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Review Article

A REVIEW: NANOSTRUCTURED LIPID CARRIER FOR TREATING FUNGAL DISEASE

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ABSTRACT

Topical fungal infections are very predominant around the globe. Topical therapy is the primary choice for treating fungal infections because it has advantages such as lowering the risk of systemic adverse effects and directing the drug to the location of fungal infection. The treatment of a fungal infection is dependent on drug molecules penetrating the outermost layer of skin (stratum corneum) at an effective concentration. Nanostructured lipid carriers (NLC) is an alternate carrier system to address difficulties in topical therapies for superficial fungal infections. This review summarizes different about fungal infections, Structure & types of NLC, formulation & characterization, advantages & its application in treating fungal infection.

Keywords: Fungal infections, Nanotechnology, Nanostructure lipid carrier, Topical drug delivery.

INTRODUCTION

Fungal infections are extremely common in the current situation. Every year, billions of people are diagnosed with either superficial or severe systemic fungal infections. Although antifungal medicines are successful in treating fungal infections, they are associated with serious side effects such as liver damage, oestrogen disruption, and allergic reactions. In the early 1840s, David Grubby, a Hungarian microscopist stationed in Paris, revealed that fungi may cause human sickness. During the 2003 SARS outbreak, 14.8-33% of people were infected, with SARS being the cause of death in 25-73.7% of cases. Fungi are found everywhere, but only a subset of them cause disease (Ravikant *et al*., 2015).

Fungal infections arise when fungus are inhaled, come into touch with the skin, or enter the body through a cut, wound, or injection on the skin. It is more common in persons who have a weakened immune system. This includes persons suffering from illnesses such as HIV/AIDS and those undergoing cancer therapy. Yeasts and moulds are examples of fungi that cause infections in humans. Candida is a form of fungal infection. Candida generally lives within the body and does not cause any difficulties. Candida overproduction can result in infection. Signs and symptoms, microscopy, and cultures are commonly used in prevention. Treatment is usually with antifungal medications, depending on the type of infection. Fungal infections are widespread throughout the world, impacting over one billion individuals each year (Richardson, 2005; Lai *et al*., 2008).

In 2020, an estimated 1.7 million fatalities from fungal illness were reported.Other animals can get a variety of fungal illnesses, and some of these can be passed on to

humans. Mycoses are classified as superficial, subcutaneous, or systemic, depending on whether the infection is deep, widespread, or involves internal organs. They can have an impact on the nails, genitalia, skin, and mouth. Some, such as blast mycosis, Cryptococcus, coccidioidomycosis, and histoplasmosis, affect people who live or travel to specific parts of the world. Other diseases that affect patients with low immunity include aspergillosis, pneumocystis pneumonia, candidiasis, mucormycosis, and talaromycosis. Yeasts, moulds, and some fungi that can exist as both a mould and a yeast cause fungal infections. They are inhaled, come into touch with skin, or enter the body through a cut, wound, or injections. Candida albicans is the most prevalent cause of human fungal infection. Fungal infections are more common in those who have a weakened immune system, have had an organ transplant, have tuberculosis, are undergoing cancer therapy, or have had a corona. People with diabetes and HIV/AIDS are more likely to get fungal infections (Pathakumari *et al*., 2020; Vallabhaneni *et al*., 2016).

Commonly occurring fungal infections

Pneumocystis pneumonia

The fungus Pneumocystis jirovecii causes Pneumocystis pneumonia (PCP). The fungus spreads from person to person through the air. In healthy people, PCP is exceedingly rare, but the fungus that causes the disease can live in their lungs without creating symptoms (Morris *et al*., 2004).

Yeast Infections

Skin yeast infections are known as cutaneous candidiasis. When a fungus called candida overgrows, it causes various infections. Yeast infections are not spreadable. Most infections occur in warm, wet, wrinkled areas of your body, such as your armpits and groyne. They frequently occur in obese or diabetic individuals. Antibiotic users are also more vulnerable (Hay, 1996).

Ringworm

Ringworm, commonly known as tinea corporis, is a fungal skin infection rather than a worm. It gets its name from the ring-shaped rash that has a looping, worm-like edge. Ringworm can be transmitted by direct contact with sick humans or animals. It can also be obtained via clothing or furniture. Heat and humidity can aid in the spread of the virus. Ringworm is characterised by a red, circular, flat sore that may be accompanied by scaly skin. The skin on the outside of the sore may be elevated, while the skin in the centre appears normal. Patches or red rings may intersect (Fuller *et al*., 2003).

