

Formulation and Evaluation of Terbinafine HCL loaded Nanoparticles for Transungual delivery of drug in Fungal infection

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ABSTRACT

In this review we mainly concern about the transungual delivery of drug to treat nail infection which is caused by the infection of a fungus. Transungual drug delivery is regarded as a very desirable treatment for various diseases in nail treatment due to its localized effects, which promote adherence while causing less unfavorable systemic effects. The nail is one of the toughest portions of the human body, and the nail plate presents a challenging barrier for drugs moiety to pass through. Topical medication delivery treatment is useful for treating numerous nail problems since it has localized effects, resulting in less systemic side effects and a better outcome. As compare to oral drug delivery the transungual delivery of drug is more effective it act on targeted site, increase the penetration, improve bio-availability and show rapid action. So for the transungual delivery of a drug there are many formulations such as gel, cream, patches, lotion, and nail lacquer etc. As compare to oral drug delivery the transungual delivery is viscous preparation used as a cosmetic items or to decor our nail of finger and toes. It is more stable formulation for longer use. On the basis of above conclusion nail lacquer is used in transungul drug delivery with addition of nanoparticle (drug loaded) and as cosmetic item to enhance beauty of the nail. The recent advancement on delivery of drug through nail system has lead to the development of anti-fungal nail lacquer.

Keywords: Transungual, Nail Lacquer, Porosis, Pseudomonas bacterial infection, and Onchomycosis.

1. INTRODUCTION

Pharmaceutical science investigates the quantitative and qualitative aspects of drugs and their delivery. It entails the design, development, and evaluation of drugs in conjunction with an appropriate dosage form [1]. It is a fluid and multidisciplinary discipline that seeks to integrate basic concepts of physical, organic chemistry, engineering, and biology to try to understand how to enhance drug delivery in the body and explain new and improved treatments for human diseases [1-3]. Drug delivery is a processor the method of administering an API (active pharmaceutical ingredient) to a person or animal in order to provide a therapeutic effect, as well as a system utilized as a vehicle or "carrier" for delivering a therapeutic agent/drug to the patient's body for the treatment of acute and chronic diseases. The following topical medication delivery systems are available for nail treatment [1,2,10], including:-

- i. Aerosol Foams
- ii. Dendrimer
- iii. Micro sponges
- iv. Ointments
- v. Pastes
- vi. Gels
- vii. Cream
- viii. Liniment
- ix. Nail lacquer

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2. NAIL

Nail is part of body which also used to enhance the beauty of the body and overall appeal of the women specially. Regular nail care is necessary to keep the nails in good shape and as a crucial component of grooming. They should be regular shaped and trimmed regularly $_{[3,4]}$. The general health of the nail has been found to be dependent on certain physical condition, dietary shortages of amino acids, vitamins, and some important fatty acids, as well as several other components that are essential for nail growth $_{[5,22]}$. A Diagrammatic representation of the human nail mentioned below in **Fig-1**.

2.1 Nail Health and Abnormality

- i. Hygiene
- ii. Colour of the Nail
- iii. Tip of a nail (colour /dirt)
- iv. Inflamation of the nailfold
- v. Lifting of nail plate
- vi. Thickness nail
- vii. Traumatic disease of nail origin
- viii. Discoloration



Fig. 1- A Diagrammatic representation of human nail

2.2 Anatomy of Nail

Nail form on the dorsal surface as a protective, translucent covering of the fingers and toes tips. Nail provide a protection to the finger and toes which help limit their distortion when they are subjected to various mechanical stresses, such as while running or grasping object [5.10,13].

Keratin-packed dead cells that are firmly compressed make up the nail's body. Variation in the color, form, and structure of the nail can also aid in the identification of the disease because the cells that produce the nails can be impacted by conditions regulated by the body's metabolism. In certain blood diseases, they start to function as a concave [14,28]. A diagrammatic representation of the human nail anatomy is mentioned below in **Fig-2 and 3**.

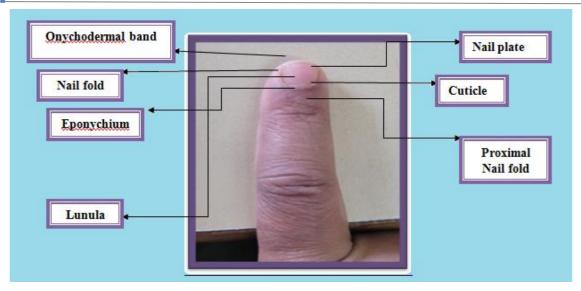


Fig-2 A diagrammatic representation of human nail anatomy.

2. Cuticle Film of the Eponychium

2.3 Composition of Nail

- 1. Nail Plate
- 3. Lunula (Half moon)
- 5. Nails root
- 7. Nail groove
- 1.1 (411 1 1410

- 4. Matrix6. Nail Bed
 - o. Nan bed

8. Lateral nail folds

- 9. Free Edge

Fig. 3 Composition of human nail.

2.4 Nail Plate

Nail is a visible and fleshy attached portion of the nail plate that covers our fingertips; it acts as a protective covering and layer that provide a support to our finger tips. The nail plate is formed by specialized cells called keratinocytes that are produced in the matrix which is laoded beneath the cuticle. These kertinocytes are become compacted and tightly packed together to form the hard and protective structure we know as the nail plate [14, 15,16]. They serve as a durable shield to protect your fingertips from external forces and Potential injuries.

