WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.453
Volume 15, Issue 1, 271-290. Review Article ISSN 2277–7105

ENGINEERING TERBINAFINE-LOADED NANOSPONGES FOR NEXT-GENERATION ANTIFUNGAL DRUG DELIVERY: A COMPREHENSIVE REVIEW

Thurupu Sowmya*[1], Dr. Shoaeb Mohammad Syed[1]

[1]Shri Venkateshwara University, Gajraula, Amroha, Uttar Pradesh, India.

Article Received on 29 Nov. 2025,
Article Revised on 20 Dec. 2025,
Article Published on 01 Jan. 2026,

https://doi.org/10.5281/zenodo.18092865

***Corresponding Author**
Thurupu Sowmya
Shri Venkateshwara University,
Gajraula, Amroha, Uttar Pradesh, India.

How to cite this Article: Thurupu Sowmya*, Dr. Shoaeb Mohammad Syed. (2026). Engineering Terbina fine- Loaded Nanosponges For Next-Generation Antifungal Drug Delivery: A Comprehensive Review. World Journal of Pharmacy and Pharmaceutical Sciences, 15(1), 271–290.

ABSTRACT

Fungal infections persist as a major health challenge worldwide with a significant portion of the affected population being those whose immunity is compromised and patients suffering from skin diseases. On the other hand, although various antifungal agents are already in the market, the therapy really is hard to handle due to drug solubility being poor, bioavailability being limited, systemic toxicity being high, and patient compliance being low in conventional dosage forms. Terbinafine, which is a commonly prescribed allylamine antifungal agent, has strong but not limited to a particular group of dermatophytes due to its fungicidal activity; however, the biopharmaceutical limitations like low aqueous solubility and variable absorption do not allow its full therapeutic efficacy. The use of nanotechnology-based drug delivery systems has become the most recent strategy to tackle these challenges. To mention one, nanosponges have turned into hot topics because of their resounding porous structure, large drug-loading capacity, release regulation and stability. Nanosponges not only overcome the poor solubility, low rate of dissolution and sporadic delivery of lipophilic drugs like terbinafine but also increase antifungal efficacy and decrease side effects at the same time. This all-encompassing review not only assesses the function of nanosponges as an advanced drug delivery medium for terbinafine critically, but also reveals the particulars of their structure, mechanisms of drug incorporation, release characteristics, and applications in antifungal therapy. Furthermore, the review addresses formulation aspects, evaluation

criteria, and future perspectives while at the same time inferring the translational capability of terbinafine-loaded nanosponge systems for the forthcoming generation of antifungal treatment.

KEYWORDS: Terbinafine, Nanosponges, Antifungal therapy, Drug delivery systems, Nanotechnology, Controlled release.

1. INTRODUCTION

The growing global health problem, fungal infections are comprised of a variety of infections starting from the superficial ones affecting skin, hair, and nails to the more serious ones that could eventually lead to death, termed systemic mycoses. The list of causes for the increasing prevalence of fungal diseases includes but is not limited to, prolonged antibiotic use, immunosuppressive treatments, organ transplants, and the growing number of chronic diseases. The several antifungal agents that are available for clinical use do not provide a solution for the problem of fungal infections that is still being limited by drug resistance, poor pharmacokinetic profiles, systemic toxicity, and noncompliance of the patient with treatment. These challenges are a strong indication of the need for new and advanced drug delivery methods that would not only make the treatment more effective but also lessen the side effects.[1,4]

Terbinafine is the most potent allylamine antifungal drug that is used extensively to treat dermatophyte infections, especially onychomycosis and cutaneous mycoses. The fungus killing ability, in this case, is the inhibition of squalene epoxidase, the enzyme that takes part in ergosterol production and in the end, leads to the death of the fungus by breaking down its cell membrane.[5,6] In spite of the fact that terbinafine is highly antifungal potent, it is not always the case that its clinical effectiveness is determined by its poor aqueous solubility and limited bioavailability especially when it comes to the use of conventional dosage forms. These restrictions require the use of higher doses or longer treatment that may cause systemic side effects and thus, lower patient compliance as a result.

Pharmaceutical nanotechnology's progress has paved the way for new solutions for the conventional antifungal formulations' drawbacks.[7,8] Along with other techniques, nanoparticles, solid lipid carriers, liposomes, and nanoemulsions have successfully contributed to making the solubility, stability, and targeted delivery of antifungal agents. Of

these, nanosponges have become a very good drug delivery system due to their three-dimensional, porous polymeric structure that can hold a diverse range of drug molecules.

Nanosponge drug delivery systems are characterized by a network made of nanosized cavities that can trap both types of drugs, lipophilic and hydrophilic. With this, controlled and sustained drug release can be achieved while the drug and the environment are separated. The unique structural characteristics of nanosponges make them remarkably fit for the delivery of the poorly soluble drugs like terbinafine. By drug solubility enhancement and release rate control, nanosponge-based systems promise a win-win for the antifungal efficacy, dosing frequency reduction, and systemic toxicity minimization.[9,10]

This review intends to give an all-encompassing view of the terbinafine-loaded nanosponges which are considered as an advanced drug delivery system for the treatment of fungi. It describes the constraints of the traditional formulations of terbinafine, the basic concepts of nanosponge technology, and the merits of the nanosponge-based delivery system in improving the efficacy of the antifungal drugs. Moreover, the review covers the major factors related to formulation, the criteria for evaluation, and the future research directions, thus underlining the relevance of the translational aspect of the technology in today's antifungal therapy.