Athlete's Foot

Athlete's foot, commonly known as tinea pedis, is a fungal condition that affects your feet. Fungi thrive in warm, damp environments, such as shoes, socks, swimming pools, locker rooms, and public showers. They are more common during the summer and in hot, humid settings. It occurs more frequently in those who wear tight shoes, do not change their sweaty socks, and frequent public baths and pools (Crawford, 2006).

Dermatophytosis

Dermatophyte fungi are keratin-digesting organisms. Dermatophytes infect the epidermis' stratum corneum and keratinized tissues generated from it, such as hair and nails. Trichophyton spp., Microsporum spp., and Epidermophyton spp. cause the majority of superficial fungal infections, while some yeast and non-dermatophyte moulds can also cause them (Robert and Pihet, 2008).

Malassezia infection

Malassezia spp. are ubiquitous surface commensals of oily skin and have been linked to pityriasis versicolor, seborrheic dermatitis, and folliculitis (Velegraki *et al*., 2015).

Topical treatment of fungal infections

The stratum corneum is the best test for dermal delivery, and innovative ways have been developed to increase its permeability. Microemulsions, vesicular transporters containing ethosomes, liposomes, and niosomes are examples of colloidal drug carriers. Among the new carrier dermal administration of antifungals through dermal targeting are lipid and polymeric particulate carrier systems. There have been a few improvements in the treatment of fungal infections, such as focusing on the site of disease, lowering the risk of adverse responses, increasing treatment viability, and improving patient compliance. A variety of topical antifungal agents have been utilised in the treatment of dermatological skin infections. Polyenes, azoles, and allyl amine/benzylamines are the most common types of topical antifungals. Cicloprox is a topically applied antifungal agent. These medications are currently commercially available in traditional dose forms such as creams, gels, salves, and showers (Kyle and Dahl, 2004).

Nanotechnology in fungal disease treatment

Nanotechnology is a multidisciplinary idea that originated in the early 1920s and has numerous uses. It is defined as the use of matter having at least one component in the nanoscale, typically spanning from 1 to 1000 nm, for health products. Nanomaterials have demonstrated remarkable applications in the pharmaceutical field, particularly in diagnostic devices and drug delivery systems, leading to the development of a hybrid science known as pharmaceutical nanotechnology, which has gained popularity due to its ability to improve the pharmacological and biopharmaceutical properties of drugs. Pharmaceutical nanotechnology currently represents a whole new world of therapeutic resources for repurposing the use of medicines, allowing the clinical use of a large number of drugs that could not previously be used properly with conventional formulations or dosage forms, owing to poor bioavailability and physicalchemical instability. Many publications highlight the potential of lipid nanosystems and their ability to overcome drug resistance, decrease systemic toxicity, and target the site of infection and/or the microorganism (Higa *et al*., 2013).

Nanosttructured lipid carrier

Lipid-based (Drug Delivery System) DDS is a well-known, well-established, and commercially viable method of producing pharmaceuticals in a variety of dosage forms. Lipid formulations, such as (Nano Lipid Carriers) NLCs, necessitate the incorporation

of a wide range of components. The bioavailability and solubility of insoluble medicines are two major factors that can be improved with formulations such as NLCs. Many pharmaceutical companies have developed well-established industrial processes for the production of large-scale batches of nanostructured lipid carriers, but all major parameters such as lipid choice, surfactants, other essential excipients, and methods of preparation vary, resulting in changes in parameters such as particle shape and size, phase transition, solubility, drug bioavailability, and so on. Lipid nanoparticles have extraordinary features that are required and extremely important for their therapeutic activity. The unique qualities of nanoparticles (NP) such as surface to mass ratio include extra colloidal particles and their ability to attach and convey chemicals, making an NP more intelligent to employ as a therapeutic product (Haider *et al*., 2020; Beloqui *et al*., 2016).

Components of NLC

Surfactants

Surfactant type and concentration have an impact on the quality and efficacy of NLC. It has been discovered that the surfactant used has a significant impact on the toxicity, physical stability, and crystallinity of NLC. Surfactant systems influence the degree of drug dissolution and drug permeability. Surfactants are chosen based on their route of administration, hydrophilic-lipophilic balance (HLB) value, particle size influence, and lipid modification. Because of their amphipathic nature, surface active agents (emulsifiers) are adsorbed on the interface and lower the tension between the lipid and aqueous phases. The crystallisation of colloid particles occurs concurrently with solidification during the formulation of NLC, however the surface area of the particle increases dramatically during crystallisation, causing the entire system to become unstable. As a result, surfactant is required to increase the interface quality of nanoparticles in order to achieve stability (Karn-Orachai, 2014; Han *et al*., 2008).