- **2.4.1 Cuticle film of the Eponychium** It is a thin flatted strip of skin that overlaps and seals the base of the nail plate. Its work to protect us and act as a barrier to protect against bacteria and fungi.
- **2.4.2 Lunula** (Half moon) It refer as the half moon, crescent shape area located at the base of your nail, it does not indicate overall health or vitamin deficiencies. The Half moon on your finger, often referred to as the lunula is not actually a separate structure itself, It is an area that is visible beneath the cuticle and is in charge of creating new cells from the nail plate The lunula's size and appearance can differ from person to person and even alter over time due to factors such as heredity, nail development rate, and individual characteristics [7,8,11, 12].
- **2.4.3 Matrix** The matrix is the area beneath your cuticle that produces new cells for nail growth. It plays an important function in establishing the shape and thickness of your nails
- **2.4.4 Nail root** It is situated in the beneath of the skin at the base of each fingernail or toenail where it is grow from specialized cells in the matrix region [5, 13, 14]
- **2.4.5** Nail Bed It is located just below the nail plate and extends from the root to the free edge of the nail, delivering nutrients for adequate development.
- **2.4.6 Hyponychium** It refers to soft tissue located underneath each free edge of your nails near its tip, it act as a barriers against external elements [6,13,14].
- **2.4.7 Nail Grooves** It is a small grooves depression on either side of each fingernail or toenail. They help the nail plate to provide stability and it do not grow back.
- **2.4.8 Lateral Nail folds** Nail folds is the folds of the skin surrounding your nails from 3 sides, they help to direct the growth of the nail plate, they also provide support to the nail plate and help to protect the delicate nail bed and its surrounding tissue from external damage.
- **2.4.9 Free Edge** The free edge is the part of your nail that extends beyond your fingertip or toe tip.

2.5 Disease related with Nails

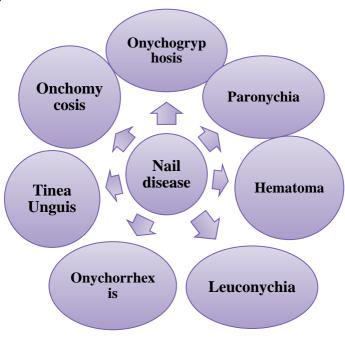


Fig no.4 Disease related with nail.

3. TRANSUNGUAL DRUG DELIVERY

Transungual delivery of drug is a technique for getting the medication to the nail plate for drug administration. It is preferred for treating nail diseases as mentioned above in **Fig-4** because it has fewer systemic side effects, better adherence to the targeted site, and localized effects_[28] We can also say that transungual delivery of drug refers to the movement of drugs across the nails to receive a targeted drug delivery for the treatment of nail disease. Bacteria and fungus are among the many microorganisms that often inhabit our bodies. Some of these are very beneficial to our systems, while others might cause

illnesses. Fungi can grow over the dead tissues/cells of the hairs and nails. Nail infections are typically caused by prolonged exposure of the nail to warm, moist conditions. The primary pathway for drug entry is the nail plate $_{[8,9]}$. To treat nail infections, a variety of traditional formulations are available, including gel, cream, nail lacquer, and oral antifungal. We consider the fact that "trans" means "through" and "unguis" means "nails" when studying transungual medication delivery. In other words, a transungual drug delivery system is simply a technique that involves delivering a medication through the nail to treat disorders of the nail itself. The nail's hardness and impermeability make it an unreliable channel for medication administration. Topical therapy, on the other hand, is highly desirable due to its localized effects, which may result in less unpleasant systemic reactions and improved adherence. Drug penetration through the nail plate is one of the barriers to absorption. Only a small portion of the topical medicine goes through it. because of low absorption, leading to low bioavailability $_{[8,9,10]}$. As a result, the therapeutic concentration is not achieved adequately. Taking into account the structure and physiology of barriers is essential for the effective delivery of APIs across the nail. To more efficiently deliver the appropriate quantity of medication to the appropriate location at the appropriate time $_{[28,28,30]}$.

3.1 Advantages and Disadvantages of transungual drug delivery

3.1.1 Advantage:

- a) One of the benefits is that the fabrication of formulation is easy comparison to other like Electrical techniques, Radio-frequency thermal Ablation, Tape stripping etc.
- b) It enhances the Patient compliance because of easy to apply.
- c) It more useful for the patients who cannot take systemic medications.
- d) It helpful in preventing drug-drug interactions in elderly patients taking multiple medications Prevent systemic negative effects.
- e) It is a topical preparation, it is simple to remove.
- f) Useful for both beautification and treatment, demonstrating dual properties.

