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TRANSUNGUAL: THE NOVEL DRUG DELIVERY SYSTEM

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ABSTRACT

The tranungual drug delivery system or nail drug delivery system is very effective on nail disorders. The transungual drug delivery is directly interact with infected part of nail and it cure infected part very rapidly as compared to oral route drugs or other any route of administration of drugs. And this drug delivery system is with minimum adverse effects on body. But after too many good things the some difficulties are also present in this system i.e. the permeability of nail is quite low which affects permeability of drug across the nail. Hence in this review article we discussed about anatomy of nail, some disorders of nail and penetration enhancing methods. The drug delivery through nail plate are used in nail plate e.g. onychomycosis, green nail syndrome, paronychia and leukonychia. The nail disorders are mainly cause due to fungal or any microbial infection. The some formulations which are generally prescribed are Ciprofloxacin, Levofloxacin, Itraconazole, and Fluconazole. The some factors also affects the penetration power of nail are molecular size of drug, concentration of nail and vehicle used in formulation. In this review article we collect the information about nail anatomy, disorders of nail, drug penetration enhancing methods and treatment on the nail disorders.

KEYWORDS: Transungual drug delivery, Nail disorders, Onychomycosis, Penetration enhancers, Micro needles.

INTRODUCTION

Transungual drug delivery system is the type of root of drug administration. The 'trans' means 'through' and 'ungual' means the nail. That is the transungual drug delivery system is related to the administrate the drug through the root of nail, which transfer the drug through the nail and shows the particular effect on the infected part of nail.[1] The nail plates responsible for the penetration of drug through it. But the nail is very hard structure very few drugs can penetrate that hard membrane to show the effect. Hence the topical drug delivery system is very effective in than the oral drug delivery system and it also have the very less side effects on body or infected part of nail. When the concentration of drug is higher in the tissue it leads to the infection of skin as well as nails also. Now days the new drug delivery system is invented that is delivery through the nail root. By this method we can easily deliver the drug from the nail to treat the fungal or infectious diseases of nails. The nail drug is delivered in the way that it makes the thin film or coating over the nail.

The nail lacquer system is also known as Film Forming System (FFS). FFS is mainly used for the topical and transdermal formulations. That FFS formulation is made from the volatile solvent, when we apply it on skin or nail the volatile solvent is get evaporated and the active ingredient form the layer on the nail or skin. The structure of film is like a polymer which releases the drug in the skin.

As the nail is very hard structure many of formulations contains the penetration enhancer's chemicals. The process of penetration is may also increase by some ways like physical, chemical or mechanical methods to increase the penetration power of drug through the hard network of keratin of the nail. The nail permeability is very important in the treatment of various disorders of nails.[2] The physicals methods for the penetration enhancing are Iontophoresis, Acid etching, Carbon Dioxide laser, Hydration and Occlusion, Electroporation, UV-light, Photodynamic Therapy, Sonophoresis, Phonophoresis .The penetration power of drug is enhanced by chemicals like sulphites, mercaptans, hydrogen peroxides, urea, water, Keratolytic agents, keratinolytic enzymes etc. And the mechanically enhancement of penetration is done by the nail abrasion and nail avulsion.[3]

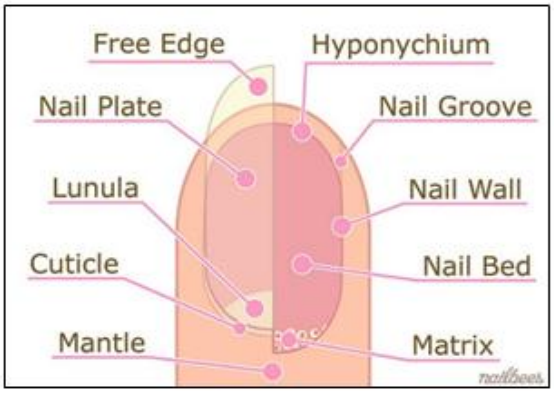
From the last two decade the scientist research over the transungual drug delivery system by physical, chemical or mechanical methods of penetration enhancing. By disarranging the dorsal surface of nail we can improve the effect of drug on the infectious part of nail.[4] The

human nails are highly susceptible to various diseases like Leuconychia, Onychauxis, and Onychatrophia etc. and may be infections cause due to bacteria, viruses or fungi. Sometimes this majorly leads to loss of appetite as well as psychological stress.[5] There are many treatments on that disorders but mainly oral drugs and antifungal treatment is given. The newly discovered techniques shows that, we can developed the more effective drug by the other root of administration such as nail drug delivery system which is also known as Transungual drug delivery system. To treat the many types of nail disorders mainly the ultrasound technique is used by which the permeability of nail is somewhat increased. The physiochemical properties of nail shows that the nail behaves more like a hydrophilic membrane. Which results into the very typical drugs can penetrate that membrane to show there effect. The topical application of drug is mostly preferred because of localised action, very less or no adverse effects and drug interaction which make patient compatible to therapy and it is also have the low cost.