Lipids

The selection of appropriate lipids is critical prior to their use in the manufacture of nanoparticulate carriers. The kind and structure of lipid influences the properties of nanocarriers. Solubility or the apparent partition coefficient of bioactives in the lipid has been proposed as the most fitting parameter for selecting a suitable lipid. The drug molecules' solubility in lipid is crucial because it impacts drug loading and encapsulation efficiency.The degree of crystallisation of the various lipids used affects drug entrapment and loading, size and charge, and efficacy (Shah *et al*., 2015).

Other ingredients

To solve the problem of encapsulating water soluble medicinal molecules, organic salts and ionic polymers may be used as counter-ions in the formation of nano structure carriers. Surface-modifiers are another type of excipient that is utilised in the formulation of NLC to reduce phagocytic absorption by macrophages in the reticuloendothelial system (RES). To increase the residence period of therapeutic molecules in systemic circulation, lipid particles are coated with hydrophilic polymers such as PEG, poloxamines, or poloxamers. Surface modification may

provide additional benefits such as improved physical stability and biocompatibility, medication targeting, and greater transport across the epithelium (Uner and Yener, 2007).

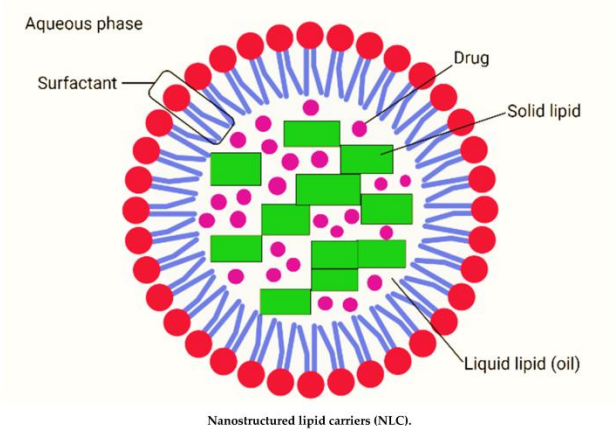

Figure 1: Structure of Nanostructure lipid carrier

Advantages of NLC

•Enhanced physical stamina.
•More space for medicine storage.
•Perfect for loading lipophilic and hydrophilic medicines.
•Easy to scale up production.
•Assist with the regulated release of encapsulated medicines.
•Preventing first-pass metabolism.
•Reduced risks of drug burst release.
•Better control over drug release.
•Through the passage of p-glycoprotein efflux pumps.
•Defending the medication against intra-enterocyte metabolism (Naseri *et al*., 2015).

Types of NLC

Imperfect NLCs

Imperfect NLCs are created by mixing structurally different lipids, such as glycerides and fatty acids, resulting in crystal order flaws.

Amorphous NLCs

Lipids are mixed in such a way in the amorphous form of NLCs that they cannot crystallise, resulting in a structure-less amorphous matrix. The solid lipid is combined with special lipids such as hydroxyoctacosanyl hydroxystearte or isopropyl myristate. As a result, NLCs reside in an amorphous state rather than an ordered one, eliminating medication exclusion due to alterations during storage (Araujo *et al*., 2020).

Multiple O/F/W NLCs

In general, the solid matrix of numerous O/F/W-type NLCs has distributed nanosized liquid oil compartments, which increases the DL as the drug solubility increases. These lipid particles are most suited for incorporating lipophilic medicines, while hydrophilic medications can only be integrated in low concentrations. In some circumstances, water-soluble medicines are converted into water-insoluble lipid conjugates by conjugating them with lipids via covalent bonding or salt creation. These lipid conjugates can be melted and processed to produce lipid-drug conjugation nanoparticles, with 30-50% DL for water-soluble pharmaceuticals (Doktorovova and Souto, 2009).

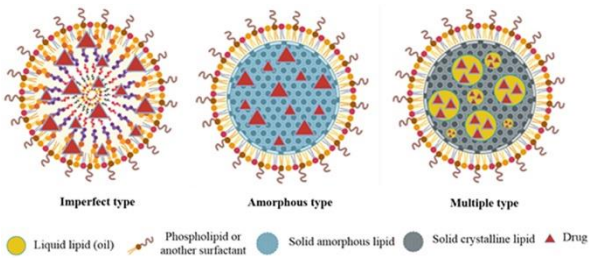

Figure 2: Structure of Nanostructured lipid carrier Methods of NLC preparation

Phase Inversion Method:

It entails magnetic stirring of formulation components followed by heating and cooling cycles with dilution under cooling conditions. At a rate of 4 oC/min, three cycles of heating and cooling from room temperature to 85 oC and back to 60 oC are then applied. The emulsion is inverted as a result of this heat treatment (Gomes *et al*., 2019).

