Advances in Pharmacology and Pharmacy 13(2): 160-167, 2025 http://www.hrpub.org
DOI: 10.13189/app.2025.130202

Lipidic Nanotechnology Carriers: A Secure and Excellent Fungicide and Hepatoprotective Transporting Devices

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Received March 9, 2024; Revised August 16, 2024; Accepted December 24, 2024

Cite This Paper in the Following Citation Styles

(a): *[1] Bhavana Madupoju, Subhakar Raju Rapaka, Narender Malothu, Ankarao Areti, "Lipidic Nanotechnology Carriers: A Secure and Excellent Fungicide and Hepatoprotective Transporting Devices," Advances in Pharmacology and Pharmacy, Vol. 13, No. 2, pp. 160 - 167, 2025. DOI: 10.13189/app.2025.130202.*

(b): *Bhavana Madupoju, Subhakar Raju Rapaka, Narender Malothu, Ankarao Areti (2025). Lipidic Nanotechnology Carriers: A Secure and Excellent Fungicide and Hepatoprotective Transporting Devices. Advances in Pharmacology and Pharmacy, 13(2), 160 - 167. DOI: 10.13189/app.2025.130202.*

Abstract Throughout the past three decades, there has been a notable rise in the incidence and variety of invasive fungal infections due to modifications in medical and surgical care, especially in intensive care units that employ invasive catheters for observing, as well as the use of more potent immune suppression and antibiotic agents. The types, benefits, and limitations of various nanoformulations for the topical and intravenous delivery of antifungal medications are investigated in the current investigation. A couple of instances of NPs used in the delivery of medicines include solid lipid nanoparticles, nanostructured lipid carriers, polymeric NPs, polymeric micelles, phospholipid vesicles (liposomes, deformable liposomes, ethosomes, transferosomes, transethosomes, etc.), non-phospholipid vesicles (noisome and plastics) and dendrimers. Collectively with these features hepatic diseases persist to be a major global health concern and one of the greatest risks to the general population. Even with all of the excellent advances in modern medicine, there are currently no fully effective drugs that improve liver function, provide total organ protection, or promote liver cell regeneration. Therefore, pharmaceutical substitutes for the therapy of liver conditions need to be explored to make them more secure and successful. Focusing liver illnesses may benefit from the use of liposomes, metallic nanoparticles, ceramic nanomaterials, polysaccharides, Carbon-nanotubes, multifunctional NPs, and dendrimers can be made much more effective when these are paired with particular targeted agents.

Keywords NPs-nanoparticles, Solid Lipid Nanoparticles, Hepatic Diseases, Antifungal Medications, Metallic Nanoparticles

1. Introduction

Throughout the past three decades, there has been a notable rise in the chronicity and variety of invasive fungus-related illnesses due to modifications in laparoscopic and healthcare settings, particularly in emergency rooms that employ devices that are invading to observing, in conjunction with using more potent immune suppression added to antimicrobial agent [1]. Around 20–25 percent of the human population is thought to be affected by superficial mycoses. Extensive contagions involving fungi also become a notable participant in fatalities and death in individuals receiving organ transplants, immune-compromised those diagnosed with acquired immunodeficiency syndrome, myeloid & lymphatic tumors, severe bone marrow failure, acute myeloid leukemia, preterm neonates and the elderly [2]. Candidemia-related mortality has reduced annually since its peak, thanks to recent breakthroughs when managing invasive candidiasis. Despite this, systemic candidiasis

continues to rank as the 4th most common nosocomial bloodstream infection in hospitals [3]. Major advancements in the identification of novel antifungal medications have led to the release of improved generations that provide superior therapeutic results for those individuals who are at threat [4]. An azole of the original class medicines, among these are itraconazole and fluconazole launched around the nineties after a more than 20-year hiatus. Azole of the following class medications, comprising voriconazole, posaconazole, and isavuconazole, as well as echinocandins (anidulafungin, caspofungin, and micafungin) became available during the decade of 2000 [5].

Particles with a diameter of 1–1000 nm are referred to as nanoparticles (NPs). However, items with a size between one and one hundred nanometres are referred to as "nanomaterials" or "nanoscale". For this review, particles utilized in drug delivery applications ranging in size from 1 to 1000 nm shall be referred to as NPs. When compared to their larger-scale counterparts, NPs have unique chemical, physical, and biological features, making them promising drug-delivery vehicles [6].

Keeping a closer eye on how nanotechnologies are used in biomedical research, those substances can be used for several applications including dressings for injuries, laser ablation treatment, drug delivery, therapy, modification of genes, immunizations fabricated devices heat exhaustion and medicinal automation. These include their large surface-to-volume ratio, their simplicity of functionalization through the incorporation of biologically compatible substances as a hat, and their distinct visual magnetic features [7].

