [8]

Perionyx:

The perionyx is the eponychium's protruding border that covers the proximal strip of the lunula. [5]

Lateral Margin

Margo lateralis, or the lateral margin The lateral margins are inserted into the cutaneous slits known as the nail groove or fold (sulcus matricis unguis), which are located on the sides of the nail beneath the nail wall. [5]

Paronychium:

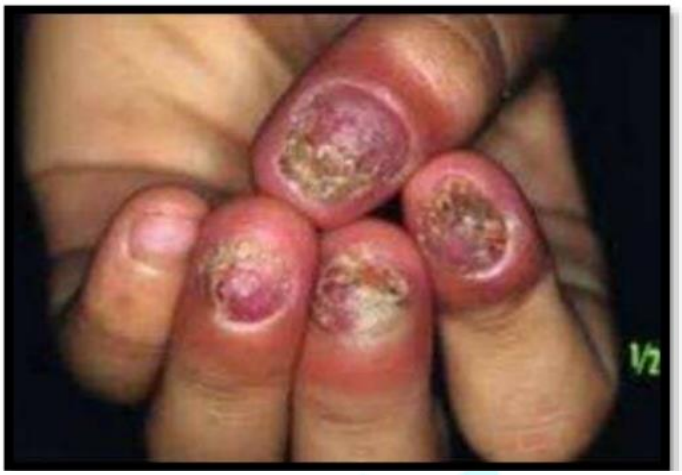
An infection in the paronychium, which is the border tissue surrounding the nail, is known as paronychia. [6]

3**. NAIL DISORDERS**

A) Onychomycosis:

The most prevalent nail infection in the world is onychomycosis, a fungal infection that causes the affected nail plate to thicken and become discolored. For the diagnosis of onychomycosis, microscopy and fungal culture are considered the gold standard methods. Oral antifungals, topicals, and devices are among the potential therapy methods. Compared to topical treatments, oral antifungals offer better cure rates and shorter treatment times, but they also come with unfavorable side effects such hepatotoxicity and medication interactions. The most widely used oral antifungals are terbinafine, itraconazole, and fluconazole; other medications such fosravuconazole are

being studied. Topical medications with less severe side effects include amorolfine, ciclopirox, tavaborole, and finaconazole. [9]



B) Green nail syndrome:

Also known as chloronychia, "green nails" are an illness mostly brought on by Pseudomonas ueruginosa, however other bacterial or fungal contaminants can also cause the condition. The classic triad of the clinical presentation is a green staining of the nail plate linked to disto-lateral onycholysis and proximal chronic paronychia. [11]

C) Paronychia infection:

Paronychia is an infection of the hands or toe nails caused by fungi or bacteria. The infection happens around the edges of the nails, or where the skin and nails meet. There are two primary classes into which the paronychia is divided: [12]

1.Acute Paronychia:

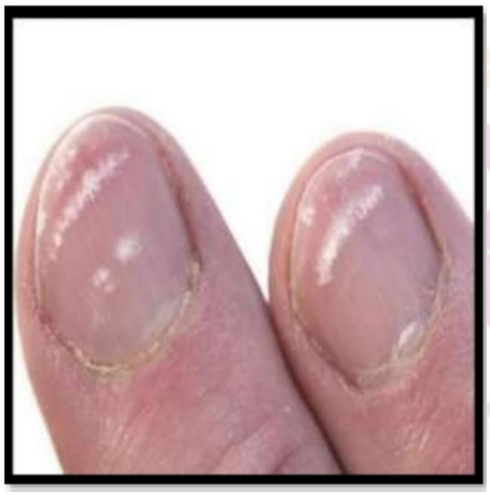
Penetrating injuries, nail biting, finger sucking, aggressive manicures, hanging nails, and retained foreign bodies are the most prevalent causes of acute paronychia. Placement of artificial nails, or sculptured fingernails, has also been linked to the development of paronychia.