2. Overview of Antifungal Drug Delivery Systems

The delivery of antifungal drugs has been based on the use of conventional dosage forms such as tablets, capsules, creams, ointments, and topical solutions. Despite these formulations being the ones most commonly applied in clinical settings, they are normally not very successful due to the issues of poor drug penetration, low bioavailability, drug clearance and side effects associated with high doses. These drawbacks are especially prominent when treating chronic and recurrent fungal infections, where lengthy therapy is necessary for total pathogen eradication.[11,12]

Suboptimal oral antifungal formulations very often suffer from poor dissolution in water and a large extent of first-pass metabolism, leading to inconsistent absorption in the body. The result could be that the drug levels at the infection site are below the therapeutic range and thus the treatment has a greater chance of failure. Topical formulations, on the other hand, while being preferred for external fungal infections, still have the problems of not sufficiently permeating the skin and getting lost quickly at the site of action, hence they require frequent

application and will likely lead to the problem of noncompliance on the part of the patient.[13,14]

As a result of the above-mentioned problems, new drug delivery systems have been developed for antifungal treatment. The advanced methods of drug administration are aimed at the elevation of drug solubility, enhancement of stability, release control or sustained release, and high drug concentration at the site of infection coupled with minimal systemic exposure. In recent times, nanotechnology-based drug delivery systems have become widely recognized for their capacity to alter pharmacokinetics and enhance therapeutic outcomes.[15] Numerous kinds of nanocarriers, including metallic nanoparticles made from polymers, liposomes, solid lipid nanoparticles, emulsions, and lipid carriers, were tested for antifungal drug delivery purposes. Such systems provide certain benefits like drug solubilization, improved permeability across the barriers of biological systems, and drug protection from decay. A number of research works have shown that nanoscale carriers can double the antifungal efficacy of poorly soluble drugs by increasing their dissolution rate and availability. Out of these systems, the one called nanosponges is the most advanced one but it is still considered a relatively new class of nanocarriers because these are characterized by a porous three-dimensional polymeric network. Conventional nanoparticles are basically relying on surface adsorption or matrix entrapment for their delivery but, in contrast to them, nanosponges are fully encapsulating the drug molecules through inclusion or adsorption mechanisms because of their internal cavities. Their distinctive structural feature allows nanosponges to provide controlled and prolonged release of drugs, while at the same time, maintaining high drug-loading efficiency levels. The multifunctionality of nanosponges renders them to be an excellent choice for antifungal drug delivery, mainly for lipophilic drugs like terbinafine. Through the enhancements of solubility, stabilization of the drug, and gradual release, the delivery systems based on nanosponge have the potential to not just cope with the limitations of conventional antifungal formulations but also boost therapeutic efficacy.

Table 1: Comparison of Conventional and Nanotechnology-Based Antifungal Drug Delivery Systems.

Delivery System	Key Characteristics	Limitations	Advantages
Conventional oral formulations	Tablets, capsules, suspensions	Poor solubility, first-pass metabolism, systemic side effects	Ease of administration

Conventional topical formulations	Creams, gels, ointments	Poor skin penetration, frequent dosing	Localized delivery
Polymeric nanoparticles	Solid colloidal carriers	Limited drug loading, burst release	Improved stability and bioavailability
Liposomes	Phospholipid vesicles	Physical instability, leakage	Enhanced penetration and targeting
Solid lipid nanoparticles	Lipid-based nanocarriers	Drug expulsion during storage	Controlled release
Nanosponges	Porous polymeric network	Formulation complexity	High drug loading, sustained release, improved solubility

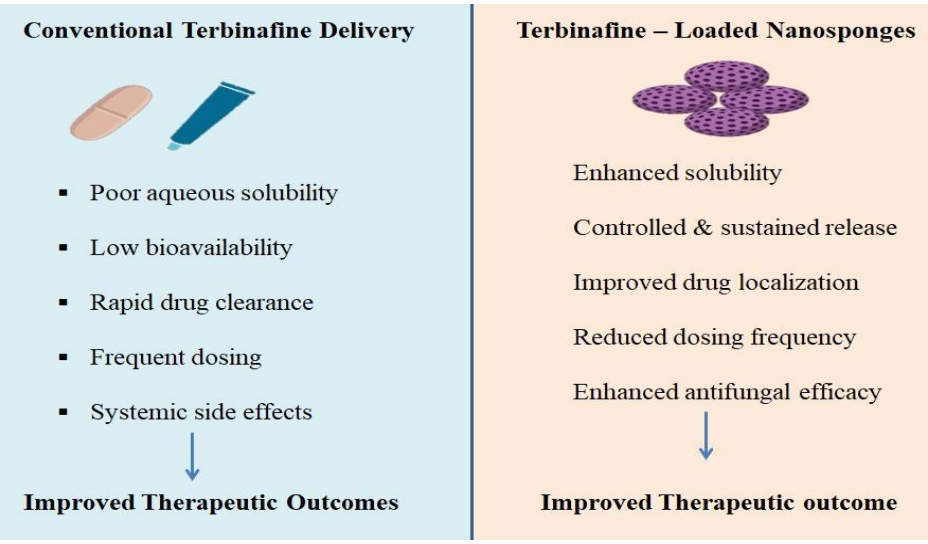

Figure 1: Schematic representation of challenges in conventional antifungal therapy and advantages of nanosponge-based drug delivery.

3. Terbinafine: Drug Profile and Delivery Challenges

Terbinafine is a man-made allylamine antifungal agent used worldwide for the treatment of superficial fungal infections. The drug is mainly dermatophyte, that is, it occurs in skin, hair and nails, hence being one of the most effective drugs in dealing with dermatophytes, besides being widely prescribed for tinea corporis, tinea pedis, and onychomycosis. The powerful anti-fungal effect of terbinafine notwithstanding, its use is limited due to challenges that arise from formulation- and delivery-related factors that hinder its clinical efficiency.