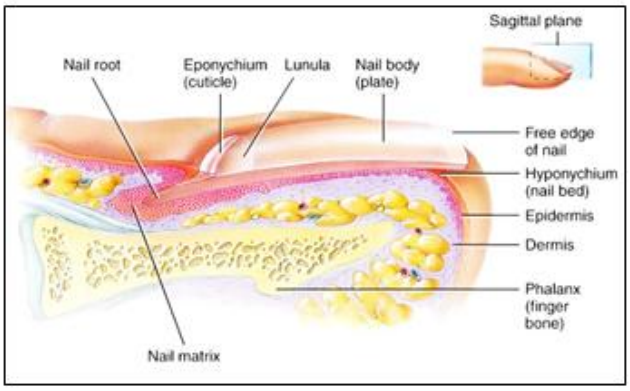
The main purpose of this review paper is to check the difficulties of drug during penetration through the nail and also to increase the availability of antiseptic and antifungal drugs. The researchers conducted on human skin and nails gives us the information about the permeability of specific drug across the skin, it also shows us the structure and functions of skin and nail in our body mechanism. But the thing is that the scientists knows very little about the nail and nail keratin properties. The purpose of this study is to understand the permeability of drug across the nail plate to treat the various nail disorders and other thing is it is also necessary to study that, the drug is goes through the systemic circulation and show effect of neighbouring target sites or infected sites.

The current situation is that the drugs do not show much more good activity on the infection because they cannot penetrate the nail plate to show the effective therapeutic effect on body. The current situations are mainly focuses on the nail permeability and to reduce the barrier across the nail plate by physical, chemical or mechanical method,[6,7] and penetration enhancers also.[8]

Anatomy of human nail



a) Outer structure of The Human Nail



b) Section of Human Nail Showing Inner parts

The nails consists of the nail plate, the nail matrix and the nail bed below it, and the grooves surrounds all the above structures.[9] The chemical composition of nail is very different from the other bod parts. It consists of many disulphide bonds. It consists of lipids. The nail is more likely to lipophilic in nature.

- **The Matrix**

The Matrix is also known as *matrix unguis*, Keratogenous membrane, nail matrix or onychostroma. It is made of tissues which provide the protection to the nail.[10] The matrix is the part of the nail bed which is present below the nail bed where the nerves and blood vessels are also present which supply the nerve impulse and blood to the nail.[11] The width of nail plate is detected by the size, length and thickness of the of the matrix. If the nail plate is flat, hocked or arched it is shown by the fingertip. The matrix produces that cells which forms the layer known as nail plate.[12] The production of nail plate layer is depend on the nutrition's and keep the nail in healthy condition.[13] As the new layer is continue forms they pushes the old layer on upper side. The old nail plate is converts into flat compressed and transparent layer. That makes the nail pinkish in colour because of presence of blood vessels below to the old nail plate.[14]

- **Nail bed**

The nail bed is the skin below to the matrix.[15] Like the skin is made up of dermis and epidermis.[16] That is the layer which is just below to the nail plate which covers the fingertip. The epidermis and dermis are attached to each other by matrix crests (*cristae matricis unguis*).[16] During the old age the matrix crests are easily visible to eyes.[12]

- **Nail sinus**

It is also known as *sinus unguis.* It is present there where the nail root is present. Nail root is the base of nail present below and behind the skin. The nail sinus is formed from the tissues made by the matrix.[10, 11]

- **The Lunula**

It is also called as "Moon" or "Small Moon". It is visible part of nail which is whitish yellow half circle shaped or half-moon shaped structure which is present at the base or root of the nail.[15] The lunula is clearly seen on the thumb and may not be seen on little finger.

- **The Nail plate**

The another name for nail plate is *corpus unguis.*[10] It is most hard part of nail made up of transparent keratin protein. It is made up of several layers of dead cells which are highly compact in nature which makes nail strong as well as flexible also.[12] The shape of nail plate is depend on the underlying bone i.e. The shape of nail plate is changes from person to person.[12] The peoples tell the nail to this visible part.