3.1.2 Disadvantage:

- a) Transungual treatment take a prolonged time to work.
- b) Some time nail lacquer (transungual treatment can be ineffective because of the nail keratin content.
- c) Disruption of the nail surface with the penetration enhancer may also cause some time

4. NAIL LACQUER

Human fingernails or toenails can be decorated and protected by using nail lacquer, commonly referred to as nail varnish or nail enamel. As mentioned below in **Fig-5 and 6**. The recipe has undergone numerous revisions to improve its aesthetic qualities, make it safer for consumers to use, and prevent peeling or cracking. Nail paints aren't just for enhancing appearances [29,30]



Fig-5 Use of nail lacquer

Nail lacquers have been long used as cosmetics to protect or adorn nails. One novel form of formulation that has been utilized for transungual drug delivery is medicated nail lacquers. The biggest and most crucial category of manicure preparation is nail lacquer. The water and air impermeable membrane that the nail lacquer covers the nail with lasts for days and is typically the only thing that can be removed .Nail lacquers have been used to protect the nails. This new family of formulations, often known as medicated nail paints, has been used for transungual drug administration. In addition to being safe for infections of the skin and nails, model nail lacquer should be easy to use and convenient to apply. When stored, it should remain stable for a long time and, with the right solvent, generate an acceptable nail film [31,36].

In order to create the antifungal lacquer, the film-forming polymer was first dissolved in a suitable solvent while being stirred, either with or without heat, depending on the polymer. The plasticizer was added to the solution while stirring once the polymer had completely dissolved. The active ingredient was then introduced after the drug solubilizer, which was constantly stirred. The formulation was then finished by adding the permeation enhancer to the solution while stirring and letting it dissolve [32].

4.1 Properties

- 1. It shouldn't be bad for the nails and skin.
- 2. It should be simple to use and convenient.
- 3. It ought to be stable when being stored.
- 4. It should form a suitable nail film.
- 5. Product should be long lasting to use.
- 6. The product should produce a good and satisfactory film.

4.2 Essential ingredients of nails Lacquer

- **4.2.1 Film formers** It is a combination of recipients that form a smooth and shiny film or layer on the nail plate, in appearance its hard and water proof system example nitrocellulose, cellulose acetate, Ethyl cellulose [26,39].
- **4.2.2 Resins** It can be a solid or highly viscous liquids, they can be natural and synthetic and often used in adhesives ,vanishes and food additives. It should be help in reducing the tendency of nitrocellulose to shrink; it gives good luster to nail film for examples Santolites.
- **4.2.3 Solvents** Solvent are normally volatile organic liquid that combine all the ingredients of lacquer and make a homogenous viscous preparation. It dissolves the non volatile constituents.
- **4.3.4 Plasticizers** A plasticizer is a substance that is added to a material to make it soften and more flexible to increase its plasticity, to decrease its viscosity, and also decrease friction during its handling for example Diethyl phthalates.
- **4.3.5 Pigments** It is a compound that are intensely colored and used to color the other material. Basically it is used to add color, they are nearly insoluble and chemically unreactive in water or any other medium.

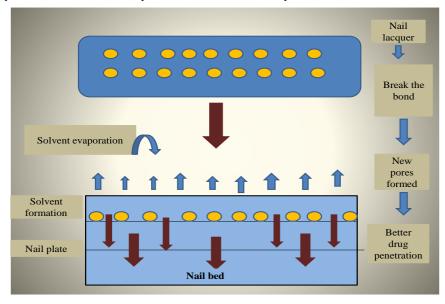


Fig-6 Function of Nail Plate

4.4 Advantages

- 1. It is difficult to remove with rubbing or water washing. A initial coat of lacquer offers protection for 7-8 days, and the effect lasts for a long time.
- **2.** By modifying the lacquer formulation's solvents, polymer, and plasticizer, the release and diffusion rate can be conveniently optimized.
- **3.** The preparation process is simpler than with an oral dose form.
- **4.** Systemic side effects are either negligible or nonexistent.
- **5.** Considering nail pharmacokinetics, only a very small fraction of oral drug reaches the nails.

4.5 Factors affecting nail permeation

4.5.1 The compound's molecular size or diffusing species:

As the molecular weight rises, the permeability coefficient falls. Drug molecules must therefore be tiny and free of electric charge in order to have the best transungual penetration.

4.5.2 Ionization level:

Compared to their non-charged counterparts with permeability coefficients, ionic chemicals are less permeable through the nail plate.

4.5.3 Hydration of nail plate:

The amount of nail plate hydration is a key determinant for determining medication penetration into the nail..

4.5.4 An intact dorsal layer is present:

Overlapping cells are the most effective barrier to drug penetration over the nail plate. If this layer has partially or completely penetrated the medication.

4.5.5 Drug binding to keratin and other nail components:

Nails are made of keratin, which is thought to have a PI of around 5 and is hence positively and negatively charged at pH values below and above this value. Depending on the charge of the molecules, it can attach to or repel them. This could explain why ionic compounds have lower nail permeability.

4.5.6 Nail thickness and disease status:

The thicker the nail, the more difficult it is for medications to enter the nail bed.

4.5.7 Type of vehicle:

It is believed that replacing water with a non-polar solvent that does not hydrate the nail may minimize medication absorption into the nail plate. As mentioned below in **Fig-7** and Various type of drug formulations with their related excipient uses are mentioned in **Table-1** and **2**.

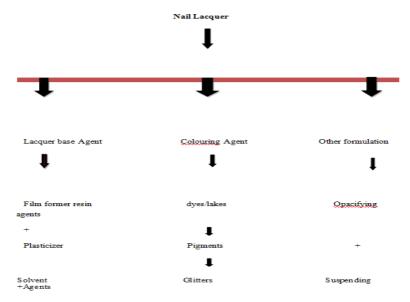


Fig-7 Nail lacquer composition

Table no.1- Different marketed preparation of antifungal nail lacquer.