3.1 Chemical Structure and Physicochemical Properties

Terbinafine hydrochloride is a chemical compound with the name (E)-N-(6,6-dimethyl-2-hepten-4-yn-1-yl)-N-methyl-1-naphthalenemethanamine hydrochloride. It belongs to the class of lipophilic compounds, which means that it has high affinity for membranes and low

solubility in water. The drug has a very high partition coefficient (log P ≈ 5.9), which tells that it is extremely hydrophobic and this is the reason that it dissolves poorly in gastrointestinal fluids and consequently, only a small amount is absorbed systemically after oral administration.[16,17]

Terbinafine's water solubility deficit is one of the main reasons for the difficultly in its formulation, since oral bioavailability of lipophilic drugs is mainly dependent on dissolution rate. The same property also causes the drug to be ineffective in topical formulations, where the lack of shift through the stratum corneum may not make the drug available at the site of infection.

3.2 Mechanism of Antifungal Action

Initially, the major part of the mechanism of action of terbinafine is the selective inhibition of the enzyme squalene epoxidase, which is a very important part of the ergosterol biosynthesis pathway in fungi and it is only in the fungal cells. Inhibition results in the depletion of ergosterol that constitutes the fungal cell membrane and the accumulation of toxic levels of squalene within the fungi. The dual mechanism brings about the breaking down of the membrane and results finally in the death of the fungus, thus making the drug terbinafine fungicidal rather than fungistatic. The reason behind the selective affinity of terbinafine for fungal squalene epoxidase over the mammalian one is that it is a contribution to its good safety profile. Nevertheless, the achievement and maintenance of the drug's effective concentrations at the target site is still a major limitation of the conventional dosage forms.

3.3 Pharmacokinetics and Biopharmaceutical Limitations

Terbinafine taken orally is subject to the metabolism in the liver which comprises almost complete first-pass metabolism and is done mainly through the cytochrome P450 complex. It is true that it gets good tissue distribution and that especially in the keratin-rich areas like skin and nails, but its oral bioavailability is limited and variable hence causing the drug to have poor solubility and go through metabolic degradation. When long-term oral therapy is used, one of the problems is that in such cases, therapeutic outcomes may not be achieved especially with nail infections, thus increasing the risk of systemic side effects like hepatotoxicity and gastrointestinal disturbances.

Topical formulations of terbinafine are the first choice for treating fungus only on a small scale. However, the penetration of the drugs through the skin barrier is very limited, so the

effectiveness is often troubled. The stratum corneum, the outermost layer of the skin, is the main barrier that limits the permeation of the drug and the patient is required to apply the cream frequently to create a continuous therapeutic level. Furthermore, uneven distribution of the drug at the site of application and rapid loss of the drug from the site are some of the drawbacks of conventional topical formulations.

3.4 Need for Advanced Drug Delivery Approaches

The challenges regarding biopharmaceutical properties of terbinafine clearly highlight the necessity for advanced drug delivery systems that would be capable of not just solubility enhancement but also bioavailability improvement and providing sustained drug release. The delivery strategies that are novel in nature target to optimize the localization of drug at infection site and at the same time reduce systemic exposure and related adverse effects. The nanotechnology-based systems for the delivery of drugs have opened up new possibilities to quite a large extent in this area through improved behavior of dissolution, enhancement of permeation and controlling the release of antifungal drugs.[18,19]

Considering the lipophilic character of terbinafine, it would be an advantage to use nanocarriers that are able to encapsulate the lipophilic drugs and control their release rates. The nanosponges, with their unique structure and ability to hold large amount of drugs, provide a very good platform for overcoming the solubility and delivery limitations of terbinafine. The process of entrapment of the drug in the internal cavities of the nanosponges will increase the dispersion of the drug in water, keep the drug safe from deterioration and also make the drug exhibit its antifungal properties for a longer period of time.

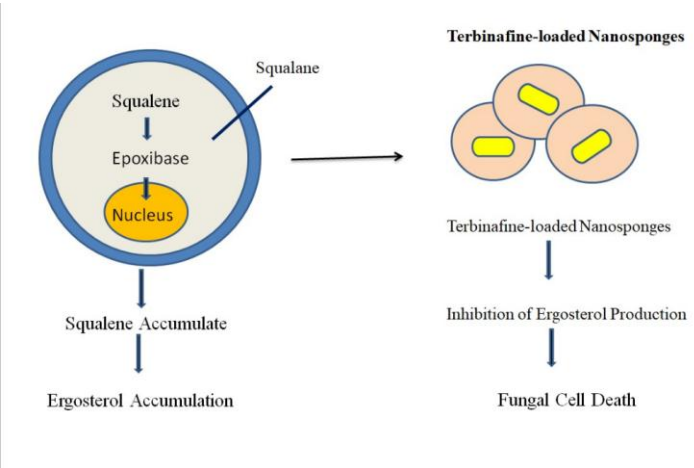

Figure 2: Mechanism of action of terbinafine and its interaction with fungal cell membrane.