High-Pressure Homogenization Technique:

This is a dependable method for larger-scale production. Lipids are pushed under high pressure (100-200 bars) through a tiny space of a few microns in this process. Shear tension and cavitation cause particle disruption to the submicron range. Normally, the lipid content ranges between 5 and 10%. In comparison to alternative preparation techniques, high pressure homogenization has the advantages of enhanced product texture and consistency with little scaling up issues (Kasongo *et al*., 2012).

Microemulsion:

Microemulsions are created using procedures similar to the high shear homogenization/sonication method. The hot microemulsion is then combined with cold water to form the nanoemulsion, which recrystallizes to form the NLC (Joshi *et al*., 2019).

Double emulsion

Adding the generated microemulsion to cold water (2-10 C) enables the precipitation of evenly distributed NLCs particles (Jang *et al*., 2017).

Membrane contractor

Molten lipid is forced on a porous membrane to form microscopic lipid droplets in this process. They are moved around inside the membrane module while being swept out of the pore. NLCs form when normal temperature is cooled (Dandagi *et al*., 2014).

Microfluidics

Microfluidics is a relatively modern technique that has been introduced as a revolutionary way for producing nanoparticles with optimised homogeneity. The nanoliter quantities of these reagents collide and swiftly mix under exact pressure by forcing liquids into a microfluidic device at constant flow rates. Submitting a pre-emulsion to high-pressure microfluidics and cooling it to room temperature can reduce particle polydispersity, shorten production times, and eliminate the use of organic solvents. Overall, it appears to be a promising strategy for large-scale manufacture of drug-loaded SLNs and NLCs (Garg *et al*., 2016).

Characterization

Size & Morphology

Lipid nanocarriers' physical properties, particularly particle size distribution, influence their accumulation in target tissue. As a result, for the formulation of safe, stable, and efficient nanocarriers, homogeneous (monodisperse) populations of nanocarriers of a certain size are required. Laser diffraction (LD) and photon correlation spectroscopy [also known as dynamic light scattering (DLS)] are routinely used to measure the size of lipid particles (Das *et al*., 2011).

Entrapment Efficiency

Drug entrapment efficiency is defined as the amount of drug entrapped in the carrier as a proportion of the total amount of drug present in the dispersion. Analytical [UV spectrophotometry or highperformance liquid chromatography (HPLC)] and separation

processes (ultrafiltration, centrifugation, and dialysis) were used to measure entrapment efficiency. These approaches can be used to quantify the active component. Entrapment efficiency can be measured in two ways: directly and indirectly (Elmowafy *et al*., 2018).

Zeta Potential

The amount of charge on the surfaces of the particles in aqueous dispersion is defined by the zeta potential, which is an important quantity in predicting the formulations' long-term physical stability. In most cases, the electrophoretic mobility of lipid nanoparticles predicts their zeta potential value, which is determined using photon correlation spectroscopy and LD techniques. The zeta potential of the electrostatically stabilised nano dispersion is greater than 30 mV in absolute terms (Parveen and Sahoo, 2008).

***In vitro* drug release**

The drug release profile from SLNs and NLCs is heavily influenced by biodegradation and diffusion processes. To estimate in vitro drug release from these nanocarriers, side-by-side diffusion cells with a biological or artificial membrane-like reverse dialysis sac, ultra-centrifugation, dialysis bag, centrifugal ultra-filtration, and ultrafiltration are often utilised. The pharmaceutical release profile is examined using a UV spectrophotometer or HPLC (Torchilin and Amiji, 2011).

Stability

The ICH recommendations state that the stability profile of SLNs and NLCs can be examined by measuring the mean particle size, size distribution, entrapment efficiency, and drug release profile over time and at different temperatures. Samples are taken and examined for these criteria at regular intervals. The % drug entrapment efficiency and drug release patterns are determined using a UV spectrophotometer or HPLC (Araújo *et al*., 2011).

Various applications of NLC

Cardiovascular Treatment:

In-vitro incubation studies with Tashinone (TA) loaded NLCs demonstrated that TA-NLC could specifically bind to apoA-I. Macrophage studies revealed that TA- NLC incubated with native HDL could become endogenous by connection with apo-lipoproteins, which do not elicit immunological reactions and may avoid identification by macrophages (Wen *et al.*, 2010).