S.no	Formulations	Name of Product	Drug used	Indications	Pharmaceutical companies
1.	Nail Lacquer	Penalc	Ciclopirox	Psoriasis , Onychomycosis	Dermik Laboratories Inc., Berwyn
2.	Nail Lacquer	Ciclopirox 8%	Ciclopirox	Psoriasis, Onychomycosis	Vers Pharma Incorporeted
3.	Nail Lacquer	Curanail 5%	Amorolfine	Psoriasis, Leuchonychia, Melanonychia	Galderma Swizaland
4.	Nail Lacquer	Eco nail	Econazole(5%) +SEPA 18%	Onychomycosis, Onchodystrophy, Onychogryposis	MacrochemCo- operation, Newyork
5.	Nail Lacquer	Amorolfine	Amorolfine 5 % w/v	Onychomycosis	Made in India
6.	Nail Lacquer	Loceryl	Amorolfine 5% w/v	antifungal	Galderma , India
7.	Nail Lacquer	Cico 8%	Ciclopirox 8 %w/v	Psoriasis	Brinton Pharmceutical Pvt. Ltd
8.	Nail Lacquer	Loprox	Ciclopirox	Psoriasis	Aventis Parma Ltd s. (Mumbai, India)
9	Nail Lacquer	Ciclopoli	Ciclopirox (8%	Onychomycosis, Psoriasis	Polichem SA (Pazzallo, Switzerland)

Table no-2 Various drug formulations with their related excipient uses.

S.N.	Drug	Formulation	Excipient used	References
1.	Terbinafine hydrochloride	Nail Lacquer	Eudragit® RL100, Eudragit® RS100, HPMC E15, 2-Mercaptoethanol , N-acetyl-L-cysteine , thioglycolic acid, PEG 400, ethanol	Patel and Vora (2016)
2.	Amorolfine hydrochloride	Nail Lacquer	Eudragit RL, triacetin, ethyl alcohol, ethyl acetate, ethylcellulose	Charyulu et al. (2017)
3.	Oxiconazole	Nail Lacquer	Nitrocellulose, ethylcellulose, salicylic acid, ethyl alcohol, propylene glycol	Nikhath and Sanjana (2022)
4.	Cissus quadrangularis	Nail Lacquer	Nitrocellulose, ethyl cellulose salicylic acid, ethyl acetate, dibutyl phthalate, acetone	Shubhangi Bhausaheb et al(2022)
5.	Econazole nitrate	Nail Lacquer	Ethanol, eudragit RL, PEG-400, 2-mercaptoethanol, HPMC, urea	Puri et al. (2022)

4.6 Evaluation of Nail Lacquers

Evaluation of nails lacquer is divided into two parts as mentioned below in Fig-8.

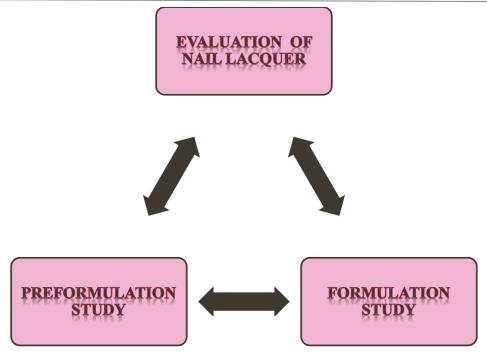
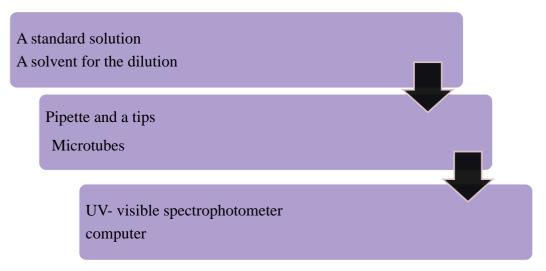


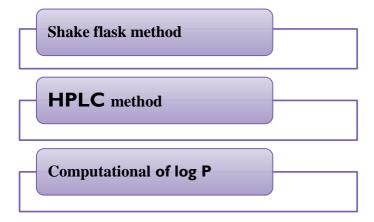
Fig. 8 Evaluation of nail Lacquer

- **4.6.1 Preformulation:** Preformulation is the study of the chemical and physical property of a drug formulation prior to the compounding process of a formulation. The main reasons of the study is to understand the physical and chemical characteristics of each components during manufacturing. The main purpose of the study is to established a physicochemical relationship between new drug substances and also establish drug excipients compatibility to know the pharmacokinetic of the drug [36,38].
- **4.6.2 Calibration curve** It is sometimes referred to as the standard curve, or simply put, it is a method of determining an unknown substance's concentration by comparing it to that of a standard or known component. A calibration curve illustrates how the material's concentration alters the analytical signal or instrumental response.

The following is required in order to create a calibration curve.



- **4.6.3 Solubility:** Solubility study is done by choosing a suitable solvent to dissolve the drug or a amount of a substance that dissolves in a given solvent at a specific pressure and temperature.
- **4.6.4 Partition coefficient:** The ratio of a compound's concentration in a mixture of two immiscible phases at equilibrium is known as the partition coefficient (P) or distribution coefficient (D). It can be measured by using following method [38,39,]



4.6.5 Compatibility: Compatibility test for formulation is a process that assesses how a products formulation interact with its packaging and other materials. The purpose of this test is to confirm the safety and quality of the product of drug and also help to predict the stability of the drug product and prevent the unwanted issues related with the product [26,36].