4. Nanotechnology in Antifungal Drug Delivery

The application of nanotechnology in pharmaceutical sciences has revolutionized drug delivery by enabling the design of carrier systems that operate at the nanoscale, typically ranging from 1 to 1000 nm. These systems offer unique physicochemical and biological properties that are not achievable with conventional formulations. In antifungal therapy, nanotechnology-based drug delivery systems have emerged as effective tools to address challenges such as poor solubility, limited bioavailability, rapid drug degradation, and inadequate penetration into infected tissues.[20]

Nanocarrier-based drug delivery systems enhance antifungal therapy primarily by increasing drug solubilization, protecting the drug from environmental and enzymatic degradation, and facilitating controlled or targeted drug release. Due to their small size and large surface area, nanocarriers can interact more effectively with biological membranes, leading to improved permeation and retention at the site of infection. This is particularly beneficial for lipophilic antifungal drugs such as terbinafine, which exhibit limited aqueous solubility and variable absorption.[21,23]

Different nanocarrier systems have been studied for antifungal drug delivery, such as polymeric nanoparticles, liposomes, nanoemulsions, solid lipid nanoparticles, nanostructured lipid carriers and dendrimers. Every system has unique advantages and limitations regarding drug administration. Polymeric nanoparticles are characterized by their higher stability and controlled release while lipid-based carriers are superior in drug solubilization and making drugs pass through membranes. Nevertheless, the widespread use of these systems in clinics has been limited by reasons like drug leakage, physical instability, and challenges related to scaling-up.

One of the principal reasons for the extensive investigation of nanoemulsions in topical antifungal delivery application is their ability to augment skin penetration and to provide rapid effect. Nevertheless, these benefits are not without a cost; they usually go hand-in-hand with the need of high amounts of surfactants used for the formulation, which may lead to skin irritation and thus restricting the long-term usage. Similarly, the case of liposomal formulations which although effective in augmenting the antifungal efficacy may still face problems of stability and high production costs.

Among the new alternatives, the nanosponges are a novel and very promising option to the conventional nanocarriers. In contrast to solid nanoparticles or vesicular systems, nanosponges are made of a porous polymeric network that can trap the drug molecules in nanosized cavities. This peculiar design results in a high drug loading capacity, increased stability, and controlled drug release. Nanosponges can hold both hydrophilic and lipophilic drugs, thus they are versatile carriers for antifungal agents having diverse physicochemical properties.[24,25]

The sustained drug release and improved aqueous dispersibility properties of nanosponges m ake them especially useful for antifungal treatment, where drug by fungal pathogens prolonge d exposure is often necessary. Besides, the use of nanosponge systems can also lower the number of doses and reduce the probability of systemic toxicity, thus patient compliance and the success of therapy can be increased.

Table 2: Nanocarrier Systems Explored for Antifungal Drug Delivery and Their Key Advantages.

Nanocarrier System	Structural Characteristics	Advantages in Antifungal Delivery	Limitations
Polymeric nanoparticles	Solid polymer matrix	Sustained release, improved stability	Limited drug loading
Liposomes	Phospholipid vesicles	Enhanced penetration, biocompatibility	Physical instability
Nanoemulsions	Oil-in-water nanosystems	Improved solubility and skin permeation	High surfactant requirement
Solid lipid nanoparticles	Solid lipid core	Controlled release, low toxicity	Drug expulsion
Dendrimers	Branched polymeric structures	High drug loading, targeting	Toxicity concerns
Nanosponges	Porous polymeric network	High encapsulation, sustained release, stability	Formulation complexity

5. Nanosponges as an Advanced Drug Delivery Platform

Nano-sponge is a new class of ultra-small drug delivery systems that are characterized by a very porous and three-dimensional polymeric network that can hold a huge amount of different kinds of drug molecules. The main difference between conventional drug-loaded nanoparticles and nano-sponge is that the latter holds the drug in its internal pockets also through inclusion, adsorption, or complexation mechanisms, which is the same as the drug-stocking process. This unique property of nanosponges makes them particularly good for delivering drugs that are poorly soluble in water and lipophilic like terbinafine.[26,28]

5.1 Concept and Structural Characteristics of Nanosponges

Nanosponges are synthesized by linking polymers in such a way that they form a hard yet porous network with nano-sized holes. This quality enables a wide variation of the drug's loading capacity and releasing mechanism depending on the mix of the polymers and cross-linking agents chosen. The porous structure of nanosponges allows them to hold drug molecules inside while at the same time keeping their size at the nanoscale, thus making them easily dispersible in water.

One of the most researched and pronounced types of nanosponge systems is cyclodextrin-based ones owing to their biocompatibility, biodegradability, and aptness for forming inclusion complexes with hydrophobic drugs. Though, polymeric nanosponges made from natural or synthetic polymers have also been recognized for their capability and modifiable physical-chemical properties. The hard nature of the nanosponges acts as a barrier around the drug protecting it from being degraded through light, heat, or chemical reactions, thus maintaining the drug's stability even during the storage and administration periods.[26]

5.2 Drug Loading Mechanisms

The process of drug loading into nanosponges primarily takes place either through the physical entrapment in the porous structure or through very weak chemical interactions like hydrogen bonding, van der Waals forces, and hydrophobic forces. The factors affecting the efficiency of drug loading include drug solubility, mycological size, the composition of the polymer, and the degree of cross-linking. Lipophilic drugs with the right molecular size can be easily trapped in the nanosponge cavities, thus high encapsulation efficiency and uniform drug distribution can be achieved. The internal spaces of nanosponges serve as reservoirs for the drug and release the drug slowly over a long time. This release pattern minimizes the initial burst effect that is generally seen with traditional nanoparticles and makes it possible to maintain the level of drug concentration at the target site that is needed for therapy. For antifungal treatment, where drug given over a long time is necessary to completely kill the fungus, such controlled release is particularly beneficial.[27,28]

5.3 Drug Release Behavior

The release of active substances from nanosponges is a complex process involving the simultaneous action of diffusion, erosion, and desorption. The active substance is released from the cavities of the nanosponges into the biological fluids in a controlled manner. The rate of release can be affected by changing parameters like the type of polymer, density of

cross-linking and size of the particle. With such flexibility, it becomes possible to create nanoconfiguration-based systems that can offer instant, prolonged, or deferred release the way it is required for the disease treatment. Sustained release from nanosponges, in the case of antifungal drug delivery, can keep the drug concentration at an effective level for a long time, and this will consequently lead to a decrease in the frequency of medication and an increase in the patient compliance. In addition, the controlled release of the drug will also manage the plasma drug levels to a certain extent, thus, it may help to eliminate the adverse effects that are related to the dose in the case of conventional formulations.