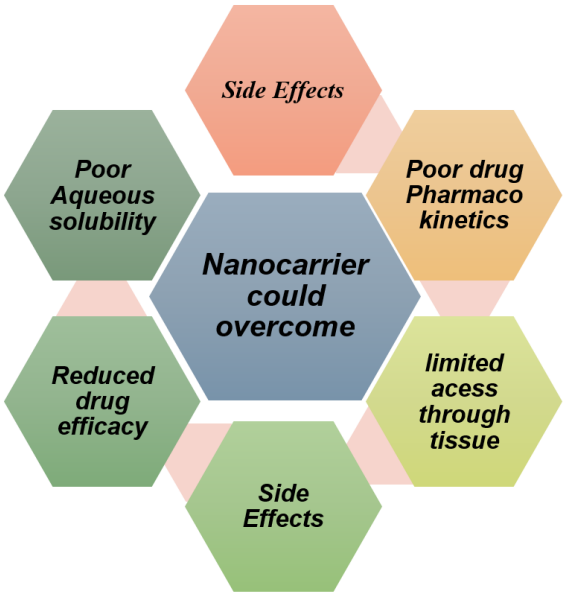

Figure 1. Unfavorable drug properties that can be improved through amalgamation into various nano-formulations

Figure 1 illustrates how nanocarriers lessen adverse effects and increase tissue penetration while improving medication solubility, effectiveness, and pharmacokinetics. The current study examines the kinds, advantages and restrictions of several nanoformulations for the cutaneous and central administration of antifungal drugs. Additionally, it highlights how these NPs may be used to combat aggressive as well as peripheral fungal illnesses. The difficulties that this research faces, as well as the roadblocks to the clinical application of a few potential nanoformulations, were explored.

2. Nanoparticles (NPs) as a Means of Dispensing Antifungal Agents

Solid lipid nanoparticles, nanostructured lipid carriers, polymeric NPs, polymeric micelles, phosphoglyceride vesicles (liposomes, deformable liposomes, ethosomes, transferosomes, transethosomes, etc.), non-phosphoglyceride vesicles (niosomes and plastics) and dendrimers are a few examples of NPs used in drug delivery [8]. In accordance with Figure 2, dendrimers, polymeric nanoparticles, solid lipid nanoparticles, phospholipid vesicles, and non-phospholipid vesicles are the components of antifungal nanoformulations.

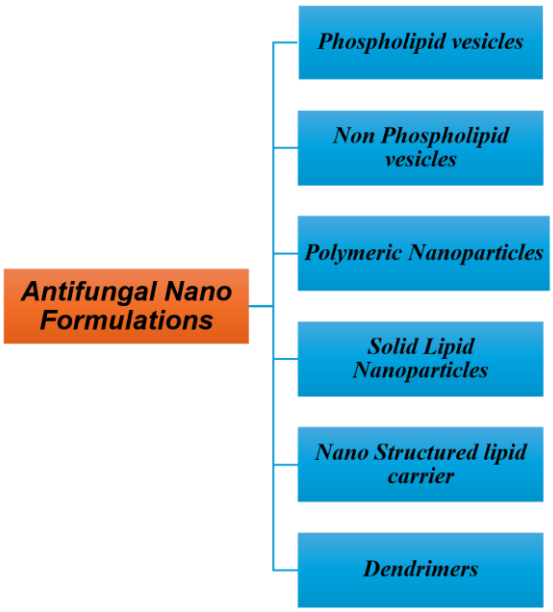

Figure 2. Various antifungal Nano formulation

3. Phospholipid-based Vesicles

3.1. Liposomes

Liposomes are a set of concentric phospholipid membranes encased in an aqueous shell operating as reliable drug-transporting vehicles for the pair of water-loving and repelling medications due to their unique structure. Biocompatibility, minimum noxious effects, extended release of drugs, low pharmacological adverse

effects, significant loading ability, enhanced bioavailability of drugs, and stability are some of the other appealing characteristics of liposomes as drug delivery vehicles. Cholesterol is generally integrated into the lipid bilayers of liposomes to increase membrane stiffness, stabilize vesicles and regulate the pace of drug release [9].

3.1.1. *Amphotericin B*

The initial and most effective commercially available antifungal nanoformulation is liposomal AmB (**AmBisome®**) [10]. To address the nephrotoxicity and infusion-related adverse effects of AmB deoxycholate injection (**Fungizone®**) was created. Treatment for patients with endophthalmitis, Candida meningitis, or disseminated histoplasmosis with AIDS now involves liposomal AmB [11].