- **The Distal edge**

It is also known as free edge, *margo liber* or anterior margin. It is the margin of nail which is come out from the nail or that part which does not have contact with skin. The hyponychium also known as "quick" is the layer of epithelial cells which is located below to the nail plate and at distal edge.[17] The hyponychium forms the cover for the protection of nail bed.[16]

- **Onchodermal band**

In some peoples, the greyish coloured layer is seen known as onchodermal band. This band is present in all the peoples but in some cases it can be easily seen by naked eyes. The onchodermal band is present in between the hyponychium and the nail plate.[12]

- **The Nail root**

It is the last part of nail present in the nail sinus. It is also known as *radix sinus* or germinal matrix. It is form from the matrix tissues.[10] This par extends in the nail about several millimetre. It forms the maximum mass of the nail.

- **The Nail wall**

The nail wall is fold of cutaneous membrane which covers the both side of nails and the root of nail also. The scientific name of nail wall is "*valum unguis"*. Below to the nail wall and to both sides of nail the margin is seen known as "lateral margin" or "*margo lateralis"*.

The Hyponychium

It is another part of nail which forms the junction in between free edge and skin of fingertip. The functions of hyponychium is to form the cover over the nail and protect the nail from any infection from any type of microorganism. The other function is that to make nail water resistant.[18]

The Eponychium

The eponychium is also known as "cuticle" or "The proximal fold". The proximal fold is present at end of eponychium. Proximal fold acts as a shield over the newly formed nail bed. This layer is made up off dead cells and it is almost invisible skin.[20] It is the layer of epithelial cells which extends from nail wall to the nail root.[19] The cuticle is formed from layer of dead cells and this layer is may remove during manicure, but the eponychium is formed from layer of living cells and touching to it may cause any disorder of nail.[20] The Periyonix is the edge of eponychium which covers the strip of the lunula.[19]

The Paronychium

It is the layer of soft tissues present around the complete nail.[21] The infection of this area is known as paronychia. Paronychium is bordering of the nail formed from epidemic layer.

Growth of Nail

In mammals, the rate of growth of nail is depend on the length of last phalanges of finger. As in humans the index finger has long phalanges the rate of growth of nail is fast in index finger as compared to the little finger. In humans the hand finger nails are grows at higher rate than the leg fingers.[22]

The growing part of nail is present below the skin under the epidermis. The epidermis is only living part of the nail. In humans the average rate of growth of finger nail is about 4-5 mm (0.20 in) per month and average growth rate of toenail is about 2-3 mm (0.08 in) per month.[23] To regrow completely the finger nail requires 6-8 months and the toenail requires 16-18 months to regrow completely. The growth rate of nail is faster in the summer season as compared to another seasons.[24] The growth rate of nail is depend on the age, sex, diet, nutrition, environmental conditions, season and exercise. The nail growth rate also depend on the hereditary factor also.[25] Some researchers says that the nails grows after death but the reason behind this is when the death of person occurs the skin present around the nail is get continues shrinking due to dehydration process, hence it looks like the nails are growing. As this is slow process this took much more time.[26]

Permeability

The nail are made up of very highly complex structure of keratinized tissues. Hence the researches considered that the nails are impermeable to any type of substance, but this is not completely true. The nails are permeable to some drugs, which shows the effect on nail drugs. The interesting thing is that the nails are more permeable than the skin. The aquatic concentration in nail is about 10-15%.[27] This permeability is very useful for the penetration of drugs on nail disorders. But toxic substances are also penetrate the nail and hence they are also cause nail risks. Water can easily penetrate the nail and hence for the treatment of nail disorders the pharmaceutically active ingredient are prepared as base water. The active ingredients are such as salicylic acid, miconazole, natamycin and sodium hypochlorite.

Clinical Importance of Nails

The nail are very important for any disease manifestations. When the any person get dehydrated then the colour of nails get changed which is indication. The nails also give the indication about shock of any person.[28] That test is known as CRT (Capillary Nail Refill Test) or Blanch test. As this tests are conducted on the nails and hence this test are not suitable for old age peoples. The tests are performed by EMT (Emergency Medical Technician).[29]

The CRT test is very simple to do. This test is carried out on nail. Firstly the pressure is applied on the nail so colour of nail changes to white. After the pressure is released. Here there are two cases; first is if the colour of nail become red then you are in healthy state and if after removal of pressure if the colour is remain as it is means white then it is concluded that you are in shock.[30, 31]

The growth rate of nail and colour of nail also for the indication for many disorders and hence our ancestors also knows that thing.[32] The Beau's line present in the nail, that line is indication for ageing. The some symptoms of disorder of nail are thinning, thickening, splitting, convex nail, concave nail, white spots, decolourization, flat nail, etc. are all the indication for deficiency of various nutrients within body.