5.4 Advantages of Nanosponges Over Conventional Nanocarriers

Nanosponges are indeed a better option than the conventional nanocarriers among the likes of liposomes, polymeric nanoparticles, and nanoemulsions by all means. The drug and nanocarrier permeation is restricted through their rigid and porous structure. This is one of the reasons why drug leakage in such cases is not uncommon. Moreover, in contrast to vesicular systems, nanosponges are not easily subjected to aggregation or fusion in case they are stored for a long time, hence their shelf life is prolonged. On the other hand, the usage of these nanocarriers can be done in the case of both hydrophilic and lipophilic drugs which increases the number of pharmaceutical agents that can be administered through them.

In drug delivery, nanosponges represent a highly compatible combination with several routes of administration. Among those, oral, topical, and transdermal deliveries are the major ones. The increased solubility of the drug, the protection of the unstable drug, and the sustained release are all handled by the nanosponges thus making them an advanced platform for antifungal drug delivery which is particularly true for drugs with poor biopharmaceutical properties like terbinafine.[29,30]

6. Terbinafine-Loaded Nanosponges: Formulation and Performance

The use of terbinafine in nanosponge-based delivery systems has become a trend that contributes to overcoming the drug's inherent biopharmaceutical issues. Terbinafine being a poor water-soluble and highly lipophilic drug makes it a perfect candidate for the nanosponges' porous structure encapsulation. The internal spaces of the nanosponges function as a microenvironment that not only solubilizes the drug but also protects it from degradation and delivers it in a controlled manner, thereby improving the effectiveness of the antifungal agent.

6.1 Rationale for Nanosponge-Based Delivery of Terbinafine

The standard terbinafine drugs usually take a long time to get rid of the illness, especially in chronic fungal infections. The long treatment periods may cause severe side effects in the patients and lead to non-compliance with the therapy. Nanosponge-based systems eliminate these issues by providing a constant drug release and better drug supply to the infection site. The large surface area and porous nature of the nanosponges speed up the dissolution of terbinafine, which is one of the key factors determining the drug's bioavailability.

Moreover, the nanosponge systems can restrict the drug action to the specific area of application, especially in topical or transdermal uses, hence reducing the amount of drug entering the bloodstream and thus, minimizing the side effects. Controlled and localized delivery is a great advantage in antifungal therapy because the fungus at the infection site has to be exposed to the drug for a long time in order to be killed.[31]

6.2 Formulation Approaches

Terbinafine-loaded nanosponges are usually made by employing methods like solvent evaporation, emulsion-solvent diffusion, or cross-linking techniques, according to the type of polymeric network used. The choice of formulation parameters such as polymer type, cross-linker concentration, and drug-to-polymer ratio has an important impact on the size of the particles, the efficiency of encapsulation, and the release behavior of the drug. The process of formulation optimization has resulted in the development of formulations with high encapsulation efficiencies, which reflect a strong affinity between terbinafine and the nanosponge matrix. The tiny size of the terbinafine-loaded nanosponges aids in their dispersibility and even drug distribution. Moreover, the rigid framework of nanosponges inhibits drug crystallization, which in turn eases dissolution and ensures uniform drug release profiles.

6.3 Drug Release and Antifungal Performance

The ability to provide controlled and sustained drug release is one of the most important benefits of the terbinafine-loaded nanosponges. In vitro release studies have shown a continuous release pattern that is significantly longer than the case with conventional terbinafine formulations, which leads to a conclusion of effective drug retention in the nanosponge cavities. The sustained release behavior helps in maintaining the therapeutic drug concentrations for a longer time, which is vital for antifungal treatment.

Terbinafine formulations based on nanosponge have shown to possess even stronger antifungal activity against the usual fungal strains like Trichophyton rubrum and Candida albicans. The reason for this better result is the synergistic effect of the factors like increased solubility of the drug, longer exposure to the drug and better interaction with the cell membranes of the fungi. The implications of the results are that delivery systems based on nanosponges can potentially be used for better antifungal treatment**.**

6.4 Comparison with Conventional Terbinafine Formulations

Terbinafine-loaded nanosponges outperform conventional oral and topical formulations in solubility enhancement, controlled release, and antifungal efficacy. While conventional formulations frequently show quick drug release and reduced retention at the infection site, nanosponge systems give prolonged release and better drug localization. All these benefits could lead to lower dosing frequency, higher patient compliance, and less systemic toxicity.

Table 3: Reported Studies on Terbinafine-Loaded Nanosponges and Their Key Outcomes.