3.1.2. Nystatin

Nystatin is a polyene antifungal medication with a broad spectrum of activity that has been effectively introduced into liposomal medications to treat systemic fungal infections. It comes from *Streptomyces noursei* and has a wider range of effects than AmB (Amphotericin B). Because of its limited oral absorption, nystatin is solely utilized topically. Furthermore, Parenteral dosing cannot occur in the presence of thrombophlebitis, high temperature, shivers or nausea. According to *in vitro* experiments liposomal nystatin exhibited an equivalent level of activity compared with that of the unbound drug [12]. The liposomal formulation allowed for intravenous nystatin administration. In Hale-Stoner rodents, the highest tolerated dosage was raised concerning 4-16 mg/kg of body mass per day. Mice diagnosed with *Candida albicans* displayed a substantial rise in their survival rates when liposomal nystatin was administered [13]. Figure 3 depicts the structural elements and drug encapsulation techniques of four different types of nanocarriers: liposomes, ethosomes, transferosomes, and transethosomes.

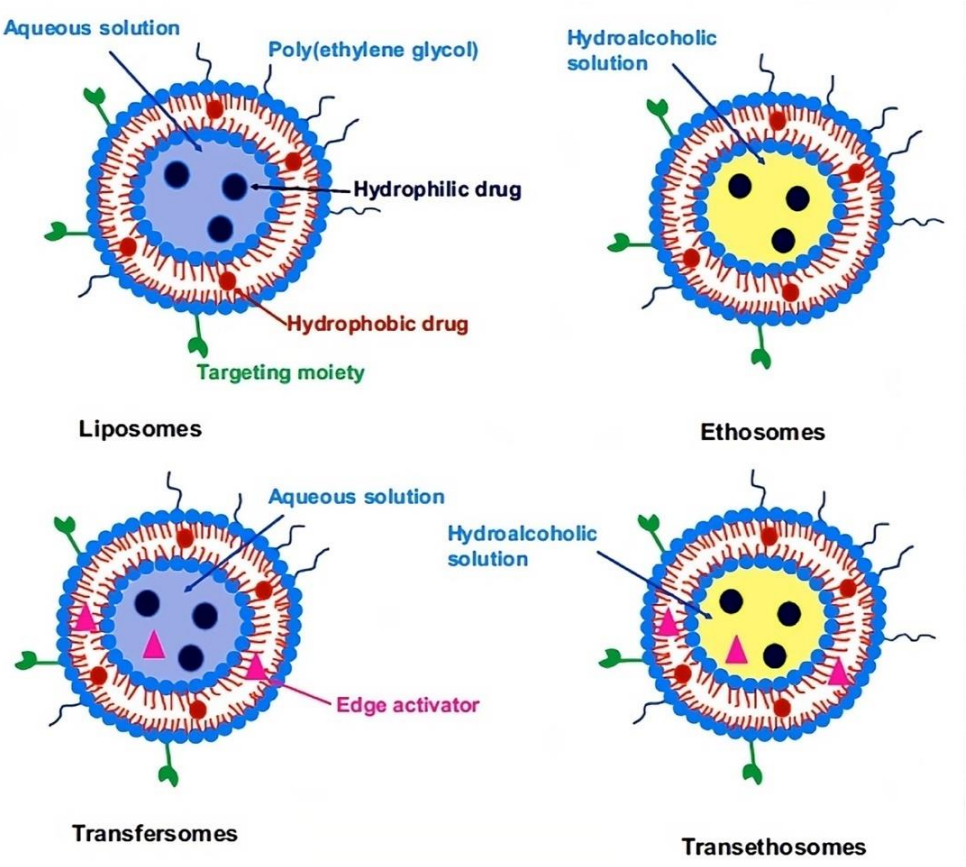

Figure 3. Phospholipid based drug delivery systems

3.2. Transferosomes

Transferosomes are ultra-deformable, self-optimized aggregates containing lipids and biocompatible membrane softeners for transdermal administration. Liposomes' low penetration into cornified layers inspired the change of the makeup of their twin layer to get around this constraint, notwithstanding their advantages and achievements. Wetting agents with a great degree of transportation like edge-activating agents include dipotassium glycyrrhizinate, sodium cholate, polysorbate 20, polysorbate 60, polysorbate 80, and Sorbitan Tri stearate 65, Sorbitan monooleate 80, etc. The edge activator is in charge of deteriorating and increasing the deformability of vesicle lipid bilayers. In terms of medication penetration and skin contact, it was discovered that these pliable vesicles outperformed conventional liposomes [14].

3.3. Ethosomes

Ethosomes are soft vesicles that are made up of phospholipids, ethanol, and water. Typically, these consist of 100 percent water, 20–45 percent ethanol, and 2-3% phospholipids *Touitou et al.,* first proposed them in 2002 as a way to overcome the poor epidermal invasion of traditional liposomes [15]. Ethosomes had a higher penetration impact than ethanol by itself, grade alcohol phosphoglyceride solution, give direction to drinking alcohol, the vesicular configuration and moisture barrier work in concert. Ethanol's propensity to lubricate ethanolic triglycerides and interpersonal fats of stratum granulosum allows ethosomes to penetrate the skin more effectively than liposomes [16].