The some diseases and their indication are given below

1. Onychogryphosis- Nail become thick
2. Onychodystrophy-Nail degenerates
3. Oncholysis- Nail is detaches from body
4. Onychomycosis- Nail is infected by fungus
5. Onychocryptosis- The toe nail ingrown within skin
6. Koilonychias- The nail ridges become flat and concave
7. Psoriasis- The nail bed detaches from skin.

Function of nails in human body

Nails have many functions in human body such as the nails protect the delicate tips of finger nails and toe nails tip from any type of external injury. They exerts an opposite pressure or counter pressure on fingertip, which helps in the movement of tip and touch sensation.[9] Nails also work as a valuable tool for cutting, scraping or pinching very small particles. The main function of nail is that the helps in holding of any object by hand that is known as "extended precision function grip".[32]

Effect of different nutrients on nails

1. Vitamin A

Vitamin A is an essential micro-nutrient. The vitamin affect the many organs of our body such as eyes, reproduction and immune system also. The deficiency of vitamin A in nails can cause brittleness, dryness and increases fragility of nails.

2. Calcium and Vitamin D

The calcium and vitamin are both work in pair means they are dependent on each other. They caught the muscle contraction, maintains the body homeostasis mechanism, blood clotting mechanism and transmission of impulse through nerve cells is also do by this two nutrients.

3. Vitamin B12

Deficiency of Vitamin B12 can cause dryness of nails and dark colour of nails. Insufficient Vitamin B12 level changes the shape of nail i.e. rounded or curled nails and ridges on nails.[27]

4. Proteins

The proteins are the building blocks of our body therefore insufficient dietary protein can cause the reduce Haemoglobin level in body and due to reduced Haemoglobin level the oxygen carrying capacity of blood decreases and body suffers with anemia like condition. Resulting to this below the nails the white patches are begin to seen. In iron deficiency anemia like condition the colour of nails become pale yellow and they become fragile and shape of nails become convex.[28]

5. Fatty Acids

Not all the fatty acids are involved in skin and nail metabolism but only the essential fatty acids are play important role for healthy skin and nails. Due to deficiency of fatty acid (Linoleic Acid) the splitting or flatting of nails can occur.

Nail Diseases and Disorders

1. Onychomycosis (Tinea unguium)

Fig. 1: Onychomycosis (Fungal Infection).

The Onychomycosis is a fungal and yeast infection to the nail. The other name for this disorder is Dermatophytic onychomycosis.[29] The name Onychomycosis is given to this disorder because in this disorder the "Oncholysis" occur. The oncholysis means separation of nail plate from nail bed. The infection nail discoloration, thickening of the nail and separation of the nail from the nail bed.[30,31] In this disorder both finger nails as well as toe nails are infected.[31] The cellulitis of nails may also occur in this disorder. The fungus which cause Onychomycosis are dermatophytes, *Fusarium*, *Trichophyton rubrum* and *T.mentagrophytes*. The other causes of this disorder are athlete's foot, other nail diseases, peripheral vascular diseases and low immune power is also one of the reason to cause this disorder.[31] The diagnosis is carried out in equipped laboratory.

The treatment for Onychomycosis is not always necessary. The antifungal drugs terbinafine is very effective on this disorder but this drug has side effect on liver.[32] The mechanical method for this disorder is that to remove the infected nail. The medications for this

disorder have some antifungal drugs like Terbinafine, Itraconazole, Fluconazole, and Ketoconazole.[30] The topical agents like Ciclopirox, Amorolfine and Efinaconazole.[34]

The Onychomycosis is mainly has four types-

a. Distal subungual onychomycosis - This is most common type of Onychomycosis. The causative agent is *Trichophyton rubrum*, which occupies the space in between nail plate and nail bed.[30]
b. White superficial onychomycosis (WSO) - It is the fungal accumulation in nail plate which looks like 'White patches'. Sometimes white patches are also occurs due to the protein deficiency. Hence for diagnosis the laboratory test is carried out.[33]
c. Proximal subungual onychomycosis – This is not more common but this may occur into the immunosuppressed peoples. In this case the fungus penetrates into the newly formed nail plate.[30]
d. Candidal onychomycosis – This is occurs due to microorganism of species *Candida*. This type of onychomycosis may cause due to continuous contact of nails with water.