Study Focus	Type of Nanosponge	Key Findings	Outcome
Solubility enhancement	Polymeric nanosponges	Significant increase in aqueous solubility	Improved dissolution
Controlled release	Cross-linked nanosponge systems	Sustained drug release up to 24 h	Prolonged antifungal effect
Topical delivery	Nanosponge-based gel	Enhanced skin retention	Reduced dosing frequency
Antifungal efficacy	Terbinafine nanosponges	Increased zone of inhibition	Superior antifungal activity

7. Role of Nanosponges in Enhancing Antifungal Therapy

Nanosponges are essential in solving the problems related to traditional antifungal drug delivery systems. They are different from other drug delivery systems because of their special porous structure, large surface area, and capacity to hold the drugs that are not easily dissolved. In the case of terbinafine, the therapeutic efficacy of nanosponge technology is enhanced considerably because of the resolution of critical issues concerning solubility, release control, and drug localization.

7.1 Improvement in Drug Solubility and Dissolution

Poor aqueous solubility is one of the main problems associated with terbinafine therapy, leading to low dissolution and absorption. However, nanosponges can overcome this problem by trapping terbinafine in their tiny cavities, thus, it will disperse the drug in the water very

well, and consequently, the increased solubility will lead to a faster dissolution rate that is a very important factor for antifungal potency especially in the case of oral and topical formulations.

7.2 Controlled and Sustained Drug Release

The use of nanosponges allows for a controlled and sustained release of terbinafine which is essential for the maintenance of therapeutic concentrations of the drug over a long time. The sustained release leads to a lower frequency of administration, which in turn results in better patient compliance. For antifungal treatment, the long-lasting presence of the drug is necessary for both preventing the return of the infection and ensuring the complete death of the fungal pathogens.

7.3 Enhancement of Antifungal Efficacy

Research has confirmed that nanosponge-based formulations of terbinafine have better antifungal properties than traditional formulations. Among the reasons for the increased potency are the solubility increase, longer drug residence time at the infection site, and larger interaction of the drug with fungal cell membranes. These factors together result in larger inhibition zones and better suppression of fungi.

7.4 Reduction in Dose-Related Side Effects

The systemic exposure to Terbinafine, together with the associated adverse effects such as hepatotoxicity and gastrointestinal disturbances, will be minimized through the use of nanosponges in localized and controlled drug delivery. The safety advantage brought by the use of nanosponges is especially critical in the case of long-term antifungal therapy, where the cumulative toxicity, eventually becoming an adherence problem and unfulfilled treatment, might be a consequence.

8. Evaluation and Characterization of Terbinafine Nanosponges

Comprehensive evaluation and characterization of the formulated nanosponge are necessary to guarantee that the quality, performance, and reproducibility of terbinafine-loaded nanosponge formulations are acceptable. Suitability of nanosponges for antifungal drug delivery is determined through the assessment of various physicochemical and biological parameters.

8.1 Particle Size, Polydispersity, and Surface Charge

The parameters of particle size and polydispersity index (PDI) are very critical and determine drug release, stability, and biological interaction. The particle sizes of nanosponges intended for drug delivery are in the nanometer range with low PDI values, implying uniform size distribution. The surface charge, indicated as zeta potential, illustrates the colloidal stability and possible interactions with biological membranes.

8.2 Drug Content and Encapsulation Efficiency

Drug content and encapsulation efficiency are critical measurements of formulation effectiveness. High encapsulation efficiency is indicative of the strong interaction between terbinafine and the nanosponge matrix, which in return prolongs the release, and enhances the therapeutic performance. These parameters are normally determined using morphologic or chromatographic techniques.[23,32,33]

8.3 In Vitro Drug Release Studies

In vitro release studies are performed to determine the release kinetics of terbinafine from nanosponge systems. The prolonged release profiles of nanosponge systems compared to conventional formulations not only confirm their use in antifungal therapy but also indicate the better patient compliance to the treatment. Kinetic models are frequently used to fit the release data which ultimately help in understanding the release mechanisms.

8.4 In Vitro Antifungal Activity

The antifungal activity of terbinafine nanosponges is normally evaluated using agar diffusion or broth dilution methods against the pathogenic fungal strains. The increase in areas of inhibition or the decrease in minimum inhibitory concentrations points to the therapeutic benefit of the nanosponges-based delivery system.

8.5 Stability Studies

Stability studies are performed to check the physical and chemical stability of nanosponge formulations at different storage conditions. The strong polymeric structure of the nanosponges provides high stability and thus reducing the risk of drug degradation and facilitating consistent performance over the time.

9. Translational Potential and Future Perspectives

The successful transition of nanosponge drug delivery systems from laboratory to clinical use depends on a number of important factors, such as scalability, reproducibility, acceptance by regulatory bodies, and long-term safety. In preclinical studies, terbinafine-loaded nanosponges showed very good abilities in terms of solubility enhancement, controlled release, and antifungal efficacy, but still, more efforts have to be made for their clinical adoption.

9.1 Scale-Up and Manufacturing Issues

Translating nanosponge formulations into commercial products is still a major challenge due to the necessity of scaling-up the manufacturing process while ensuring the same level of quality and performance all along. Particles size, drug loading, and release behavior are some examples of the characteristics that must be kept the same during large-scale production. The application ofadvanced polymer processing techniques and continuous manufacturing may become the solution to these problems, making the production of nanosponge-based formulations on industrial scale a reality**.**

9.2 Regulatory and Safety Issues

The regulatory approval process for nanosponge drug delivery systems is quite demanding in that it requires a thorough assessment of their safety, biocompatibility, and stability. In the case of nanosponges, which are primarily made of biocompatible polymers, performing long-term toxicity and biodegradation studies is a must to assure patient safety. The regulatory agencies are quite strict when it comes to the applicability of the pharmaceutical standards for nanotechnology and they also expect a clear understanding of the nanoscale material behavior.