3.4. Transethosomes

A novel class of vesicular carriers known as transethosomes merges the perks of ethosomes and collapsible liposomes. It accommodates an edge activator or permeability accelerator in addition to the typical ethosome makeup. Because transethosomes are a relatively novel drug carrier there is little research on their use for antifungal drug delivery, contrasted with the ethosomes, medicine flexible liposomes and typical liposomes, polyethylene glycol solution, voriconazole transethosomes exhibited considerably higher skin permeability. Furthermore, as compared to other vesicular carriers, the transethosomes improved voriconazole skin deposition in the dermis/epidermis layers both *in vitro* and *in vivo* [17].

3.5. Niosomes

Niosomes and liposomes share characteristics in that they both have double layers formed up of non-ionized single-alkyl chain detergents rather than amphiphilic lipids. The water-resistant tail of the surfactant is submerged within the bilayer and the hydrophilic head confronts both architecture of vesicles. Although water-repellent pharmaceuticals are implanted in the hydrophobic bilayers, hydrophilic drugs can be integrated into the watery core. To increase the rigidity of the bilayer and stop drugs from releasing too soon, cholesterol is introduced. Similar to liposomes, niosomes have several advantages over liposomes, including higher chemical stability, lower cost and the capacity to keep them in a controlled environment for storage [18].

3.6. Polymeric Nanoparticles

The subject of drug delivery, notably cancer chemotherapy, has been transformed by degradable and/or bio-adaptable polymer-assembled nanoparticles (NPs). NPs have demonstrated a strong capacity to improve medication therapeutic qualities while reducing side effects and toxicity. Many cytotoxic medication formulations based on polymeric NPs have already entered clinical trials and many more are in the works. Based on their molecular makeup and production method polymeric, NPs are categorized into distinct categories i.e., three categories: polymeric micelles, nanospheres, and nanocapsules [19]. Figure 4 demonstrates a few polymeric nanocarrier structural compositions, namely nanocapsules, nanospheres, and polymeric micelles.