2. Green Nail Syndrome

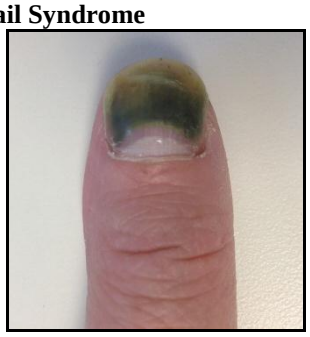


Fig. 2: Pseudomonas bacterial infection.

Green nail syndrome is also known as Chloronychia. This is an infection caused due to *Pseudomonas aeruginosa*. In this disorder the Pseudomonas bacterium get trapped in between nail plate and nail blade and it looks like green strip. If the infection is not treated on time it can separate the nail plate from nail bed. The peoples are more susceptible to this disease whose nails have always contact with moisture or water. If any person has artificial coating on nail then the infection of this disease may also cause in between artificial nail coating and natural nail bed.[35] Treatment is available on this disorder as oral dose of Quinolone (Ciprofloxacin). The topically applicable drugs are Silver Sulfadiazine, Nadifloxacin, Ciprofloxacin and Gentamicin. Some antibiotics are also have therapeutic effect on green nail such as Polymyxin B or Bacitracin.[36]

3. Paronychia Infection

Fig. 3: Paronychia Infection.

Paronychia is a fungal or bacterial infection to nails of hands or toe. The infection occurs at where the nails and skin touches i.e. at the sides of nails.

The Paronychia is mainly classified in two classes,

a. Acute Paronychia

This type of infection stars suddenly.[37] This type of Paronychia is caused due to bacteria *Candida albicans* and *Staphylococcus aureus*.[38] The infection is start with local pain, redness and swelling. The infection is last long for six weeks. The infection may cause due to trauma, injury from thorn, nail biting, finger sucking, etc.[39] The antibiotic treatment of drugs like Clindamycin (Cleocin) and combination of amoxicillin–clavulanate potassium (Augmentin).

b. Chronic Paronychia

This type of infection is long lasting and appears slowly. This was mainly caused due to continuous contact of nails with moisture. In this infection the cuticle separates form nail plate and nail plate get susceptible for infection.[40] The causative agents for chronic type of Paronychia are similar as that of acute type. The drug treatment includes combination of penicillin with cephalosporin and aminoglycosides, Acyclovir and Valacyclovir.

4. Leukonychia

Fig. 4: Leukonychia (Milky Spot).

The *leuko* means 'white' and *onyx* means 'nails'. This is the most common type of nail injury in between nail plate and nail bed. In this white line or white spot appears on one or more nails. The spot may occurs due to air bubble trapped in between nail bed and nail late due to trauma.

There are several types of Leukonychia as

1. Leukonychia totalis

As name indicates in this condition the complete nail become white. This condition is mainly causes due to the hypoalbuminaemia i.e. low albumin level in blood. The hypoalbuminaemia condition is caused due to kidney failure, liver failure and protein dysfunctioning. This is genetic type of disorder and the person having allergy from drugs of sulphonamide family can also cause this condition in that patient.

2. Leukonychia partialis

As the name indicates in this condition the some part of nail become white. If the partial leukonychia is did not treated at specific time then it leads to Leukonychia totalis.

3. Leukonychia striata

This condition is also known as transverse leukonychia or Mees' lines leukonychia. In this condition the nail become white parallel to the nail base i.e. lunula. This is mostly caused due any physical injury to nail or infection to matrix of nail. This condition cause due to heavy metal like lead, arsenic poisoning or over manicure also leads to this disorder.[41, 42] The leukonychia striata is also caused due to liver cirrhosis i.e. degeneration of liver or chemotherapy. In some cases this disorder is also genetically inherited. There is a same condition like leukonychia striata named as Muehrcke's lines (apparent leukonychia) but this is not any disorder and the white patch is easily get removed on application of pressure on nail.[43]

4. Leukonychia punctata

This is the most common type of leukonychia, which occurs in young children's and nail bitters. It caused due to trapping of air in between nail plate and nail bed and it also cause due to trauma.[44] The white spot disappear within eight months because the nail completely regrow within this time period.

5. Longitudinal leukonychia

It is not common disorder and mostly not seen in any patient. In this condition an about 1-1.5 cm white line appears on nail. For the treatment of any type of leukonychia the all nutrient level in body is checked and the necessary supplement is given.