2. Chronic Paronychia:

Although the etiology is multifactorial, chronic paronychia clinically mimics acute paronychia. b. Treatment for chronic paronychia is more challenging and typically non-supportive. Individuals who are frequently exposed to both wet settings and water that contains irritants or alkali are at risk of developing chronic paronychia. Bartenders, housekeepers, homemakers, dishwashers, swimmers, diabetics, and immunocompromised individuals are among the high-risk groups. [10]

D) Leukonychia

Leuko means "white," whereas onyx is the word for "nails." Between the nail plate and the nail bed, this is the most typical kind of nail injury. One or more nails in this case have a white line or spot on them. The area could be the result of an air bubble that was traumatized and lodged between the nail plate and the nail bed. [12]



There are several approaches laid one by one, for treating the transungual drug delivery. Few of them were discussed as follows;

4.1 Topical application:

Antifungal medication administered orally has lately been linked to gastrointestinal and systemic adverse effects. With its comparatively milder side effects and improved patient compliance—especially for younger patients—topical administration is undoubtedly the most preferred form of treatment. Regretfully, there are a minimum of two elements that may restrict the absorption and efficacy of medications when applied topically in the nail. Initially, the drug's physicochemical characteristics must be advantageous for absorption via the nail matrix. It has been reported that polar chemicals can pass through the nail matrix more easily than nonpolar ones. Second, the drug's availability is decreased when it binds to keratin. There are reports that antifungal medications have a high affinity for binding to keratin.[14]

4.2 Enhancement of chemical penetration:

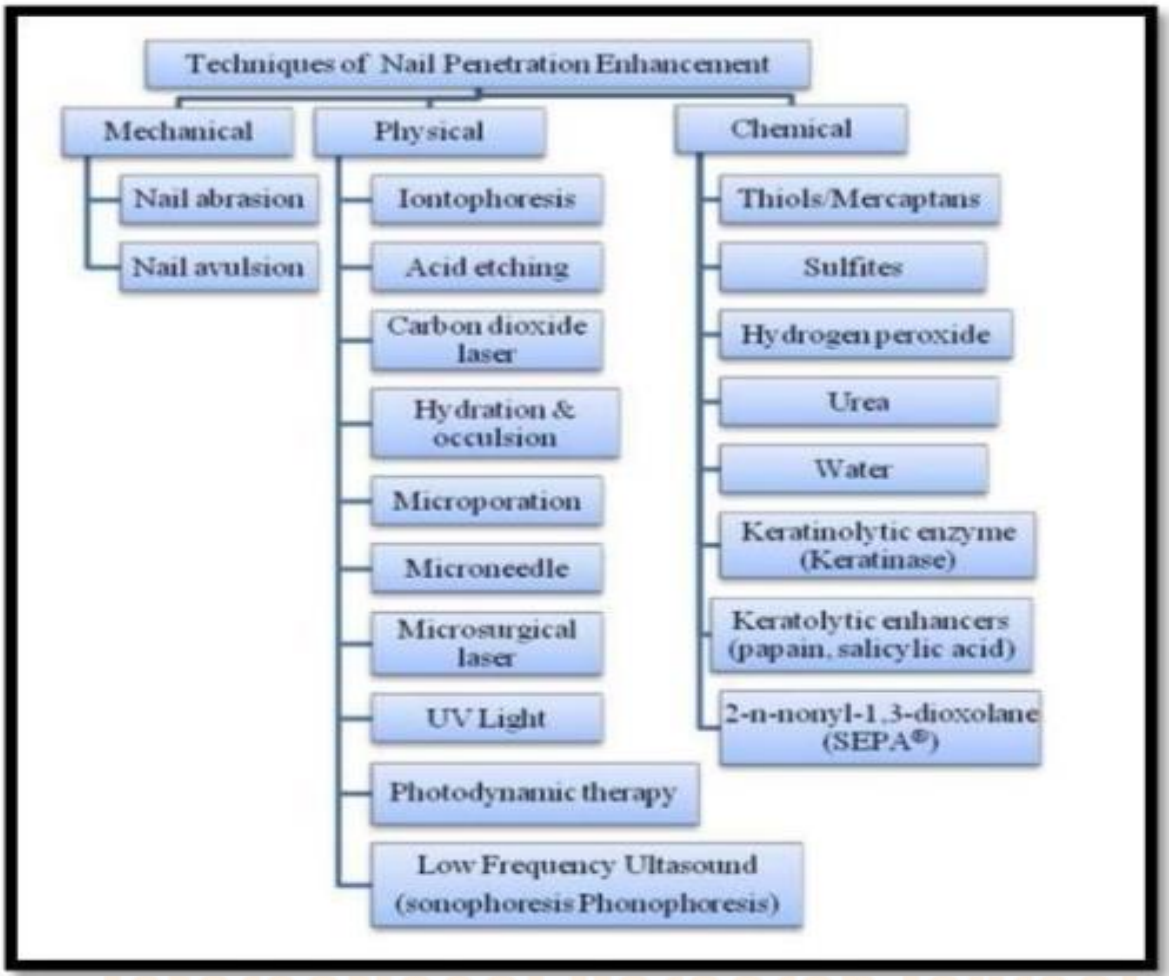
The use of keratolytic and thiolytic chemicals has been a frequent strategy for improving nail medication delivery. These substances are known to chemically alter keratin, increasing the permeability of the nail matrix. Their ability to increase permeability is, however, constrained by elements like the enhancer's penetrability and how long it remains in the nail matrix, both of which may have a major impact on the keratin's chemical alteration. Because topical monotherapy has poor drug absorption via the nail, it is thought to be less effective in treating nail problems such onychomycosis. [15]