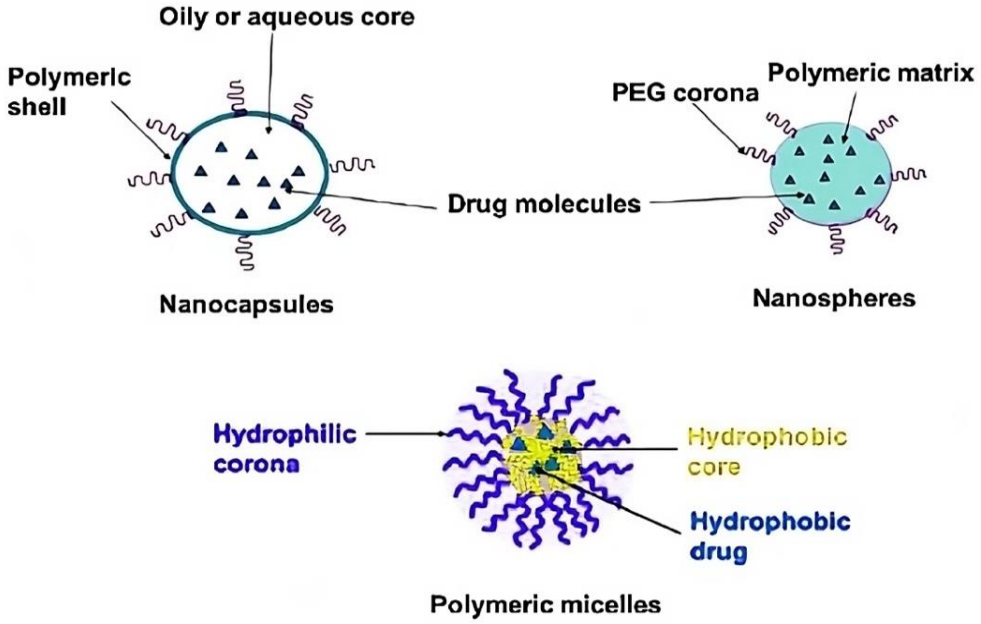

Figure 4. Polymeric nanoparticles

3.7. Lipid Nanoparticles in Solid State (SLNs) and Fat-soluble Transporters with Nanostructure (NLCs)

SLNs (Solid lipid nanoparticles) stand for therapeutically appropriate lipids suspended in an aqueous surfactant solution, forming dispersion nanostructured carriers for drugs. They were first made available as an alternative to polymeric NPs at the beginning of the nineties. Since the lipids in SLNs remain solid at human body temperature & ambient temperature release of drugs is facilitated with a prolonged process of medication dispersion via rigid fat. SLNs have some benefits to providing medication such as improved biological barrier permeability the Chemical endurance of lipids, the capacity to alter their outer layer, the space available for delivering several medications, and protection from integrated molecule breakdown. SLNs on the other hand have some drawbacks such as inadequate ability to load drugs and drug ejection upon preservation. Whenever the molecules of lipids rearrange to form an ideal crystal lattice through storage, drug evacuation happens because less space exists for therapeutic incorporation. Two-generation carrier lipids with nanostructured structures of SLNs were introduced to overcome these constraints. Better medication loading, controlled release of drugs, and stability over time are achieved by NLC's (Nanostructured lipid carriers) solid lipid matrix, which is made up of solid lipid and oil in specific ratios at ambient temperature and the temperature of the body [20]. The creation of crystallized phospholipid structures that are extremely organized is inhibited by the fluid lipid inside NLCs, which are the source of SLN's flaws. ITZ (Itraconazole) put into NLCs, for example, exhibited a 99.98 percent encapsulation efficiency and stable circumstances for storage for more than six months. Additionally, it was discovered that SLNs comprised entirely of solid or fluid lipids achieved encapsulation efficiencies of 59 and 42 percent respectively for AmB (**Amphotericin B**). These formulations on the other hand had an AmB ejection rate of 80%. AmB encapsulation efficiency was reduced to 39% medication ejection was dropped to 12% as long as a combination of liquid and solid forms of fats was utilized suggesting improved formulation stability [21].

3.8. Dendrimers

Dendrimers are three-dimensional hyperbranching and spherical macromolecules with multiple arms extending from a distinct focal core, originating from the ancient Greek word dendron, meaning "tree." Dendrimers have a lot of possibility of delivering antifungal medication because of their distinctive properties such as structural plasticity, multivalency, and low polydispersity. Hydrophobic fissures formed by dendrimer branches are conceivably utilized to remediate the hydro-based solubility of water-repellent medications by encapsulating them. At pH 7.4 poly (propylene imine) dendrimers increased AmB aqueous solubility by a factor of 25. Furthermore, one can use ionized surfaces made up of dendrimers as focal areas for attaching targeting or imaging moieties or integrating ionized medicines via ionic interactions. Dendrimers' potential as antifungal medication delivery strategies is still lacking as indicated by the small number of studies in this field and AmBisome, to name a few. Peptide-conjugated poly amidoamine dendrimers (PADRE-PAMAM) seemed additionally employed to improve AmB localization to epitope presentation cells (APC (Antigen presenting cells), macrophages, and dendritic cells) [22]. AmB effectiveness was increased by 83% with PADRE-PAMAM and its

targeting to APC by tenfold *in vivo* experiments resulting in lower AmB dose and toxicity [23].

4. Difficulties in Clinically Translating NPs

The results of the aforementioned study unequivocally show that different NPs compositions can function as efficient antifungal drug delivery vehicles. Flavonoids and phenols were found in the water-based extract of *Stephania japonica* leaflets by botanical compounds examination. The medicinal qualities that this breed exhibits are mostly due to these types of chemicals. The antimicrobial, fungicide, and antioxidant properties of "SJ-Aq" (Aqueous extract of *S. japonica*) are probably attributed to its chemical components particularly to its flavonoids some of which are phenolic chemicals with notably significant amounts [24]. Despite decades of research and hundreds of articles published on this subject, AmB is the sole antifungal medication accessible economically in compositions that employ NPs. This wide disparity could be attributable to a variety of factors, the most significant of which include industry-related issues, NPs limits, and issues with clinical investigations & preclinical research. The majority of NPs research takes place in academia, with little backing from the pharmaceutical sector. In the pharmaceutical sector, two significant obstacles to NPs manufacturing are control of quality and elevated nanostructures having coverings on their surfaces or many elements necessitating complicated manufacturing and assessment stages, which might drastically elevate the production costs and render the scale-up process impossible [25].

5. Hepatoprotection

As an integral component of the body, the liver is vital for several processes, such as the metabolic processes, secretion, detoxification, and storage of both internal and external chemicals. Hepatic illnesses remain one of the most serious hazards to public health as a result of these functions, and they continue to be a problem throughout the world. Nevertheless, despite tremendous breakthroughs within contemporary medicine, there exist zero effective medications that enhance the performance of the liver, offer complete organ defense, or assist in the regenerative process of liver cells. Therefore, pharmaceutical substitutes for the therapy of liver conditions need to be explored to make them more secure and successful. It is critical to shield the liver's tissues from the harmful consequences of ingested hepatotoxins or to reverse changes in antiradical defense mechanisms, medications capable of doing so are known as hepatoprotectives [26].

Hepatoprotective activity may be easily evaluated/screened in experimental animals using a variety of model systems of liver damage. Conditions for liver damage are implemented in all test model systems and using the material or preparation being tested, an effort is made to combat this poisoning [27].