9.3 Clinical Translation Prospects

The use of terbinafine-loaded nanosponges in clinical settings is particularly promising in the case of treating fungi on the skin or in the localized area with the help of controlled drug release and skin retention techniques thus enhance the skin's absorption and this consequently leads to better treatment outcomes. Nanosponge formulation has a potential to minimize the overall treatment pressing issues such as the time taken for treatment, frequency of doses, and occurrence of the adverse effect in the systemic part of the body. Thus, the system will be compliant to the patient. The future clinical research's primary focus on efficacy, safety, and

patient acceptability would be the decision-makers of the therapeutic benefits that the delivery systems based on nanospheres have with the application of antifungal.

9.4 Future Research Directions

Future research work is going to be all about making the best choice of the composition of nanosponge for targeted antifungal delivery, creating multifunctional nanosponges that are able to do the co-delivery of the drug or its penetration enhancer and testing their draw with advanced in vivo models. Moreover, the combination of nanoscopes with the systems responding to stimuli can be a means of providing drug release at the specific site and on-demand basis which further improvements in antifungal therapy might be.

CONCLUSION

Nanosponges have taken the place as a leading-edge and all-around platform for antifungal drug delivery due to their great versatility and similarity to other conventional, and nanocarrier-based systems. The characteristic porous structure of the nanosponges allows for efficient encapsulation of poorly soluble drugs like terbinafine, which results in better solubility, controlled drug release, and consequently, improved therapeutic efficacy. Nanosponge-based delivery systems have the potential to make a considerable impact on antifungal treatment by addressing the biopharmaceutical obstacles that come with conventional formulations of terbinafine. This thorough review points out the significance of nanosponges in the process of terbinafine delivery and focuses on formulation strategies, drug release behavior, antifungal performance, and evaluation parameters. Nanosponge's capacity for slow drug release while at the same time mitigating adverse effects related to dosage underlines the importance of their use in clinics especially when it comes to chronic and recurrent fungal infections. The persistence of challenges over large-scale production and the approval of regulatory bodies seems not to hinder the proponents of continuing research and technological advancements which would, in the not-too-distant future, make it possible for the use of nanosponge-based antifungal formulations in clinical practice. Overall, the combination of terbinafine and nanosponges constitutes a new and promising drug delivery strategy that could significantly increase the effectiveness, safety, and patient acceptance of antifungal treatment. The successful development and clinical acceptance of this product may open doors for broader use of nanosponge systems in the delivery of other therapeutic agents that are poorly soluble in the body.

REFERENCES

1. H. Bhowmik, D.N. Venkatesh, A. Kuila, K.H. Kumar, Nanosponges: A review, International Journal of Applied Pharmaceutics, 2018; 10. https://doi.org/10.22159/ijap.2018v10i4.25026.
2. A. Garg, W.C. Lai, H. Chopra, R. Agrawal, T. Singh, R. Chaudhary, B.N. Dubey, Nanosponge: A promising and intriguing strategy in medical and pharmaceutical Science, Heliyon 2024; 10. https://doi.org/10.1016/j.heliyon.2023.e23303.
3. A.Y. Pawar, K.R. Jadhav, S.P. Rathod, A.S. Sanap, M.J. Umekar, Formulation and Evaluation of Nanosponges Loaded Hydrogel of Metformin Hydrochloride, Indian Journal of Pharmaceutical Education and Research, 2023; 57. https://doi.org/10.5530/001954641980.
4. S. Koppula, S. Maddi, Nanosponges in therapeutics: Current advancements and future directions in targeted drug delivery, J Drug Deliv Sci Technol, 2024; 101. https://doi.org/10.1016/j.jddst.2024.106258.
5. A. J, A. Girigoswami, K. Girigoswami, Versatile Applications of Nanosponges in Biomedical Field: A Glimpse on SARS-CoV-2 Management, Bionanoscience, 2022; 12. https://doi.org/10.1007/s12668-022-01000-1.
6. B.H.J. Gowda, M.G. Ahmed, M.A.A. Almoyad, S. Wahab, W.H. Almalki, P. Kesharwani, Nanosponges as an Emerging Platform for Cancer Treatment and Diagnosis, Adv Funct Mater, 2024; 34. https://doi.org/10.1002/adfm.202307074.
7. P.S. Goudanavar, B. Ramesh, N.R. Naveen, B. Gowthami, Pharmaceutical/Biomedical applications of electrospun nanofibers-Comprehensive review, attentive to process parameters and patent landscape., Pharm Nanotechnol, 2023.
8. S. Desai, R. Naveen, P.S. Goudanavar, B. Gowthami, Nanobiosensors: Concepts and Emerging Clinical Applications, Pharm Nanotechnol 2023; 12: 197–205. https://doi.org/10.2174/2211738511666230901160530.
9. G. Utzeri, P.M.C. Matias, D. Murtinho, A.J.M. Valente, Cyclodextrin-Based Nanosponges: Overview and Opportunities, Front Chem., 2022; 10. https://doi.org/10.3389/fchem.2022.859406.
10. S. Iravani, R.S. Varma, Nanosponges for Water Treatment: Progress and Challenges, Applied Sciences (Switzerland), 2022; 12. https://doi.org/10.3390/app12094182.
11. R. Amer, G. El-Osaily, S. Gad, Design and optimization of topical terbinafine hydrochloride nanosponges: Application of full factorial design, in vitro and in vivo

evaluation, J Adv Pharm Technol Res., 2020; 11. https://doi.org/10.4103/japtr.JAPTR_85_19.