4.3 Physical penetration enhancement:

James and associates performed prednisolone sodium phosphate Iontophoresis on the thumb nail and ascertained the prednisolone time course in plasma. To evaluate the effectiveness and address the mechanistic issues of iontophoresis over nails, thorough preliminary investigations are nonetheless required. In treating nail fungal diseases, the iontophoretic trans-nail administration approach has demonstrated promising outcomes recently. Researchers led by S. Narsimha Murthy have examined how iontophoresis affects salicylic acid's capacity to permeate human nail plates. They used an electrode-equipped Franz diffusion cell to conduct a

diffusion research. In comparison to the traditional penetration method, the test penetrant's permeability over the nail plate increased dramatically, according to the data. [16]

5. PENETRATION THROUGH NAIL :



Chemical Method;

Chemical techniques Different mammalian nails respond differently to skin penetration enhancers. Thus, only a small number of substances that were clearly able to increase drug penetration into the nail plate have been described below.

1. **Keratolytic enhancers:**

Three imidazole antifungal medications (miconazole, ketoconazole, and itraconazole) were examined for their permeability in relation to the effects of keratolytic agents such as papain, urea, and salicylic acid. Over the course of 60 days, it was noted that no transungual antifungal permeation was found in the absence of keratolytic drugs. The spectrophotometric analysis approach, which lacked the sensitivity to precisely detect drug concentrations, further corroborated this. Pre-treating with 20% salicylic acid (for 10 days) and adding 40% urea to the donor solution did not improve the permeability of these agents. On the other hand, pre-

treatment with 15% papain for one day and 20% salicylic acid for ten days improved antimycotic penetration. [17]

2. Mercaptan and N-acetyl-l-cysteine compounds :

N-acetyl-l-cysteine and 2-mercaptoethanol together improved the antifungal medication tolnaftate's penetration into nail samples. They proposed that these substances might be generally helpful in improving medication penetration through the nail plate. In vivo investigations have documented how N-acetyl-lcysteine enhances the uptake of the antifungal medication oxiconazole.[17]

3. 2-nonyl-1,3-dioxolane.

Econzole (in a lacquer formulation) has been able to enter human nails by the application of 2-n-nonyl-1,3-dioxolane (SEPA®). According to studies, while using a lacquer containing 2-n-nonyl-1, 3-dioxolane, econazole penetrates the nail six times more effectively than when using the same lacquer without an enhancer. The "enhancer" group had considerably increased concentrations of econazole in the deep nail layer and nail bed compared to the control group. Additionally, the concentration of econazole in the deep nail layer of the "enhancer" was 14,000 times higher than the Minimum Inhibitory Concentration required to stop fungal growth.[17]

Physical methods

Physical permeation enhancement may be superior to chemical methods in delivering hydrophilic and macromolecular agents.

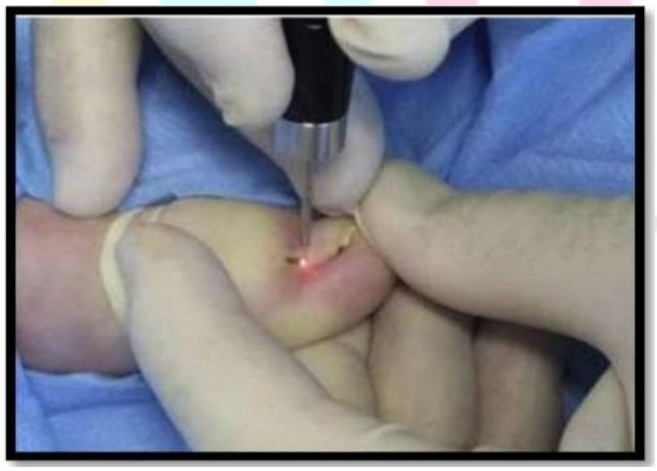
1. Carbon dioxide laser:

CO2 laser may result in positive, but unpredictable results.