5. EVALUATION OF FORMULATION

Some important evaluated Parameters are as follows [28,39].

- 1. Evaluation of Non Volatile contents
- 2. Evaluation of Gloss
- 3. Rate of drying
- 4. Color of the product
- 5. The smoothness of the film is tested
- 6. Test for the hardness of the film
- 7. Test for resistance of water permeability
- 8. Test for Adhesive property.

5.1 Non-volatile content:

The test is used to determine how much non -volatile material is present in the formulation .The technique called the dish method uses a straightforward procedure that is show below.



First the sample is spread on a flat plate as a circle of 8 cm in diameter .Then the quantity is weighed and kept in an oven at a temperature 1050 for 1 hr



Then the quantity of substance remaining substances in the plate is weighed arid this constitutes the non-volatile content.

5.2 Gloss:

works on the principle of reflection of light.



The gloss of the product can be determined by the use of an instrument.



This test is done in order to check the rate of evaporation of these Preparation.



It involves a simple procedure in which the film is applied with an applicator on a completely non-porous surface.



Then the drying time is noted by kepting it at 25° C and 50% RH•

5.3 Rate of Drying:

This test is performed in order to check the rate of evaporation of the formulation



It is a simple procedure which involves placing the film on a completely nonporous surface using an appropriate applicator.



After maintaining it at 50C and 50% relative humidity ,and drying time is recorded . If nothing sticks to the tip of your finger when you contact it , the product is said to be fully dry.

5.4 Color of the Product:

The color of the tested product is compaired with, a standard color.



Then comapred both the tested and standered product by applying it both the adjecent nails.



by this comparison, the contrast in both the nail colours can be easily noted

5.5 Test for film Smoothness:

The most crucial aspect of the formulation is its smoothness microscopic research can be used to examine this surface quality.



under a microscope, this should also not exhibit the orange peel apparence.



These should not be any foreignobject or coating material particles in the film .

5.6 Test for the film hardness:

The test is applied for the determination of the hrdnesse of the substance



It is done by spread out the film on glass plate and dried at 25°C.for 48 hours.



It is then further dried for 2 hrs at70°C.



then it is cooled for 48 hrs at 25°C.



then applying external mechanical force for checking the hardness.

5.7 Test for resistance to water permeability:

This test evaluates the film's resistance to water absorption to do this



On the surface of a metal plate, a continous layer is applied ,after the plate submerged in water



then noted the immersion of the film before and after the application.



It is calculated that the weight will increase ,the water resistance increase with decreaseing weight rise .

5.8 Test for adhesive property:

The purpose of this test is to gauge how well the film adheres to the adhering substances. This is accomplished using the following technique



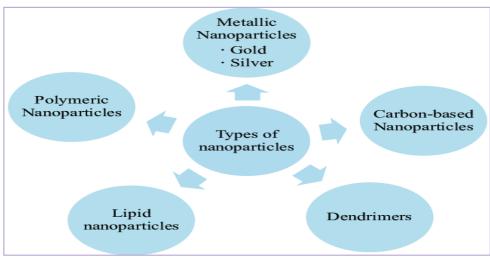
Then use a metal surface to spread out the film and settle for some time.



The adhesion character of the film is then determined by measuring the mechanical force which is applied externally to remove the film.

6. NANOPARTICLES

The nanoparticles are the spherical polymeric particles which are composed of natural or artificial polymer. The size range of these macromolecule particles is 10–1000 nm. Over the past few decades [16, 18], there has been an increasing interest in creating biodegradable nanoparticle formulations for efficient and effective drug delivery. These particles offer a broad range of possible invocation due to their spherical form and high surface area to volume ratio. A successful nanoparticle system must have a high drug loading capacity because it facilitates the administration of fewer carriers overall [19]. The Pharmaceutical nanotechnology has focused on treating diseases at the molecular level and provided more precise diagnostics [24,27]. The antigen associated with diseases including cancer, diabetes, and neurological diseases can also be identified, as can the virus and microorganisms responsible for the infection. Size reduction is one of the main uses in pharmacy since drugs in the nanoscale size range work better in a variety of dose forms. One example of this process is whereby nanoparticles are being developed to assist the transportation of chemotherapy drugs directly to cancerous growths, as well as to deliver of drugs to the areas of arteries that are damaged in order to fight cardiovascular disease. The various types of Nano particles are mentioned below in **Fig-9**.



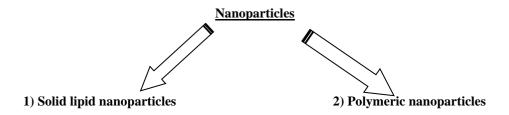
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Fig. 9 Types of nanoparticles

6.1 Types of Nanoparticles:-

Liposome Micelles

NanocapsulesNano suspensionNanoemulsionMicrosphereMicrocapsulesMicro pelletsMicroemulsionNanosphere



6.2 Advantages of Nanoparticles in Pharmacy

- a. Increased the surface area.
- **b.** Enhanced solubility of the drug .
- c. Increased rate of dissolution of the drug.
- **d.** Increased the bioavailability of the drug.
- e. Less amount of dose required & reduces the chance of loss of the doses and drugs.
- f. It provides Protection of drug from degradation.
- g. Have more rapid onset of therapeutic action on the targeted site.
- **h.** Achievement of drug targeting.