Drug Penetration Enhancing Methods across the Nail

There are mainly three methods to increase the penetration power of drug across the nail as,

1. Physical Methods

In this method that type of agents or drugs are used which degenerates the lipid molecules present in nail plate to increase drug penetration power and its activity. The physical method for penetration enhancing is better than the chemical methods. The some physical methods are enlisted below;

1. Hydration and Occlusion

In the hydration process pore size of nail matrix is increased to enhance the penetration. Due to hydration the nails become more soft and porous. The solution which used in the hydration that solutions pH and concentration do not affect the hydration process. When the layer of skin i.e. Stratum Corneum is get saturated the penetration process of drug across the skin and nail become much faster.[45]

2. Etching

In this type of physical method the nail is exposed to phosphoric acid. The phosphoric acid increases microsporocytes. The microsporocytes increases the surface area. As the nail get etched a hydrophilic or polymer film drug delivery system is applied and due to bioadhesion the tranungual drugs are applied.[46]

3. Iontophoresis

Iontophoresis is the special type of physical method in which the electromagnetic field is applied around the skin or nail. This method is applicable in various medical and paramedical fields. By this method drug penetration through the hydrated stratum corneum is enhanced. The some other types are;

- Electrorepulsion/Electrophoresis – This is interaction in between electric field and ionic field of drug.
- Electro-osmosis – Convective solvent flow in old and newly created charge pathways.
- Permeabilization/Electroporation – Electric field induces pore induction for drug.

As compared to any other type of drug penetration enhancing method the ionotophoresis is the most preferable and convenient process for treatment of nail disorders.[47]

4. Carbon Dioxide Laser

The carbon dioxide laser method give positive result but the chances are very less. In this method the nail plate is penetrated by CO2 laser beam. By this methods the antifungal drugs are given.[48]

5. Micro Needles

It is new drug delivery system. In which the small needles are used to release the drug in stratum corneum layer of skin. This is mostly preferred because it has low pain during treatment.

2. Chemical Methods

Effect of chemicals which are used as penetration enhancer is different for different organism's nails. Some of chemicals are given following;

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

The penetration of nail lacquer through the nail is enhanced by 2-n-nonyl-1,3-dioxolane. In researches it is found that the nail lacquer containing 2-n-nonyl-1,3-dioxolane can penetrate nail seven times faster than another nail lacquer containing identical enhancer. The concentration of this chemicals should ne maintain for stopping of microbial growth within nail.[49]

2. Mercaptan compounds and n-acetyl-l-cysteine

This two drugs are used in combination because they are effective in combination to increase permeability of antifungal drug through nail. The researchers studied the penetration property of n-acetyl-l-cysteine with an antifungal drug Oxiconazole.[50]

3. Keratolytic Enhancers

Some examples of keratolytic drugs are salicylic acid, urea, etc. When the keratolytic agents are studied with

some antifungal drugs such as miconazole, ketoconazole, and itraconazole. It is seen that when the keratolytic agents are not used then this antifungal drugs doesn't penetrate the nail within 60 days long period. This keratolytic drugs can induce antimycotic penetration.[51]

4. Organic Solvents

Ethanol, isopropanol, propylene glycol, etc. are especially used in transungual drugs to enhance the penetration of active ingredient through nail. The organic solvents increases the moisture level within nail and the drug penetrate the nail.

3. Mechanical Methods

This methods have high cost and they are very painful. This method is only used by the dermatologist and nail experts. Some of the mechanical methods are discussed below;

1. Nail Abrasion

It is very painful method. In this method the thickness of nail is reduced or completely removal of nail by mechanical way to penetrate the drug. To decrease the nail plate thickness health expert use the sand paper. The abrasion of nail plate is done from the edges of nail to penetrate drug. Other way is also used by doctors i.e. drilling the nail plate and make the small hole within nail plate and they place that drug in that hole.[52]

2. Nail Avulsion

The avulsion is defined as it is an injury in which body structure is torn off by either trauma or surgery. This is very painful than the nail abrasion because in this method the nail is fully or partially removed from nail bed. When the nail is removed from nail bed then nail bed again forms the nail bed.[53] On the removal of nail plate the nail bed become very sensitive to any type of impulse or injury and hence the nail bed is still covered until new nail doesn't forms.[54] For removal of nail it is necessary to make nail soft and hence the keratolytic agents are used.