Two methods were suggested so far;

1. One method involves avulsion of the affected nail portion followed by laser treatment at 5000W/cm2 (power density). Thus, underlying tissue is exposed to direct laser therapy.

2. Second method involves penetrating the nail plate with CO2 laser beam. This method is followed with daily topical antifungal treatment, penetrating laser-induced puncture holes. The first method is preferred.[17]



2. Hydration and occlusion:

Hydration may improve transungual penetration by enlarging the nail matrix's pore size. Nails with moisture have greater elasticity and porosity. Studies on iontophoresis have made use of this characteristic to increase penetration. Nail hydration has not been found to be significantly impacted by the pH or ionic strength of the

solution. Human skin gets more hydrated as a result of which things, including medications, become more diffusible. Up to about 300 percent is retained in the human stratum corneum of its weight in water; diffusivity also multiplies three times when the stratum corneum is saturated. [17]

3. Electroporation:

To make the solute particles permeable via the lipid bilayers, an electric transient aqueous hole is applied. [17]

4. Laser ultraviolet light:

Heating the nail by UV light exposure is one technique. Because of the heat, fungus cannot develop behind the nail plate.[17]

5. Micro needle:

It is an improved method of distribution. Using an array of tiny needles, this technique opens Stratum corneum pores and allows blood to reach the skin capillaries. It also benefits from being too short to activate the pain fibers, which makes it easier for drugs to seep through.[17]

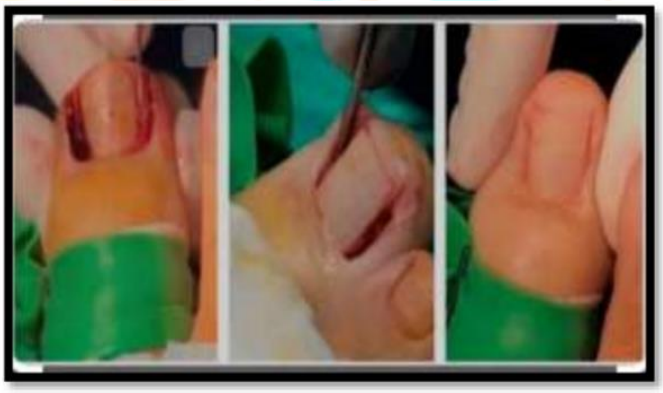
6. Iontophoresis:

Iontophoresis is the process of delivering a substance across a membrane by applying an electric field. The idea has been used in clinical settings for the treatment of herpes simplex, hyperhidrosis, antibiotic penetration, and cutaneous anesthesia. Applications for iontophoresis can be found in the transdermal, ophthalmic, dental, orthopedic, etc. fields. Iontophoresis may improve drug diffusion through the moist keratin of a nail. This enhancement is caused by a number of factors, including electroosmosis—convective solvent flow in both newly formed and pre-existing charged pathways—electro repulsion/electrophoresis—interaction between the electric field and the charge of the ionic permeant, and permeabilization/electroporation—electric field-induced pore induction. [18]

5.3 Mechanical approaches:

For many years, dermatologists and pediatricians have employed mechanical procedures, with differing degrees of success. They could hurt and are intrusive.

1. **Nail avulsion:**



Under local anesthesia, a total or partial nail avulsion is a surgical procedure used to remove the entire nail plate or just a portion of the damaged nail plate. The nail plate is made softer for avulsion by keratolytic chemicals such as salicylic acid and urea. Prior to topical treatment for Onychomycosis, urea or mixtures of urea and salicylic acid have been used in clinical research for nonsurgical avulsion (chemical avulsion). [19]

Modern transungual drug delivery strategies include:

1. Delivery of content on topic Systemic and gastrointestinal side effects are constitutionally associated with oral antifungal therapy. Topical distribution is one of the recommended approaches because of its less severe side effects and improved patient compliance, particularly for younger patients. For drugs to be absorbed through the nail matrix, they need to have favorable physicochemical properties. It has been reported that polar compounds penetrate the nail matrix more rapidly than nonpolar ones. The affinity of pharmaceuticals for keratin limits the amount of unbound drugs. Antifungal medications are said to have a considerable affinity for keratin[65].