6.3 Characterization of Nanoparticles

6.3.1 Particle size

The size of NPs assist a significant position in their cellular uptake rate. Smaller NPs often have better cellular uptake due to their increased surface area-to-volume ratio, allowing for more interactions with cells. This size-dependent internalization mechanism can impact how NPs are processed by the body, affecting factors like their *in-vivo* circulation half-life. The sizes for developing NPs for in-vivo applications are between 10 and 1000 nanometers. This size range is relevant to their patterns of clearance and distribution within living organisms [8]. SEM and TEM images gauge particles and clusters, while laser diffraction techniques evaluate bulk samples in a solid state [19]. Reducing the size of NPs leads to a larger surface area, enabling faster drug release. However, this can lead to the aggregation of smaller particles during the transportation and storage of nanoparticle dispersion.

6.3.2 Shape

Most NPs designed for drug delivery typically exhibit a spherical morphology. In certain instances, it has been observed that spherical Nanoparticles demonstrate a more significant and swifter rate of endocytos when contrasted with Nanoparticles of rod or disk shapes [28,29].

6.3.3 Surface charge

It plays a crucial role in their interaction with cells and uptake. NPs with positive charge tend to undergo greater internalization due to the ionic interactions between positively charged and negatively charged cell membranes. This phenomenon significantly affects their interaction with cells [8]. Typically, a zeta potentiometer is employed to assess the surface charges and their dispersion stability in a solution [19]. Measuring the zeta potential enables us to predict the storage stability of colloidal dispersions. To ensure stability and prevent particle aggregation, it is essential to attain high zeta potential values, whether positive or negative.

6.3.4 Surface area

The Nanoparticle's surface area plays a crucial role in its characterization. The surface area to volume ratio significantly impacts the Nanoparticle's performance and properties. Surface area measurement is typically conducted through BET analysis. The extensive surface area of Nanomaterials provides sample opportunities for diverse applications, and the most effective method for evaluating the surface area of Nanoparticles is the Brunauer-Emmett-Teller (BET) technique, which relies on the principles of adsorption and desorption according to the BET theorem

6.3.5 Non volatile content

Taking \pm 0.2 grams of a sample in a glass Petri dish of about 8cm in diameter. Then samples were spread equally with the help of a trade wire. The dish was placed in the oven at 105 ± 2 degrees centigrade for 1hour. After 1 hour the Petri dish was removed, cooled and weighed. The differences in the weight of a sample or drug sample after drying were calculated [42].

6.3.6 Film formation and Drying time

A film of the drug sample was applied on the surface of a glass Petri dish with the help of a brush. Noted the time to create a dry-to-touch film by employed a stopwatch.

6.3.7 The flows and smoothness of the film

The sample was poured to approximately 1.5 inches height and spread on a glass plate and made to rise vertically.

6.3.8 Glossiness

The gloss of the film was visually seen by applying it over the nail and a glass plate, comparing it with a standard marketed nail lacquer.

6.3.9 Water resistance

This is the measure of the resistance towards water permeability of the film. This was done by applying a continual film on a surface and immersing it in water. The weight before and after immersion was noted and the increase in weight was calculated. Higher the increase in weight it lowers the water resistance [41,42].

6.4 Quality control and Evaluation

- 1. Viscosity
- 2. Glossiness
- 3. Solid content
- 4. Color matching with lab standards
- 5. Brush ability and Drying rate
- 6. Test of setting and adhesion Suspending agents

7. CONCLUSION

The Presented review is an attempt that concluded that the research over past one decade has been focused on improving the permeability of the drug through nail plate in transungual formulation by mean of chemical treatment, penetration enhancer and by using chemical and physical methods. On the basis of above conclusion nail lacquer is one of the formulation in transungul drug delivery which is a part of noval drug delivery system with the addition of nanoparticle (loaded with the drug) and as cosmetic item to enhance beauty of the nail and provide a effective medical treatment also. The recent advancement on transungual drug delivery system has lead to the development of antifungal nail lacquer. Transungual drug delivery has experienced a healthy annual growth rate of 25%, which outpaces oral drug delivery (2%) and the inhalation market (20%). This figure clarify that transungual drug delivery system offers various advantages, including self-administration, comfort, and virtually no interaction with the GI.