Drug Delivery to Brain:

Because of their quick uptake by the brain, tolerability, and biodegradability, NLCs of this generation are considered one of the key techniques for drug administration without any alteration to the drug molecule. NLCs of asenapine (ASN) maleate were discovered to have higher bioavailability and increased ASN absorption to the brain (Qi *et al*., 2010).

Parasitic Treatment:

Novel colloidal delivery systems for antiparasitic medicines have piqued the curiosity of researchers working on three important parasitic diseases: malaria, leishmaniasis, and trypanosomiasis. Lipid Nanoparticles combine the benefits of existing colloidal drug carrier systems such as liposomes, polymeric nanoparticles, and emulsions while avoiding or minimising the disadvantages associated with them (Zhang *et al*., 2010).

Ocular Delivery:

In recent decades, SLNs have been employed for ocular medication delivery. More research

into NLCs as ocular delivery methods has recently been conducted. The mucoadhesive characteristics of the thiolated nonionic surfactant Cysteine polyethylene glycol stearate (Cys PEG SA) and NLC modified by this thiolated substance, as well as NLC loaded with cyclosporine, were investigated. The resulting NLCs offered a promising system with a lengthy residence duration (Mohammed *et al*., 2017).

Cancer Chemotherapy

To boost the anti-cancer impact, pHsensitive membranolytic and lysosomolytic nanocarriers (BSAAL-NLCs) were produced by incorporating L-arginine lauryl ester (AL) into NLCs and then coating with bovine serum albumin (BSA). This increases the lysosomolytic potential of nanocarriers while decreasing cytotoxicity, as well as the therapeutic index of loaded active drugs (Sai et al., 2012).

Table 1: Reported formulations of NLC in treatment of fungal disease

Name of drug	Uses	Preparation method	Reference
Fluconazole	Fungal infection	Ultrasonication emulsion technique	(Fernandes *et al*., 2020)
Itraconazole (ITZL)	Fungal infection	Hot homogenization method and Box-Behnken statistical design	(Ameeduzzafar *et al*., 2021)
Clotrimazole	Fungal vaginal infections	Ultrasonication method	**(**Ravani *et al*., 2013)
Miconazole	Athlete's foot	Melt emulsification and Sonication technique	(Singh et al., 2016)
Luliconazole	Dermatophytes	Hot melt emulsification followed by probe sonication	**(**Baghel *et al*., 2020)
Ketoconazole	*Cryptococcus neoformans*-mediated meningoencephalitis	High-pressure homogenization technique	(Du *et al*., 2019)
Miconazole nitrate	Fungal infections	High pressure homogenization technique	**(**Sanap and , Mohanta, 2013)
Voriconazole	Fungal infections	Hot-melt emulsification technique	(Waghule *et al*., 2019)

Oxiconazole Nitrate	Fungal infection	Ultrasonication method	(Ranpise *et al*., 2018)
Amphotericin-B	Fungal infections	Combination of homogenisation and ultrasonication techniques	(Ling *et al*., 2019)
Nystatin	Fungal infection	Hot homogenization and ultrasonication	(Khalil *et al*., 2014)
Econazole nitrate	Fungal infection	Hot homogenization technique	(Gujjar *et al*., 2019)
Sertaconazole	Fungal keratitis	Solvent-diffusion method	(Tavakoli *et al*., 2019)
Clotrimazole and ciprofloxacin	Fungal infectious diseases.	Solvent diffusion technique	**(**Sharma *et al*.,2016)

CONCLUSION

Based on the trials included in this study, it was discovered that incorporating medications into NLC for use against fungal infections improved their effectiveness, even when compared to commercial presentations. This profile of findings could be attributed to qualities associated with these systems, such as adhesiveness, sustained release, and a high contact surface, which allows for better engagement with the microbe, reaffirming both systems' ability to treat this set of illnesses. However, due to the fast flow of the micro supensions of the aforementioned systems, they must be dispersed in systems with higher adhesion, such as hydrogels, for cutaneous application. Thus, although improving medication therapeutic response, inclusion in these nanosystems and dispersion in more viscous systems may increase the cost of the end product, making it more expensive than currently available presentations. Furthermore, several hurdles remain to be overcome in order to translate these in vitro data for animal subjects as well as humans. Many encouraging results indicate the need for more specific investigations in the near future to assess their biological potential, not just in vitro. However, there are just a few studies that use NLC to treat fungal infections, making their application for this purpose a viable source for future research.