5.1. Hepatoprotective Medicaments

Hepatoprotective properties are found in a significant range of plant-based medications, either directly or indirectly. Herbal medications for the treatment of liver problems have become increasingly popular in recent years all over the world [28]. The herb's hepatoprotective qualities could be linked to the phenolic compounds, flavonoids, and saponins [29]. Flavonoids' ability to scavenge free radicals is responsible for their hepatoprotective properties [30]. Many different plants and combinations have been shown to have liver-protective properties. In contemporary therapy, no meaningful reliable hepatoprotective medication is currently available, notwithstanding major advancements. This has led to a great deal of global emphasis being paid to the invention of plant-derived hepatoprotective drugs that are effective towards a range of liver-related conditions [31].

5.2. Hepatoprotective Molecules Used in Emergency Medicine

When treating an acetaminophen/paracetamol overdose, N-acetylcysteine is the hepatoprotective medication of choice [32].

It is currently shown that a key factor in the liver-protective effects of plant-based extracts and polyherbal compositions (PHF) is their capacity as antioxidants. When treating illnesses involving oxidative damage, NMAE (Natural Methylated Alkaloid Extract) could be beneficial [33]. Silymarin is used intravenously to treat Amanita mushroom toxicity. In Polycystic rodents, excessive amounts of allicin are found to provide significant liver-protective and antioxidant functions [34]. Rats with a combination of quercetin and curcumin showed no liver dysfunction and its cytoarchitecture did not alter, indicating preserving the liver [35].

5.3. Plants that May Have Liver-protective Constituents [36]

- *Mongolian milkvetch*
- *Curcuma domestica*
- *Cruciferous vegetables, cabbages, or mustard plants.*
- *Marian thistle*
- *Andrographis paniculata*

6. Conclusions

Infections caused by fungi are becoming a global problem, causing major morbidity and death rates. Ostensibly, there is an assortment of efficient antifungal

medicines on the market, but their therapeutic benefits are restricted due to excessive toxicity or unfavorable physicochemical features. Because their advantageous qualities, including the potential to surpass numerous limitations, stem from their compactness, numerous functions, and biological compatibility. Liposomal, solid lipid nanoparticle, and Phospholipid-based tiny carriers known as lipid carriers with nanostructured structures were studied the most when it comes to the distribution of antifungal medication correlated with various nanocarrier types. Numerous such nanoparticles (such as liposomes) were been tested in clinical studies to treat invasive mycoses. Indeed, a major advancement in the medicinal application of this powerful antifungal medication with little or no side effects was made possible by the availability of liposomal amphotericin B. Nanocarriers have a lot of promise for delivering drugs to specific cells. To present, a vast number of formulations for liver targeting using polymeric nanocarriers as targeting ligands have been developed. Only a few delivery systems for liver-targeted drugs are currently on the market. The presence of flavonoids, alkaloids, terpenoids, glycosides, and steroids in plants is thought to be responsible for their hepatoprotective properties. Plant active extracts, fractions, or a combination of fractions/extracts could be very effective medications.

REFERENCES

[1] Correa-Moreira D., Baptista B. O., Giosa D., Oliveira M. M. E., "Emerging fungal pathogens: perspectives," Front Fungal Biology, vol. 5, pp. 1369062, 2024. DOI: 10.3389/ffunb.2024.1369062.

[2] Bouz G., Doležal M., "Advances in Antifungal Drug Development: An Up-To-Date Mini Review," Pharmaceuticals (Basel), vol. 14, no. 12, pp. 1312, 2021. DOI: 10.3390/ph14121312.

[3] Al-Ahmadey Z. Z., Al-Ahmadi S. S., Aljohani E. D., Al-Rashidi N. H., "Candida Bloodstream Infection and Antifungal Susceptibility Over Three Years in a Single Center from Medinah, Saudi Arabia," Microbiology Research Journal International, vol. 33, no. 2, pp. 1-7, 2023. DOI: 10.9734/mrji/2023/v33i21363.

[4] Garg A., Sharma G. S., Goyal A. K., Ghosh G., Si S. C., Rath G., "Recent advances in topical carriers of anti-fungal agents," Heliyon, vol. 6, no. 8, pp. e04663, 2020. DOI: 10.1016/j.heliyon.2020.e04663.

[5] Lombardo D., Kiselev M. A., "Methods of Liposomes Preparation: Formation and Control Factors of Versatile Nanocarriers for Biomedical and Nanomedicine Application," Pharmaceutics, vol. 14, no. 3, pp. 543, 2022. DOI: 10.3390/pharmaceutics14030543.

[6] Yusuf A., Almotairy A. R. Z., Henidi H., Alshehri O. Y., Aldughaim M. S., "Nanoparticles as Drug Delivery Systems: A Review of the Implication of Nanoparticles' Physicochemical Properties on Responses in Biological Systems," Polymers, vol. 15, no. 7, pp. 1596, 2023. DOI: 10.3390/polym15071596.