4. Latest methods in nail drug delivery system

In this methods the latest drug formulations are used such as nail lacquer, nail patches, etc. The some of the latest method are discussed below;

1. Mesoscissioning technology

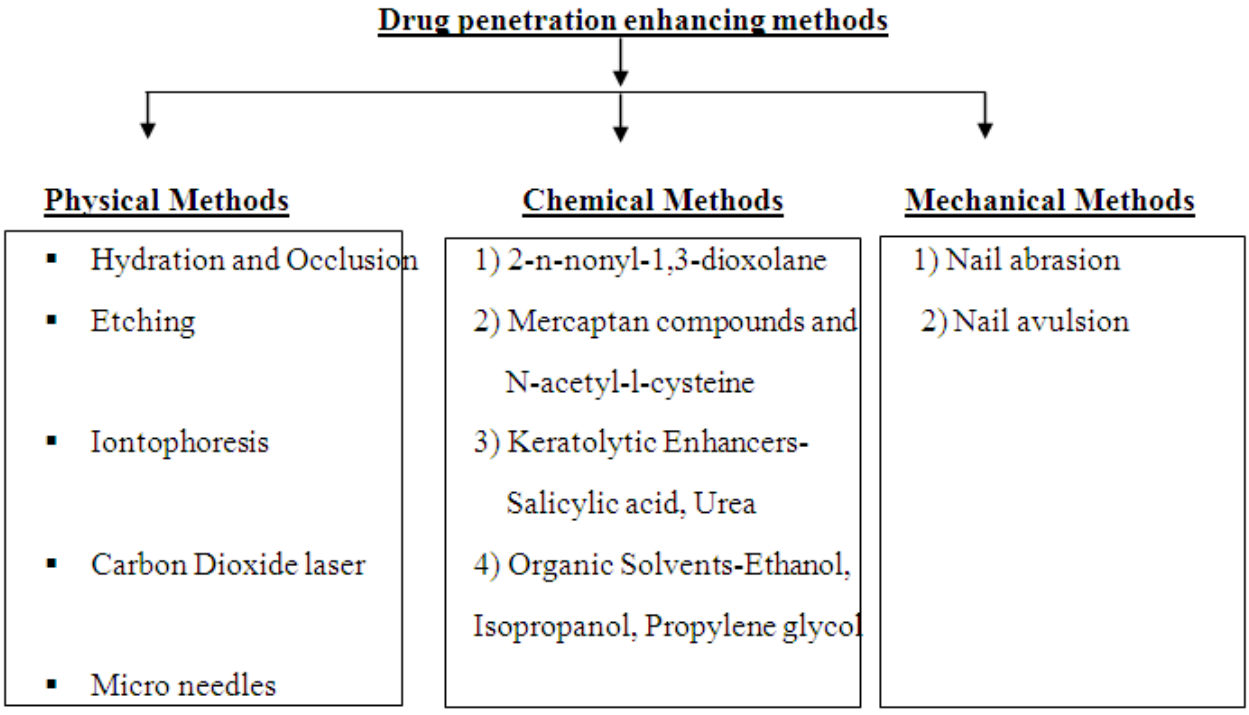
This is painless method for drug delivery. In this method firstly approximately 300-400 micron cut is given on skin or nail. This process is very fast and without any sensation of pain. The micro conduits are also used for blood glucose level testing. In nail they reduces painful pressure.[55, 56]

2. Electro Chemotherapy

It is believed that this method have the high success rate and it decreases the time period of treatment, because it is very effective. This method is similar to iontophoresis but it enhances the drug delivery.[55]

3. Nano Patch Nail fungus

In this method the drug is supplied by alternate current or direct current. Both of the currents push the active ingredient to the actual location i.e. infected area of nail by fungus. The drug is delivered over the nail membrane i.e. cuticle.[57]