REFERENCES

- Ameeduzzafar, Q.M., Qumber, M., Alruwaili, N.K., Bukhari, S.N.A., Alharbi, K.S., Imam, S.S., Afzal, M., Alsuwayt, B., Mujtaba, A. & Ali, A. (2021) BBD-based development of itraconazole loaded nanostructured lipid carrier for topical delivery: In vitro evaluation and antimicrobial assessment. *Journal of Pharmaceutical Innovation*, 16, 85–98

- Araújo, J., Nikolic, S., Egea, M.A., Souto, E.B. & Garcia, M.L. (2011) Nanostructured lipid carriers for triamcinolone acetonide delivery to the posterior segment of the eye. *Colloids and Surfaces. B, Biointerfaces*, 88, 150–157
- Araujo, V.H.S., da Silva, P.B., Szlachetka, I.O., da Silva, S.W., Fonseca-Santos, B., Chorilli, M., Ganassin, R., de Oliveira, G.R.T., da Rocha, M.C.O., Fernandes, R.P., de Carvalho Vieira Queiroz, M.D., Azevedo, R.B. & Muehlmann, L.A. (2020) The influence of NLC composition on curcumin loading under a physicochemical perspective and in vitro evaluation. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, 602, 125070
- Baghel, S., Nair, V.S., Pirani, A., Sravani, A.B., Bhemisetty, B., Ananthamurthy, K., Aranjani, J.M. & Lewis, S.A. (2020) Luliconazole-loaded nanostructured lipid carriers for topical treatment of superficial tinea infections. *Dermatologic Therapy*, 33, e13959
- Beloqui, A., Solinís, M.Á., Rodríguez-Gascón, A., Almeida, A.J. & Préat, V. (2016) Nanostructured lipid carriers: Promising drug delivery systems for future clinics. *Nanomedicine: Nanotechnology, Biology, and Medicine*, 12, 143–161
- Crawford, F. (2006) Athlete's foot. *BMJ Clinical Evidence*, 2006, 1712–
- Dandagi, P.M., Dessai, G.A., Gadad, A.P. & Desai, V.B. (2014) Formulation and evaluation of nanostructured lipid carrier (NLC) of lornoxicam. *International Journal of Pharmacy and Pharmaceutical Sciences*, 6, 73–77.
- Das, S. & Chaudhury, A. (2011) Recent advances in lipid nanoparticle formulations with solid matrix for oral drug delivery. *AAPS PharmSciTech*, 12, 62–76
- Doktorovova, S. & Souto, E.B. (2009) Nanostructured lipid carrier-based hydrogel formulations for drug delivery: A comprehensive review. *Expert Opinion on Drug Delivery*, 6, 165–176
- Du, W., Li, H., Tian, B., Sai, S., Gao, Y., Lan, T., Meng, Y. & Ding, C. (2019) Development of nose-to-brain delivery of ketoconazole by nanostructured lipid carriers against cryptococcal meningoencephalitis in mice. *Colloids and Surfaces. B, Biointerfaces*, 183, 110446
- Elmowafy, M., Ibrahim, H.M., Ahmed, M.A., Shalaby, K., Salama, A. & Hefesha, H. (2017) Atorvastatin-loaded nanostructured lipid carriers (NLCs): Strategy to overcome oral delivery drawbacks. *Drug Delivery*, 24, 932–941
- Elmowafy, M., Shalaby, K., Badran, M.M., Ali, H.M., Abdel-Bakky, M.S. & Ibrahim, H.M. (2018) Multifunctional carbamazepine loaded nanostructured lipid carrier (NLC) formulation. *International Journal of Pharmaceutics*, 550, 359–371
- Fernandes, A.V., Pydi, C.R., Verma, R., Jose, J. & Kumar, L. (2020) Design, preparation and in vitro

characterizations of fluconazole loaded nanostructured lipid carriers. *Brazilian Journal of Pharmaceutical Sciences*, 56