[7] Naik A. Y., Sundarrajan P., "Applications of nanomaterials in biomedical science," Annals of Phytomedicine, vol. 12, no. 1, pp. 171-179, 2023. DOI: 10.54085/ap.2023.12.1.54.

[8] Sivadasan D., Ramakrishnan K., Mahendran J., Ranganathan H., Karuppaiah A., Rahman H., "Solid Lipid Nanoparticles: Applications and Prospects in Cancer Treatment," International Journal of Molecular Sciences, vol. 24, no. 7, pp. 6199, 2023. DOI: 10.3390/ijms24076199.

[9] Matos C. M., "Liposomes: The Brave Old World," International Journal of Molecular Sciences, vol. 24, no. 5, pp. 4343, 2023. DOI: 10.3390/ijms24054343.

[10] Faustino C., Pinheiro L., "Lipid Systems for the Delivery of Amphotericin B in Antifungal Therapy," Pharmaceutics, vol. 12, no. 1, pp. 29, 2020. DOI: 10.3390/pharmaceutics12010029.

[11] Noor A., Preuss C. V., "Amphotericin B," StatPearls [Internet], Treasure Island (FL): Stat Pearls Publishing, 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482327/. DOI: 10.9734/mrji/2023/v33i21363.

[12] Panda P., Mohapatra S., Sahoo R., "Formulation And In Vitro Evaluation of Nystatin's In Liposomal Drug Delivery System," International Journal of Pharmaceutical Sciences, vol. 1, no. 9, pp. 31-40, 2023. DOI: 10.5281/zenodo.8312639.

[13] Sousa F., Nascimento C., Ferreira D., Reis S., Costa P., "Reviving the interest in the versatile drug nystatin: A multitude of strategies to increase its potential as an effective and safe antifungal agent," Advanced Drug Delivery Reviews, vol. 199, pp. 11496, 2023. DOI: 10.1016/j.addr.2023.114969.

[14] Simrah, Hafeez A., Usmani S. A., Izhar M. P., "Transfersome, an ultra-deformable lipid-based drug nanocarrier: an updated review with therapeutic applications," Naunyn-Schmiedeberg's Archives of Pharmacology, vol. 397, no. 2, pp. 639-673, 2024. DOI: 10.1007/s00210-023-02670-8.

[15] Emanet M., Ciofani G., "Ethosomes as Promising Transdermal Delivery Systems of Natural-Derived Active Compounds," Advanced Nano Biomed Research, vol. 3, no. 2300020, 2023. DOI: 10.1002/anbr.202300020.

[16] Chauhan N., Vasava P., Khan S. L., Siddiqui F. A., Islam F., Chopra H., Emran T. B., "Ethosomes: A novel drug carrier," Annals of Medicine and Surgery (Lond), vol. 82, pp. 104595, 2022. DOI: 10.1016/j.amsu.2022.104595.

[17] Nayak B. S., Mohanty B., Mishra B., Roy H., Nandi S., "Transethosomes: Cutting edge approach for drug permeation enhancement in transdermal drug delivery system," Chemical Biology & Drug Design, vol. 102, no. 3, pp. 653-667, 2023. DOI: 10.1111/cbdd.14254.

[18] Ghafelehbashi R., Memarzadeh F., Mansouri A., Akbarzadeh I., Abtahi M. S., Hejabi F., Ren Q., "Current advances in niosomes applications for drug delivery and cancer treatment," Materials Today Bio, vol. 23, pp. 100837, 2023. DOI: 10.1016/j.mtbio.2023.100837.

[19] Elmowafy M., Shalaby K., Elkomy M. H., Alsaidan O. A.,

Gomaa H. A. M., Abdelgawad M. A., Mostafa E. M., "Polymeric Nanoparticles for Delivery of Natural Bioactive Agents: Recent Advances and Challenges," Polymers, vol. 15, no. 5, pp. 1123, 2023. DOI: 10.3390/polym15051123.

[20] Lopez K. L., Ravasio A., Gonz áez-Aramundiz J. V., Zacconi F. C., "Solid Lipid Nanoparticles (SLN) and Nanostructured Lipid Carriers (NLC) Prepared by Microwave and Ultrasound-Assisted Synthesis: Promising Green Strategies for the Nanoworld," Pharmaceutics, vol. 15, no. 5, pp. 1333, 2023. DOI: 10.3390/pharmaceutics15051333.

[21] Khan S., Sharma A., Jain V., "An Overview of Nanostructured Lipid Carriers and its Application in Drug Delivery through Different Routes," Advanced Pharmaceutical Bulletin, vol. 13, no. 3, pp. 446-460, 2023. DOI: 10.34172/apb.2023.056.

[22] Mhlwatika Z., Aderibigbe B. A., "Application of Dendrimers for the Treatment of Infectious Diseases," Molecules, vol. 23, no. 9, pp. 2205, 2023. DOI: 10.3390/molecules23092205.