Different Drugs Used in the nail disease treatment

1. Antibacterial drugs

a. Fluroquinoles

E.g. - Ciprofloxacin, Levofloxacin, Ofloxacin

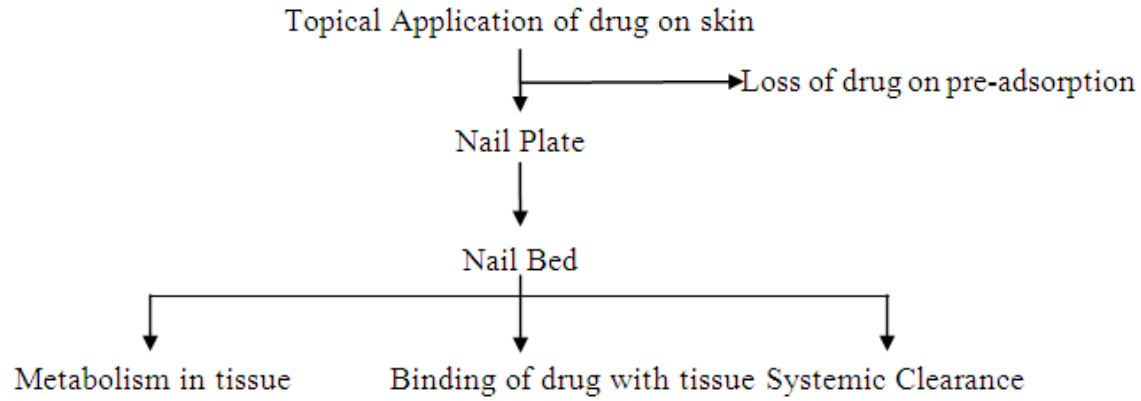
b. Antipseudomonals

E.g. - Penicillin, Cephalosporin

c. Aminoglycosides
E.g. - Amikacin, Neomycin, kanamycin, Tobramycin, Gentamycin.
d. Echinocandins & Heterocyclic benzofurans
E.g.-Caspofungin, Micafungin, Anidulafungin, Griseofulvin, etc.

2. Antifungal drugs
a. Azoles
E.g.-Itraconazole, Fluconazole, Posaconazole, Voriconazole, Ravuconazole, etc.
b. Ally amines and Benzyl amine
E.g.-Terbinafine hydrochloride, Naftifine, Butenafine.

Fate of drug applied on surface of nail



Factors affecting drug penetration through nails

1. Molecular size

The drug penetration across the nail is inversely proportional to molecular size of drug. That means that penetration of drug increases as molecular size of drug decreases. Hence the doctors always prescribes that drugs for nail disorders which have low molecular size.[58]

2. Hydrophilic and Lipophilic molecules

The lipopilic drugs penetrates the nail by lipid pathway, if the size of lipophilic drug molecule is large then it can't penetrate nail membrane. The hydrophilic pathway is completely opposite to lipophilic pathway. When the hydrophilic drug come in contact of nail the nail membrane become hydrated as result the pores of nail are get opened and drug get easily penetrate from nail.[59]

3. Nature of drug vehicle

The polar solvents like water are mainly used as a base or vehicle for transungual drugs. The water wets the nail membrane which results into swelling of keratin network present in nail. As the keratin network swells the pores get open and the drug can easily penetrate. But if the non-polar solvent is used as a vehicle then it can't hydrate the nail and the chances of penetration of drug decreases.[60]

Concentration of formulation

The concentration of formulation of drug is also affects the penetration period through nail. The weak acidic formulation rapidly penetrate nail plate but weak basic formulation can't do that.[61]

RESULT

Topical drug delivery or transungual drug delivery system is typically used for treatment of various types of nail disorders such as onchiomycosis, paronychia, etc. In the world about 3% to 4% of total population suffers with different type nail or skin disorder. The transungual drug therapy is usually applied topically to treat the nail disorders. The treatment includes antifungal as well as antibacterial drugs. The pharmaceutical formulations are mainly placed in between nail plate and nail bed. But the success rate of nail treatment is very less due to less permeability of nail. As the permeability of nail is less in market very small formulations which can successfully penetrate the nail plate and show their good effect on infected area. The penetration power of formulation is very important to treat any nail disorder. As the nail plate permeability is low it acts as a barrier to the drug.

In this review article we describe the anatomy of nail. In this paper the four diseases are briefly described which are onychomycosis, green nail syndrome, paronychia and leukonyhia. In this article various methods for the drug penetration through the nail are discussed. We also involved the factors affecting the nail permeability for drugs like molecular size, concentration of formulation, etc. the Physical, Chemical and Mechanical methods for drug penetration enhancement. The researchers need to research in this field because in this field it is needed to explore more about the nail and their disorders. The use of suitable or identical penetration enhancer should be preferred for nail disease treatment. Finally, in this review article we included all of the information which is necessary to treat nail disorders.

CONCLUSION

It is most necessary to identify the different nail barriers for pharmaceutical formulation to enhance the success rate of nail disease treatment. The more research should be done on permeability of nail plate for efficient drug delivery. Hence the drug delivery through the nail is

major challenge for doctors due to barriers. The barriers should be physical or chemical. But over the all of the above the transungual drug therapy is always better than the oral drug therapy because the effect of drug is directly on the infected part of nail. But the researchers doesn't found the specific permeability enhancer which can used in all formulations. If we want to improve the nail formulations then it is necessary to study the physiochemical properties of drug, property of penetration enhancers and final is use of formulation. It is possible in future the researchers found the best acting drug on nail disorder.

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