- Fuller, L.C., Child, F.J., Midgley, G. & Higgins, E.M. (2003) Diagnosis and management of scalp ringworm. *BMJ*, 326, 539–541
- Garg, S., Heuck, G., Ip, S. & Ramsay, E. (2016) Microfluidics: A transformational tool for nanomedicine development and production. *Journal of Drug Targeting*, 24, 821–835
- Gomes, G.V.L., Sola, M.R., Rochetti, A.L., Fukumasu, H., Vicente, A.A. & Pinho, S.C. (2019) β-carotene and α-tocopherol coencapsulated in nanostructured lipid carriers of murumuru (Astrocaryum murumuru) butter produced by phase inversion temperature method: Characterisation, dynamic in vitro digestion and cell viability study. *Journal of Microencapsulation*, 36, 43–52
- Gujjar, S., Blr, M. & Karki, R. (2019) Formulation and evaluation of topical gel containing nanostructured lipid carriers dispersion of an antifungal drug. *Acta Pharmaceutica Sciencia*, 57
- Haider, M., Abdin, S.M., Kamal, L. & Orive, G. (2020) Nanostructured lipid carriers for delivery of chemotherapeutics: A review. *Pharmaceutics*, 12, 288
- Han, F., Li, S., Yin, R., Liu, H. & Xu, L. (2008) Effect of surfactants on the formation and characterization of a new type of colloidal drug delivery system: Nanostructured lipid carriers. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, 315, 210–216
- Hay, R.J. (1996) Yeast infections. *Dermatologic Clinics*, 14, 113–124
- Higa, L.H., Schilrreff, P., Perez, A.P., Morilla, M.J. & Romero, E.L. (2013) The intervention of nanotechnology against epithelial fungal diseases. *Journal of Biomaterials and Tissue Engineering*, 3, 70–88
- Iglic, A., Kulkarni, C. & Rappolt, M. (2016). *Advances in Biomembranes and Lipid Self-Assembly*, 1st edn. Academic Press: UK.
- Jang, J.H. & Park, S.Y. (2017) pH-responsive cholesteric liquid crystal double emulsion droplets prepared by microfluidics. *Sensors and Actuators. Part B*, 241, 636–643
- Joshi, M.D., Prabhu, R.H. & Patravale, V.B. (2019). *Fabrication of Nanostructured Lipid Carriers (NLC)-Based Gels from Microemulsion Template for Delivery Through Skin. Pharmaceutical Nanotechnology: Basic Protocols*, pp. 279–292.
- Karn-Orachai, K., Smith, S.M., Phunpee, S., Treethong, A., Puttipipatkhachorn, S., Pratontep, S. & Ruktanonchai, U.R. (2014) The effect of surfactant composition on the chemical and structural properties of nanostructured lipid carriers. *Journal of Microencapsulation*, 31, 609–618
- Kasongo, K.W., Müller, R.H. & Walker, R.B. (2012) The use of hot and cold high pressure homogenization to enhance the

loading capacity and encapsulation efficiency of nanostructured lipid carriers for the hydrophilic antiretroviral drug, didanosine for potential administration to paediatric patients. *Pharmaceutical Development and Technology*, 17, 353–362

- Khalil, R.M., Abd-Elbary, A., Kassem, M.A., El Ridy, M.S., Samra, M.M., Awad, G.E. & Mansy, S.S. (2014) Formulation and characterization of nystatin-loaded nanostructured lipid carriers for topical delivery against cutaneous candidiasis. *British Journal of Pharmaceutical Research*, 4, 490–512
- Kyle, A.A. & Dahl, M.V. (2004) Topical therapy for fungal infections. *American Journal of Clinical Dermatology*, 5, 443–451
- Lai, C.C., Tan, C.K., Huang, Y.T., Shao, P.L. & Hsueh, P.R. (2008) Current challenges in the management of invasive fungal infections. *Journal of Infection and Chemotherapy*, 14, 77–85
- Li, S., Su, Z., Sun, M., Xiao, Y., Cao, F., Huang, A., Li, H., Ping, Q. & Zhang, C. (2012) An arginine derivative contained nanostructure lipid carriers with pH-sensitive membranolytic capability for lysosomolytic anti-cancer drug delivery. *International Journal of Pharmaceutics*, 436, 248–257
- Ling, J.T.S., Roberts, C.J. & Billa, N. (2019) Antifungal and mucoadhesive properties of an orally administered chitosan-coated amphotericin B nanostructured lipid carrier (NLC). *AAPS PharmSciTech*, 20, 136
- Morris, A., Lundgren, J.D., Masur, H., Walzer, P.D., Hanson, D.L., Frederick, T., Huang, L., Beard, C.B. & Kaplan, J.E. (2004) Current epidemiology of Pneumocystis pneumonia. *Emerging Infectious Diseases*, 10, 1713–1720
- Naseri, N., Valizadeh, H. & Zakeri-Milani, P. (2015) Solid lipid nanoparticles and nanostructured lipid carriers: Structure, preparation and application. *Advanced Pharmaceutical Bulletin*, 5, 305–313
- Parveen, S. & Sahoo, S.K. (2008) Polymeric nanoparticles for cancer therapy. *Journal of Drug Targeting*, 16, 108–123
- Pathakumari, B., Liang, G. & Liu, W. (2020) Immune defence to invasive fungal infections: A comprehensive review. *Biomedicine and Pharmacotherapy*, 130, 110550
- Qi, S., Marchaud, D. & Craig, D.Q. (2010) An investigation of the mechanism of dissolution rate enhancement of poorly water-soluble drugs from spray chilled gelucire 50/13 microspheres. *Journal of Pharmaceutical Sciences*, 99, 262–274
- Ranpise, H.A., Gujar, K.N., Mathure, D., Satpute, P.P., Awasthi, R., Dua, K. & Madan, J.R. (2018) Skin targeting of oxiconazole nitrate loaded nanostructured lipid-carrier gel for fungal infections. *Pharmaceutical Nanotechnology*, 6, 192–200
- Ravani, L., Esposito, E., Bories, C., Moal, V.L., Loiseau, P.M., Djabourov, M., Cortesi, R. & Bouchemal, K.