[23] Dannert C., Mardal I., Lale R., Stokke B. T., Dias R. S., "DNA Condensation by Peptide-Conjugated PAMAM Dendrimers, Influence of Peptide Charge," ACS Omega, vol. 8, no. 47, pp. 44624–44636, 2023. DOI: 10.1021/acsomega.3c05140.

[24] Krishnarao K. L., Rajeswari T. R., "Phytochemical investigation and evaluation of the antioxidant, antibacterial and antifungal activities of Stephania japonica L. leaves extract," Annals of Phytomedicine: An International Journal, vol. 12, no. 1, pp. 477-485, 2023. DOI: 10.54085/ap.2023.12.1.59.

[25] Nami S., Aghebati-Maleki A., Aghebati-Maleki L., "Current applications and prospects of nanoparticles for antifungal drug delivery," Excli Journal, vol. 20, pp. 562–584, 2021. DOI: 10.17179/excli2020-3068.

[26] Saikat Mitra, Mashia Subha Lami, Tanvir Mahtab Uddin, Rajib Das, Fahadul Islam, Juhaer Anjum, Md. Jamal Hossain, Talha Bin Emran, "Prospective multifunctional roles and pharmacological potential of dietary flavonoid narirutin," Biomedicine & Pharmacotherapy, vol. 150, pp. 112932, 2022. DOI: 10.1016/j.biopha.2022.112932.

[27] Martinez-Lopez S., Angel-Gomis E., Sanchez-Ardid E., Pastor-Campos A., Pic ó J., Gomez-Hurtado I., "The 3Rs in Experimental Liver Disease," Animals, vol. 13, no. 14, pp. 2357, 2023. DOI: 10.3390/ani13142357.

[28] Arman M., Chowdhury K.A.A., Bari M.S., "Hepatoprotective potential of selected medicinally important herbs: evidence from ethnomedicinal, toxicological and pharmacological evaluations," Phytochemistry Reviews, vol. 21, pp. 1863–1886, 2022. DOI: 10.1007/s11101-022-09812-5.

[29] Ramasamy Thilagavathi, S. Sameema Begum, Sowfika Dharshini Varatharaj, Arun Kumar Balasubramaniam, Joselin Susan George, "Recent insights into the hepatoprotective potential of medicinal plants and plant-derived compounds," Phytotherapy Research, vol. 27, no. 5, pp. 2102–2118, 2023. DOI: 10.1002/ptr.7821.

[30] Kim M., Jee SC., Sung JS., "Hepatoprotective Effects of Flavonoids against Benzo[a]Pyrene-Induced Oxidative Liver Damage along Its Metabolic Pathways," Antioxidants (Basel), vol. 13, no. 2, p. 180, 2024. DOI: 10.3390/antiox13020180.

[31] Pandey B., Baral R., Kaundinnyayana A., "Promising hepatoprotective agents from the natural sources: a study of scientific evidence," Egyptian Liver Journal, vol. 13, p. 14, 2023. DOI: 10.1186/s43066-023-00248-w.

[32] Licata A., Minissale MG., Stankevičiūtė S., Sanabria-Cabrera J., Lucena MI., Andrade RJ., Almasio PL., "N-Acetylcysteine for Preventing Acetaminophen-Induced Liver Injury: A Comprehensive Review," Frontiers in Pharmacology, vol. 13, p. 828565, 2022. DOI: 10.3389/fphar.2022.828565.

[33] Jyothilekshmi S., Valsa A.K., Ramadasan, Kuttan, "Protective effect of the polyherbal formulation Nalpamaram on the oxidative stress induced by ethanol," Annals of Phytomedicine, vol. 11, no. 2, pp. 296–301, 2022. DOI: 10.54085/ap.2022.11.2.34.

[34] Nazia Begum, Rahathunnisa Begum, Kandavalli Manipriya, B. Veeresh, "Hepatoprotective and antioxidant activity of allicin on the polycystic ovarian syndrome in rats," Annals of Phytomedicine, vol. 11, no. 2, pp. 400–404, 2022. DOI: 10.54085/ap.2022.11.2.48.

[35] Rao SS., Patel UD., Makwana CN., Ladumor VC., Patel HB., Modi CM., "Effect of quercetin and curcumin in rats sub-acutely exposed to cadmium chloride: haemato-biochemical changes, oxidative stress parameters and histopathological changes in intestine, liver and kidney of rats," The Journal of Phytopharmacology (Pharmacognosy and Phytomedicine Research), vol. 10, no. 5, pp. 399–408, 2021. DOI: 10.31254/phyto.2021.10520

[36] Shahparan Islam Shawon, Rashmia Nargis Reyda, Nazmul Qais, "Medicinal herbs and their metabolites with biological potential to protect and combat liver toxicity and its disorders: A review," Heliyon, vol. 10, no. 3, 2024. Doi:https://doi.org/10.1016/j.heliyon.2024.e25340.