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REFERENCES

- [1] Rathi R Apeksha, Popat Ritesh R, Adhao S Vaibhav, Shrikhande N Vinayak; Nail drug delivery system a review; International Journal of Pharmaceutical Chemistry and Analysis, 2020;7(1):2-21.
- [2] Verma Surender, Singh Renu and Ashima; Transungual drug delivery a pivotal remedy in onychomycosis; Journal of Chemical and Pharmaceutical Research, 2016, 8(4):370-381.
- [3] Rajendra B Vivek, Baro Anjana, Kumari Abha, Dhamecha L Dinesh, Lahoti R Swaroop, Santosh D. Shelke D Santosh; Transungual Drug Delivery an Overview; Journal of Applied Pharmaceutical Science 2012: 02 (01); 203-209.
- [4] Nikam. K Vikrant, Kotad . B Kiran, Gaware. M Vinayak, Dolas.T Raamdas, Kiran B Dhamak3, Sachin B Somwanshi1, Khadse . N Atul, Vivekanand A. Kashid . A Vivekanand; transungual drug delivery system: a review; pharmacologyonlin 2011(1)126-139
- [5] Sharma Lalit, Mehan Navneet, Chouhan Ritika, Anjali Suman, Kumar Vaibhav, KM Rekha, Kumar Kunal and Kumar Naman; Current review on nail drug delivery system and their future perspectives; World Journal of Biology Pharmacy and Health Sciences, 2024, 19(01), 337-349.
- [6] V. Aneesha, S.Gopi, Jose Jaison Rasel, S. Karan, M. Snehadevi, Jeevanandham Dr. S, and Akshara V.Anil; formulation and evaluation of herbal antifungal nail lacquer for the treatment of onychomycosis; world journal of pharmaceutical research; 2024; vol 13, Issue 1.
- [7] Chandra Ram, Kumar Sandeep, Aggarwal Ashutosh; Evaluation of Nail Lacquer; Indo Global Journal of Pharmaceutical Sciences, 2012; 2(4): 379-382.
- [8] Vejnovic, I., Simmler, L., Betz G., "Investigation of different formulations for drug delivery through the nail plate", International Journal of Pharmaceutics, 2010, 386, 185-194.
- [9] Kesharwani Roohi, Sachan Anupam, Singh Swati, Patel Dilip; Formulation and Evaluation of Solid Lipid Nanoparticle (SLN) Based Topical Gel of Etoricoxib; Journal of Applied Pharmaceutical Science Vol. 6 (10), 2016;124-131.
- [10] Upadhyay Prerna, Kaur Manjit, Choudhary Akanksha, Kujar Shaina, Nita. Dr. Transungal Drug Delivery System: A Review on Bharti Gupta; Int. J. Pharm. Sci. Rev. Res., 57(2), 2019; 50-56.
- [11] Muthukumar .M, Prabhu R, Rajeev. T, Arunpandiyan J, Thaila R, Jayalakshmi B, Senthilraja M.; Formulation Development of Antimicrobial Nail Lacquer by Transungual Delivery System for the Treatment of Paronychia; International Journal of Pharmaceutical Sciences Review and Research; 2023; 167-175
- [12] Bhattacharjee Bedanta, Dey Nikita, Barman Dhunusmita, Karmakar Arka, Ahmed Nasima; Understanding the drug delivery through nails: a comprehensive review; Journal of Drug Delivery & Therapeutics. 2021; 11(4):116-131
- [13] Azhar Danish Khan, Ayan Giri, Lubhan Singh; transungual drug delivery: a newer approach; world journal of pharmacy and pharmaceutical sciences; 2014; vol 3, issue 3
- [14] Kumar T. Praveen, Raju P. Narayana; Transungual Drug Delivery; A Promising Route to Treat Nail Disorders; International Journal of Pharma Research & Review, 2013; 2(4):22-33.
- [15] Vaghasiya Harshad, Kumar Abhinesh, Sawant Krutika; Development of solid lipid nanoparticles based controlled release system for topical delivery of terbinafine hydrochloride; 2013, Volume 49, Issue 2, 311-322.
- [16] Julia A. Balfour & Diana Faulds ; Terbinafine; A Review of its Pharmacodynamic and Pharmacokinetic Properties, and Therapeutic Potential in Superficial 1992, Volume 43, 259–284.
- [17] Aditya K. Gupta MD, , Neil H. Shear MD; Terbinafine: An update Journal of the American Academy of Dermatology; 1997, Volume 37, Issue 6 , 979-988.
- [18] Abobakr E Fatna ,Fayez M. Sahar, Elwazza S.Vivian , Srkran Wedad; formulation and optimization of terbinafine hcl solid lipid nanoparticles for topical antifungal activity; international journal of pharmacy and