(2013) Clotrimazole-loaded nanostructured lipid carrier hydrogels: Thermal analysis and in vitro studies. *International Journal of Pharmaceutics*, 454, 695–702

- Ravikant, K.T., Gupte, S. & Kaur, M. (2015);1(2) A review on emerging fungal infections and their significance. *J. Bacteriol. Mycol. Open Access.*, 00009.
- Richardson, M.D. (2005) Changing patterns and trends in systemic fungal infections. *Journal of Antimicrobial Chemotherapy*, 56 (Supplement 1)(suppl_1):i5-11, i5–i11
- Robert, R. & Pihet, M. (2008) Conventional methods for the diagnosis of dermatophytosis. *Mycopathologia*, 166, 295–306
- Sanap, G.S. & Mohanta, G.P. (2013) Design and evaluation of miconazole nitrate loaded nanostructured lipid carriers (NLC) for improving the antifungal therapy. *Journal of Applied Pharmaceutical Sciences*, 3, 046–054.
- Shah, R., Eldridge, D., Palombo, E. & Harding, I. (2015). *Lipid Nanoparticles: Production, Characterization and Stability*. Springer: UK.
- Sharma, A., Sood, A., Mehta, V. & Malairaman, U. (2016) Formulation and physicochemical evaluation of nanostructured lipid carrier for codelivery of clotrimazole and ciprofloxacin. *Asian Journal of Pharmaceutical and Clinical Research*, 9, 356–360.
- Singh, S., Singh, M., Tripathi, C.B., Arya, M. & Saraf, S.A. (2016) Development and evaluation of ultra-small nanostructured lipid carriers: Novel topical delivery system for athlete's foot. *Drug Delivery and Translational Research*, 6, 38–47
- Tavakoli, N., Taymouri, S., Saeidi, A. & Akbari, V. (2019) Thermosensitive hydrogel containing sertaconazole loaded nanostructured lipid carriers for potential treatment of fungal keratitis. *Pharmaceutical Development and Technology*, 24, 891–901
- Torchilin, V. & Amiji, M.M. (2011). *Handbook of Materials for Nanomedicine*, Vol. 1. Pan Stanford Publishing.
- Uner, M. & Yener, G. (2007) Importance of solid lipid nanoparticles (SLN) in various administration routes and future perspectives. *International Journal of Nanomedicine*, 2, 289–300
- Vallabhaneni, S., Mody, R.K., Walker, T. & Chiller, T. (2016) The global burden of fungal diseases. *Infectious Disease Clinics of North America*, 30, 1–11
- Velegraki, A., Cafarchia, C., Gaitanis, G., Iatta, R. & Boekhout, T. (2015) Malassezia infections in humans and animals: Pathophysiology, detection, and treatment. *PLOS Pathogens*, 11, e1004523
- Waghule, T., Rapalli, V.K., Singhvi, G., Manchanda, P., Hans, N., Dubey, S.K., Hasnain, M.S. & Nayak, A.K. (2019) Voriconazole loaded nanostructured lipid carriers based topical delivery system: QbD based designing, characterization, in-vitro and ex-vivo evaluation. *Journal of*

Drug Delivery Science and Technology, 52, 303–315

- Zhang, W.L., Gu, X., Bai, H., Yang, R.H., Dong, C.D. & Liu, J.P. (2010) Nanostructured lipid carriers constituted from high-density lipoprotein components for delivery of a lipophilic cardiovascular drug. *International Journal of Pharmaceutics*, 391, 313–321
- Zhang, X., Liu, J., Qiao, H., Liu, H., Ni, J., Zhang, W. & Shi, Y. (2010) Formulation optimization of dihydroartemisinin nanostructured lipid carrier using response surface methodology. *Powder Technology*, 197, 120–128