2. Topical administration using nanocarriers Applying nanoparticles topically to the nail is an easy way to cure it without going through the systemic adverse effects of taking medication orally. The use of nanoparticles improves medication targeting and increases drug permeability and profile[66]. Highlights from the content include the concept of topical medication delivery using nanocarriers to treat nail disorders.

Nanoemulsion: Liquid droplets and surfactants with a size range of 10 to 500 nm are combined to create nanoemulsions. The properties required for antifungal therapy are stability, improved solubilization, increased

penetration impact, and focused activity. They're an excellent substitute for liposomes that are unstable[67]. The dispersion of the nanoemulsion in the gel-like state is referred to as "nanoemulgel".

Liposomes: Liposomes are a type of spherical, bilayered phospholipid vesicles that have an aqueous interior and a phospholipid outer membrane. They work well for delivering medications in both hydrophilic and hydrophobic environments. Liposomes are used in topical drug administration because of their many benefits, such as improved skin penetration, biocompatibility, durability, low toxicity, and extended release. It is thought that liposomes and ethosomes can target particular lipophilic routes in the nail, which makes them a viable choice for medication delivery to the nail. As shown in Table No. 1, several antifungal drugs have already been added to liposomes and ethosomes for topical antifungal therapy[68].

4. Nail Patch: Nail patches are a preferred noninvasive drug carrier for the topical treatment of nail issues since they eliminate the negative effects of oral or injectable medications. Following treatment, the patch would remain in place over the affected area and deliver the drug gradually over time. Commercially available skin patches cannot simply be loaded with drugs for nail illnesses due to variances in the surfaces of the skin, nails, and pharmaceuticals[72].Making nail patches from scratch is essential. A combination of theoretical, experimental, and modeling approaches must be used to establish the appropriate patch components, such as the adhesive, backing membrane, and solvents, as well as to create drug-loaded nail patches. iii) testing the produced patches for adherence to the nail plate, effects on hydration of the nail plate, drug transfer into the nail plate, and the illness-fighting effects of the medication afterward[73].

6. FACTORS AFFECTING DRUGS TRANSPORT INTO/ACROSS THE NAIL

When a medication formulation is applied topically to the nail plate, it must penetrate the plate, diffuse into the deeper layers of the nail, and perhaps even reach the nail bed. According to Walters et al., the nail plate functions more like a concentrated hydrogel than a lipophilic membrane.

- The physicochemical properties of the drug molecule to be applied.
- The type and nature of formulations.
- The presence of permeability enhancers in the formulations,
- The properties of the nail.
- The interactions between the permeant and the keratin network of the nail plate all have an impact on drug delivery into and through the nail plate.

Molecular size of drug :

Drug penetration is reduced and drug diffusion via the keratin network is hindered by higher molecular sizes. Mertin and Lippold showed how an increasing molecular size of a series of alkyl nicotinates resulted in decreased permeability coefficients across human nail plate and through bovine hoof membrane.

Hydrophobicity

Walters et al. investigated the penetration of a range of homologous alcohols (C1–C12), diluted in saline, through human nail plates that had been avulsed. The permeability coefficient decreased as the chain length increased from one to eight carbon atoms; however, the permeability coefficient increased when the chain length increased (>C12). According to the findings of Walters et al.'s study, the nail plate is classified as a hydrophilic gel membrane. [21]

Nature of Vehicle used in formulation :

The permeability coefficients of plain alcohols were five times lower than those of alcohols diluted in saline via nail plates. Water hydrates the nail plate, causing it to enlarge as a result. Given that the nail plate is a hydrogel, swelling causes the keratin fibers to spread farther apart and creates bigger pores that allow molecules to

penetrate more readily. This increases the molecules' ability to penetrate the nail plate. It is therefore anticipated that substituting a non-polar solvent for water may lessen medication penetration into the nail plate because this solvent does not hydrate the nail. [21]

Vehicle and solute charge potential:

Weakly acidic/basic medications' ionization is influenced by the pH of aqueous formulations, which in turn affects the drugs. The characteristics to consider are hydrophilicity or hydrophobicity, medication solubility, nail plate solubility, formulation, and interactions with the keratin matrix. It appears that the medication's ability to pass through the nail plate is significantly impacted by the formulation's pH. [21] 6.5

Ionization Degree: Ionic chemicals tend to be less permeable through the nail plate than their non-charged counterparts with higher permeability coefficients.[22]

Nail plate hydration:

An essential component in determining medication penetration is the degree of nail plate hydration. The penetration of ketoconazole under varying relative humidity (RH) conditions, ranging from 15% to 100%, demonstrated a threefold enhancement in the administration of the radiolabeled medication.[22]

The dorsal layer is present and intact:

The biggest obstacle to a drug's entry through the nail plate is an overlap of cells. Drug permeability rises if this layer is destroyed entirely or partially, for example, by debridement, chemical etching with 30–40% phosphoric acid, or the use of keratinolytic enzymes.[22]

The drug's binding to keratin and other nail constituent:

Keratin is positively and negatively charged at pH values below and above 5, which is assumed to be its pH. Therefore, depending on the charge of the molecules, it may bind or repel them. This could contribute to the reduced ionic compound permeability in nails.[22]

Disease presence and nail thickness Drugs will have a harder time getting to the nail bed the thicker the nail].[22]

7. Drugs used for treatment of nail disorder:

Amorolfine:

● Amorolfine is a morpholine derivative that possesses fungistatic and antifungal qualities. It was invented in 1981. Amorolfine inhibits the synthesis of ergosterol in two ways: first, by blocking the enzymes delta 14 reductase and delta 7-8 isomerase, which impact the synthesis of pathogen membranes; second, by reducing ergosterol and generating non-typical spherical sterols that build up in the fungal cytoplasm membranes[74].

● Amorolfine's pharmacokinetic properties minimize bloodstream absorption of active components while facilitating efficient nail-to-nail bed penetration. Most fungi can be detected in the nail for around two weeks and are sensitive to its low concentration. Treatment with amorolfine continues until a mycological and clinical cure is achieved. Depending on the extent and location of the infection as well as the growth of the nail plate, the course of treatment usually lasts six to twelve months. It is advised to assess the treatment's efficacy every three months[75–78].

● The amorolfine lacquer formulation is applied once or twice a week on a clean nail plate, and it is left to cure for three to five minutes. Organic solvents should not be used to remove the preparation. Negative symptoms that have been noted include onycholysis, erythema, and a burning sensation in the nails[78,79].

Ciclopirox

is a hydroxy-pyridone derivative. Lacquer has been manufactured from it since the 1990s, but it has been investigated since 1973. Ciclopirox is used to treat onychomycosis of the skin and scalp. It is available in many forms, such as cream suspension, shampoo, gel, solution, powder, and globules. It also relieves seborrheic dermatitis, pityriasis versicolor, and vaginal candidiasis. It demonstrates antifungal activity by chelating trivalent cations such as Fe3+ and Al3+. This lowers the amount of nutrients taken in and decreases ion transport via pathogen cytoplasmic membranes by inhibiting metal-dependent enzymes such as cytochromes, catalases, and peroxidases. Potassium ions are lost, leucine and other amino acids, such ciclopirox, are kept out of cells, and the arachidonic acid cascade is stopped. Ciclopirox displays a variety of anti fungal action. By inhibiting the arachidonic acid cascade, which stops polynuclear granulocytes from synthesizing prostaglandins and leukotrienes, the material also has anti-inflammatory qualities[80–81].

● Systemic absorption is incredibly low. It successfully penetrates mycotic nails' keratin. The duration of treatment should normally last between six and twelve months. Four weeks following the conclusion of treatment, a mycological test ought to be conducted in order to verify the cure and rule out the likelihood of any residual active ingredient acting[82–83].

Urea:

● Urea has been reported to be a safe and effective treatment for skin disorders for more than a century. The organic molecule urea is created by chemically joining two amine residues with a carbonyl group. From a physiological standpoint, urea is essential for the metabolism and excretion of nitrogen-containing substances. Both a topical bacteriostatic agent and a proteolytic agent for wound debridement have been applied with urea. The precise mechanism by which urea acts on skin is still unknown, but research indicates that it causes the keratolytic and moisturizing effects of topical urea through the breaking of hydrogen bonds in the stratum corneum, the loosening of keratin in the epidermis, and the increase of water-binding sites[88-91].