12. S. Iravani, R.S. Varma, Nanosponges for Drug Delivery and Cancer Therapy: Recent Advances, Nanomaterials, 2022; 12. https://doi.org/10.3390/nano12142440.
13. S. Baner, Dr.R.B. Sharma, Development and Evaluation of Terbinafine Loaded Nanosponges, Int. J Pharm Sci Rev Res., 2023; 82. https://doi.org/10.47583/ijpsrr.2023.v82i02.023.
14. S.M. Syed, T. Sowmya, P. Koteswari, Topical Delivery of Terbinafine via Nanosponge-Embedded Gel: A Novel Approach to Combat Superficial Fungal Infection, Biomedical Materials and Devices, 2025. https://doi.org/10.1007/s44174-025-00557-1.
15. D. Gorakh, D. Shashikant, D. Satish, Design and Evaluate Terbinafine Hydrochloride Loaded gel by using Modified Tamarind for Topical Drug Delivery, Res J Pharm Technol, 2024; 17. https://doi.org/10.52711/0974-360X.2024.00324.
16. A.K. Gupta, Susmita, H.C. Nguyen, A. Liddy, V. Economopoulos, T. Wang, Terbinafine Resistance in Trichophyton rubrum and Trichophyton indotineae: A Literature Review, Antibiotics, 2025; 14. https://doi.org/10.3390/antibiotics14050472.
17. R. Kano, Y.H. Hsiao, H.S. Han, C. Chen, A. Hasegawa, H. Kamata, Resistance Mechanism in a Terbinafine-Resistant Strain of Microsporum canis, Mycopathologia 183 (2018). https://doi.org/10.1007/s11046-018-0242-0.
18. J. Leyden, Pharmacokinetics and pharmacology of terbinafine and itraconazole, J Am Acad Dermatol, 1998; 38. https://doi.org/10.1016/s0190-9622(98)70483-9.
19. M. Mustafa, Comparison of Efficacy of Terbinafine and Fluconazole in Patients of Tinea Corporis, Annals of Punjab Medical College, 2021; 15. https://doi.org/10.29054/apmc/2021.780.
20. S. Dombe, P. Shirote, Nanosponges Encapsulated Phytochemicals for Targeting Cancer: A Review, Curr Drug Targets, 2020; 22: 443–462. https://doi.org/10.2174/1389450121999201012201455.
21. N.R.N. P. Divya D. R. Bharathi, Optimization of cross linked tragacanth and comparison of drug Release rate profile with synthetic superdisintegrants on Metoclopramide orodispersible tablets, International Journal of Pharmacy and Life Sciences, 2013; 4: 2500–2505.
22. N.R.N. Ranjitha B1* Goudanavar Prakash3, Biradar Nikita1 and Asha B R, Prospection of Antifungal Loaded Nanoparticulate Topical and Transdermal System for Enhanced Therapy, Indian Journal of Natural Sciences, 2023; 14: 61525–61535.

23. M. Kurakula, N.R. Naveen, In situ gel loaded with chitosan-coated simvastatin nanoparticles: Promising delivery for effective anti-proliferative activity against tongue carcinoma, Mar Drugs, 2020; 18: 201.
24. G. Tejashri, B. Amrita, J. Darshana, Cyclodextrin based nanosponges for pharmaceutical use: A review, Acta Pharmaceutica, 2013; 63: 335–358. https://doi.org/10.2478/acph-2013-0021.
25. A.P. Sherje, B.R. Dravyakar, D. Kadam, M. Jadhav, Cyclodextrin-based nanosponges: A critical review, Carbohydr Polym, 2017; 173: 37–49. https://doi.org/10.1016/j.carbpol.2017.05.086.
26. U. Kandekar, R. Pujari, N. Munot, T. Chorge, K. Lone, P. Kamble, K. Kishanchand, Nanosponges- Versatile Platform as Drug Carrier, Recent Pat Nanotechnol, 2022; 17: 91–103. https://doi.org/10.2174/1872210516666220905092202.
27. S. Wang, D. Wang, Y. Duan, Z. Zhou, W. Gao, L. Zhang, Cellular Nanosponges for Biological Neutralization, Advanced Materials, 2022; 34. https://doi.org/10.1002/adma.202107719.
28. F. Caldera, M. Tannous, R. Cavalli, M. Zanetti, F. Trotta, Evolution of Cyclodextrin Nanosponges, Int J Pharm, 2017; 531: 470–479. https://doi.org/10.1016/j.ijpharm.2017.06.072.
29. G. Utzeri, P.M.C. Matias, D. Murtinho, A.J.M. Valente, Cyclodextrin-Based Nanosponges: Overview and Opportunities., Front Chem., 2022; 10: 859406. https://doi.org/10.3389/fchem.2022.859406.
30. S. Subramanian, A. Singireddy, K. Krishnamoorthy, M. Rajappan, Nanosponges: A novel class of drug delivery system - Review, Journal of Pharmacy and Pharmaceutical Sciences, 2012; 15: 103–111. https://doi.org/10.18433/j3k308.
31. S. Nandi, D. Karati, S. Mukherjee, Nanosponges-road Less Explored Changing Drug Delivery Approach: An Explicative Review, Curr Pharm Biotechnol, 2024; 26 1696–1715. https://doi.org/10.2174/0113892010307169240619061808.
32. N.R. Naveen, Design and characterization of sustained release matrix tablets of glimepiride by using synthetic and natural polymers, International Journal of Drug Discovery and Herbal Research, 2013; 3: 573–578.
33. M. Kurakula, N. Raghavendra Naveen, In Situ Gel Loaded with Chitosan-Coated Simvastatin Nanoparticles: Promising Delivery for Effective Anti-Proliferative Activity against Tongue Carcinoma, Mar Drugs, 2020; 18. https://doi.org/10.3390/MD18040201.