- pharmaceutical Sciences; 2019 Vol 11.
- [19] Tiwari S, Mistry P and Patel V; SLNs Based on Co-Processed Lipids for Topical Delivery of Terbinafine Hydrochloride; Journal of Pharmaceutics & Drug Development; 2020 Volume 2 227-234.
- [20] Fatma E. Abobakr, Sahar M. Fayez, Vivian S. Elwazzan, Wedad Sakran; Effect of Different Nail Penetration Enhancers in Solid Lipid Nanoparticles Containing Terbinafine Hydrochloride for Treatment of Onychomycosis; AAPS PharmSciTech; 2021;22:33.
- [21] Bhapkar P.H, Puttewar T.Y, Patil .R.Y, Nail Lacquers in Nail Diseases, IOSR Journal Of Pharmacy; 2013; Issue 9; Volume 3; 24-48.
- [22] Deshmukh.S Priya, Kadam .A Aniket; Drug Delivery through Nail Bed A Novelistic Platform; Ijppr.Human, 2022; Vol. 23 (4): 472-491.
- [23] Yadav.Vikas, Srivastava1.Viashal, Dwivedi Karunakar Parsad, Singh. Ravindra, Yadav. Anku Verma. Kumar Navneet; A review on disease of nails (fungal infection), diagnosis & treatment (nail lacquer); World journal of pharmacy and pharmaceutical sciences; 2022; Volume 11, Issue 10; 663-694.
- [24] Verma. Surender, Shweta Rani. Shweta, Yadav. Akash; A review on an emanation of nail lacquer in the management of nail disorders; World Journal of Pharmaceutical Research; 2020; Volume 10, Issue 1, 870-898.
- [25] Rathi1 .R. Apeksha, Popat. .R .Rutesg, Adhao. S. Vaubhav , Shrikhande. N. Vinayak; Nail drug delivery system a review; International Journal of Pharmaceutical Chemistry and Analysis; 2020;7(1);9-21
- [26] Salunke Pramod Rutuja, Ingale Vilas Minal, Shinde Dadasaheb Nikita, Pingale Rajendra Vaishnavi and Kumbhar Umesh Akanksha; a comprehensive review on nail lacquer; World Journal of Pharmaceutical; 2023 Volume 12, Issue 9, 2378-2390.
- [27] V. Malvade V. Pratik . , Chavan . R .Sayli , Bhagat . B Dhanashri , Ghorpade . R. Komal ; transungual: the novel drug delivery system ; World Journal of Pharmaceutical and Life Sciences; 2020, Vol. 6, Issue 6, 265-274
- [28] Sharma .Sonal , Chopra Hitesh , Pahwa Rakesh, Talha B. Emran B. Talha ; Novel transungual drug delivery system for treating Onychomycosis ; International Journal of Surgery 2023; 109; 2145–2147
- [29] Pradnya Suryabhan , Gaikwad Rutuja V. Pagare; An Overview on Transungual Drug Delivery System; transungual drug delivery: a newer approach ; International Journal of Pharmaceutical Research and Applications ;2023 Volume 8;464-478
- [30] Zahra Salehi & Masoomeh Shams-Ghahfarokhi,; Mehdi Razzaghi-Abyaneh; Antifungal drug susceptibility profile of clinically important dermatophytes and determination of point mutations in terbinafine-resistant isolates; European Journal of Clinical Microbiology & Infectious Diseases; 2018; 37;1841–1846
- [31] Tiwari S, Mistry P and Patel V; SLNs Based on Co-Processed Lipids for Topical Delivery of Terbinafine Hydrochloride; Journal of Pharmaceutics & Drug Development; 2014; V 2; 2348-9782
- [32] Duong An-Van, Nguyen Linh Thao-Thi, Maeng Joo- Han; Preparation of Solid Lipid Nanoparticles and Nano structured Lipid Carriers for Drug Delivery and the Efects of Preparation Parameters of Solvent Injection Method, Molecules 2020, 25, 4781
- [33] Fireman.Sharon, Toledano.Ofer, Neimann.Karine, Loboda. Natalia & Dayan .Nava; A look at emerging delivery systems for topical drug products, Dermatologic Therapy, 2011, Vol. 24, 477–488
- [34] Katare Om Prakash., Raza Kaisar, Singh Bhupinder, Dogra .Sunil ;Novel drug delivery systems in topical treatment of psoriasis; Rigors and vigors;Indian Journal of Dermatology, Venereology, and Leprology November-December 2010 Vol 76 Issue 6
- [35] Soni Abhishek , Jamwal Shalini . , Kumar Arvind., Thakur Shivani, Kumari Kiran; preformulation study of terbinafine for novel drug delivery system formulation ; International Journal of Research and Analytical Reviews ; September 2020, Volume 7, Issue 3
- [36] Kumar T. Praveen, Raju P. Narayana; Transungual Drug Delivery: A Promising Route to Treat Nail Disorders; International Journal of Pharma Research & Review, April 2013; 2(4):22-33
- [37] Kishun Jai, Ankur Srivastava Ankur, Vikash Chandra Vikash, Vishal Srivastava Vishal, Singh Ravindra, Navneet Kumar Verma Navneet kumar; In-vitro evaluation of an anti-fungal nail lacquer containing miconazole nitrate; neuroquantology; sep 2022; volume 20; issue 11; 2699-2714
- [38] Kumar B. Sravan , Kumar T. Praveen , Himabindu V and Eswaraiah M. Chinna ; formulation and evaluation of bi layer nail lacquer containing antifungal drug for the treatment of onychomycosis ; World Journal of Pharmacy and Pharmaceutical Sciences; 2020; Volume 9, Issue 7, 2191-2203

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- [39] Pati Nikunja Basini , Dey Biplab Kr , Das Sudip , Sahoo Subhas1; Nail Drug Delivery System: A Review; Journal of Advanced Pharmacy Education & Research ;2012 2 (3) 101-109 (2012) ISSN 2249-3379
- [40] Mali Audumbar Digambar, Bathe Ritesh and Patil Manojkumar; An updated review on transdermal drug delivery systems; International Journal of Advances in Scientific Research; 2015; 1(06): 244-254
- [41] Raj R. Arun, Kurian Nithin; Formulation and Evaluation of Transungual Drug Delivery of Fluconazole Using Permeation Enhancers Screened by Hydration of Nail Plate; Research & Reviews; A Journal of Pharmaceutical Science 7006; Volume 8, 2229-7006
- [42] Bukke Sarad Pawar Naik , Venkatesh Chandrakala , Rajanna Sowmyashree Bandenahalli , Saraswathi Tenpattinam Shanmugam , Kusuma Praveen Kumar , Goruntla Narayana , Balasuramanyam Nitin , Munishamireddy Shilpa ; Solid lipid nanocarriers for drug delivery design innovationsand characterization strategies a comprehensive review; 16 April 2024