● It is hypothesized that topical urea cream in conjunction with chemical nail avulsion will enhance topical antifungal therapy uptake and bioavailability. When concentrations of urea surpass thirty percent, it is considered a keratolytic agent. that improves drug penetration and promotes the avulsion of damaged nails by softening and hydrating the nail plate through the denaturing of the nail keratin[92–97].

Sertaconazole:

● An imidazole antifungal drug that exhibits potent antimycotic properties against a range of pathogens, pathogenic yeasts, and Grampositive bacteria. regular use and continuous topical agent shedding [5] It mostly has fungistic activity because of a limited concentration-dependent reduction of the de novo sterol synthesis. This prevents filamentous fungi and yeasts from using ergosterol, the most common sterol in their membranes[98,99].

● Sertaconazole reduces the production of ergosterol in direct proportion to the antifungal concentration used, just like other azole antifungal drugs. Nevertheless, because of its intricate structural composition, sertaconazole has the potential to directly damage the C. albicans cell membrane[100–102].

● Bseisoet al. [2015] synthesized and examined sertaconazole-loaded nanovesicles for transungual dispersion. The nano-penetration enhancing vesicles were created and examined using a variety of nail penetration enhancers. The formulation of the chosen nanopenetration enhancing vesicles and Dermofix cream were compared. The most effective nail penetration enhancer for vesicle inclusion was discovered to be N-acetyl-L-cysteine. The percentage of sertaconazole that could be encapsulated in vesicles ranging in size from 77 to 95%

was observed. The selected nanopenetration enhancing vesicles' formula displayed a larger zone of inhibition and a 1.4-fold increase in medication and hydration permeation into nail clippings (103).

Terbinafine:

Tanrverdi and Ozer et al. developed gel-based formulations of ethosome and liposome loaded with terbinafine in 2012. Together with evaluation testing, there were also releases in vitro and ex vivo experiments conducted. Following application of each composition, nail characterization testing revealed that the nail surface had changed, with gel formulations causing the greatest alterations. It was found that all of the formulations could efficiently distribute terbinafine to the nail. Consolidation trials revealed that the liposome poloxamer gel formulation performed best in terms of accumulation and application to the nail.

- The most common side effects of terbinafine that are documented include abnormal liver test results, rashes, urticaria, itching, and gastrointestinal (GI) problems include dyspepsia, diarrhea, and stomach discomfort.

- Terbinafine was first approved in the US in May 1996 and the UK in 1991 for the treatment of onychomycosis. In the US and Canada, onychomycosis is most commonly treated with this antifungal drug.[104–10]

CONCLUSION

The effectiveness of topical treatments for nail illnesses is hampered by the lack of knowledge on the barrier qualities of the nail and formulations to enable improved ungula delivery. This presents a significant problem in the delivery of drugs to the nail, or ungual drug delivery.Systemic medications delivered topically provide advantages, but there are more technical difficulties. The advantages that are most frequently mentioned are sustained release, convenience, and avoiding first pass. Yellow nail syndrome, paronychia, onycomycosis, nail psoriasis, and many other nail conditions can be effectively treated with medicinal lacquers. Longer contact time at the site of action is provided, and the oral toxicity of antifungal medications is avoided.The human nail's structure, disorders of the nail plate, nail formulations, methods for improving the medications' topical bioavailability throughout the nail, and the most recent developments in nail drug delivery are all covered in this comprehensive overview**.**

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REFERENCES:

1. Nikunja Basini, P., Biplab Kr, D., Sudip, D., & Subhas, S. (2012). Nail Drug Delivery System: A Review. Journal of Advanced Pharmacy Education & Research, 2(3), 101–101.

2. Malvade, P. v, Chavan, S. R., Bhagat, D. B., & Ghorpade, K. R. (n.d.). TRANSUNGUAL: THE NOVEL DRUG DELIVERY SYSTEM. www.wjpls.org,265

3. Nikunja Basini, P., Biplab Kr, D., Sudip, D., & Subhas, S. (2012). Nail Drug Delivery System: A Review. Journal of Advanced Pharmacy Education & Research, 2(3), 101–102.

4. Praveen Kumar, T., & Narayana Raju, P. (2013). Transungual Drug Delivery: A Promising Route to Treat Nail Disorders. In International Journal of Pharma Research & Review (Vol. 2, Issue 4).23

5. Feneis Heinz. Pocket Atlas of HumanAnatomy. 2000(4th ed.). Thieme. pp. 392–95. ISBN 3-13-511204-7

6. Praveen Kumar, T., & Narayana Raju, P. (2013). Transungual Drug Delivery: A Promising Route to Treat Nail Disorders. In International Journal of Pharma Research & Review (Vol. 2, Issue 4). 24

7. Preuss Marti. "Understanding Your Natural Nails" (http:/ / hooked-on-nails. com/natural nails. html). Hooked on Nails.Retrieved Feb 2010.

8. Lellipop. "Anatomy of the nail" (http:/ /www. salongeek. com/ health-safetyunnatural/ 40362-anatomy-nail. html).Salon Geek. Retrieved Feb 2010.

9. Gupta, A. K., Stec, N., Summerbell, R. C., Shear, N. H., Piguet, V., Tosti, A., & Piraccini, B. M. (2020). Onychomycosis: a review. Journal of the European Academy of Dermatology and Venereology, 34(9), 1972–1990. https://doi.org/10.1111/JDV.16394

10. Acute and chronic paronychia. (n.d.). Retrieved April 8, 2023, from https://www.researchgate.net/publication/5554216_Acute_and_chronic_paronychia

11. Maes M, Richert B, de la Brassinne M. Le syndrome des ongles verts ou chloronychie [Green nail syndrome or chloronychia]. Rev Med Liege. 2002 Apr;57(4):233-5. French. PMID: 12073797.

12. Malvade, P. v, Chavan, S. R., Bhagat, D. B., & Ghorpade, K. R. (n.d.). TRANSUNGUAL: THE NOVEL DRUG DELIVERY SYSTEM. www.wjpls.org,269

13. Onychomycosis: Potential of Nail Lacquers in Transungual Delivery of Antifungals - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Various-approaches-for-effective-transungual-drug-delivery_fig1_299513100

14. Forslind B, Thyresson N. On the structure of thenormal nail. Archiv für dermatologische Forschung. 1975 Sep 1;251(3):199-204.

15. Kobayashi Y, Miyamoto M, Sugibayashi K,MORIMOTO Y. Drug permeation through the three layers of the human nail plate. Journal of pharmacy and pharmacology. 1999 Mar;51(3):271- 8

16. Verma, N. K., Singh, A. K., Mall, P. C., Yadav, V., Jaiswal, R., Dwivedi, K. P., Gupta, A. K., & Kumar, S. (2020). Nails Drug Delivery: A Review. Scholars Academic Journal of Pharmacy, 09(04), 141–147. https://doi.org/10.36347/sajp.2020.v09i04.002

17. R Popat, R., R Rathi, A., S Adhao, V., & N Shrikhande, V. (2020). Nail drug delivery system a review. International Journal of Pharmaceutical Chemistry and Analysis, 7(1), 9–21. https://doi.org/10.18231/j.ijpca.2020.002 ,18

18. R Popat, R., R Rathi, A., S Adhao, V., & N Shrikhande, V. (2020). Nail drug delivery system a review. International Journal of Pharmaceutical Chemistry and Analysis, 7(1), 9–21. https://doi.org/10.18231/j.ijpca.2020.002 ,19

19. Dawber RPR, De Berker D, Baran R. Science of the nail apparatus. In: Baran, R. Dawber, R.P.R. (Eds.), Diseases of the Nails and their Management, 2nd Ed. Blackwell Scientific Publications, London. 1994;1-34.

20. De Berker DAR, Baran R, Dawber RPR. Normal nail anatomyand physical signs in nail disease. In: Handbook of Diseases of the Nails and their Management. Blackwell Science Ltd, Oxford, 1995a; 1-31

21. Bhowmik, D., Gopinath, H., Pragati Kumar, B., & Sampath Kumar, K. P. (2013). The pharma innovation drug delivery system-a novel approaches for drug delivery system. 1(7725). www.thepharmajournal.com

22. Christi, J. M., Aundhia, C., Seth, A., Shah, N., & Patel, S. (2017). Review on transungual drug delivery system. indo american journal of pharmaceutical research. www.iajpr.com