European Review for Medical and Pharmacological Sciences 2023; 27: 5257-5263

Current status and research progress of nanoparticle application in superficial fungal infection

M.-Y. REN[1], Y.-J. SHI[1], Y. DING[2], W. LU[2], S.-S. FAN[2], X.-H. TAO[1,2]

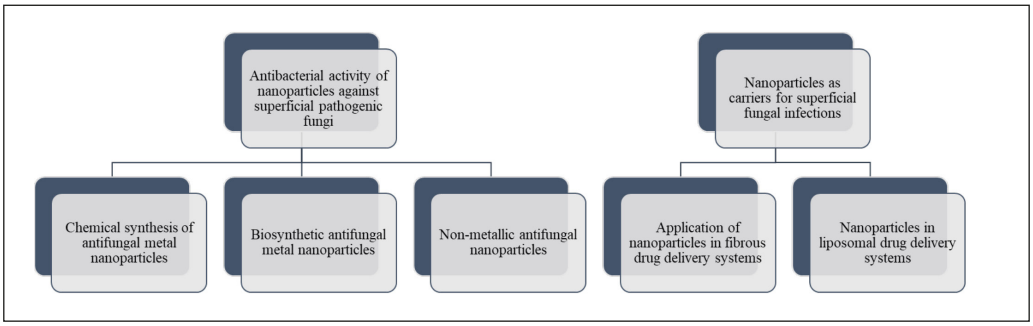
[1]Department of Graduate School, Bengbu Medical College, Bengbu, China
[2]Department of Dermatology, Zhejiang Provincial People's Hospital, Affiliated People's Hospital, Hangzhou Medical College, Hangzhou, China

Abstract. – Superficial fungal infections (SFIs) are characterized by diverse etiologies, complex pathogenesis, and marked geographical differences in patient symptoms. Conventional management of SFIs is associated with complications such as hepatotoxicity, skin problems, severe headaches, and clinical difficulties including intractable relapses and drug-drug interactions in patients with chronic diseases remain to be addressed. Moreover, in topical treatment, low penetration of antifungal drugs in hard tissues such as finger (toe) nails and drug-resistant fungi are emerging concerns in current antifungal therapy. Nanotechnology has been a leading research topic in recent years for new dosing forms of antifungal drugs, chemical modification of traditional drugs, and pharmacokinetic improvement, providing potential opportunities for the effective treatment of SFIs. The present study reviewed the direct use of nanoparticles in SFIs and the use of nanoparticles as carriers in SFIs and discussed their future medicinal applications.

Key Words:
Superficial fungal infection, Nanoparticles, Candida albicans, Dermatophytes, Drug delivery system.

Introduction

Dermatophytic fungal infections are the fourth most common public health issue, involving approximately 1 billion people worldwide[1]. Superficial fungal infections (SFIs) with keratinophilic properties are caused by dermatophytes, *Candida albicans*, and *Malassezia spp.* and easily invade the skin, hair, and nail plates[2]. Pathogenic fungi can be transmitted by contact, inhalation, or ingestion, and SFIs are classified as tinea capitis, tinea corporis, tinea manuum, tinea pedis, tinea versicolor, and tinea unguium according to their distribution sites[3]. *Candida albicans* is commonly found in superficial infections of the vagina, gastrointestinal tract, and oral cavity, and *Malassezia* is commonly located in areas of high seborrhea and is closely associated with folliculitis, seborrheic dermatitis, and pityriasis versicolor[4]. The dramatic rise in SFIs after the popularity of antibiotic therapy in the late 1960s has posed a global health threat, especially for patients with immunodeficiency diseases, cancer, acquired immune deficiency syn-



Graphical Abstract. Antibacterial activity and carrier of nanoparticles against superficial pathogenic fungi.

Corresponding Author: X.-H. Tao, MD; e-mail: txhtxh@sina.com

drome (AIDS), diabetes, organ transplantation, old age, and cystic fibrosis[5].

Topical antifungal drugs are the preferred treatment modality for SFIs, allowing penetration of the stratum corneum and high local drug concentrations. In addition, self-administration by patients results in high patient compliance with medications[6]. Despite the widespread use of various topical and systemic agents such as ketoconazole, fluconazole, itraconazole, ashwagandha, and terbinafine, the emergence of resistance with the formation of fungal biofilms and efflux pump proteins requires alternative therapeutic strategies[7]. Current research has indicated that topical preparations may elicit adverse skin reactions such as skin irritation, allergic reactions, and pruritus[8]. The stratum corneum of the skin causes low skin drug concentrations, dermatophytosis recurrence or treatment failure, and results in short retention of antifungal drugs at the site of skin action, thereby necessitating frequent drug administration[9]. Thus, multiple clinical interventions, including chemical agents, iontophoresis, and electroporation, have been developed to disrupt the integrity of the skin barrier to enhance topical drug penetration[10]. However, they may induce skin irritation due to their disruptive effect on the lipid structure of the skin and may produce stinging and burning sensations with improper use[11].

Nanotechnology is an important area of modern research involving the synthesis and manipulation of material structures, commonly referred to as nanomaterials, ranging in size from approximately 1 to 100 nm, and their surface-to-volume ratio and antimicrobial activity increase with the decrease in nanoparticle size[12]. A bidirectional relationship exists between mycology and nanotechnology, as metal nanoparticles (NPs) possess antifungal activity and fungi can produce NPs from metal salts[13]. Nanotechnology is a research hotspot for new dosage forms of antifungal drugs, chemical modifications of traditional drugs, and pharmacokinetic improvements[14]. NPs can be synthesized and administered in combination with antifungal agents to boost one or both of their antifungal abilities, and the use of NPs as potential antifungal agents is a promising research direction[15].

Antibacterial Activity of Nanoparticles Against Superficial Pathogenic Fungi

Chemical synthesis of antifungal metal nanoparticles

Kim et al[16] dissolved solid silver in nitric acid at 90°C, added sodium chloride to reduce the silver ions, synthesized silver nanoparticles (AgNPs) with a diameter of 3 nm for the first time, and verified the minimum inhibitory concentrations (MICs) of AgNPs in *Candida albicans*, *Candida tropicalis*, *Candida smoothis*, *Candida subsmoothis*, *Candida krusei*, and *Trichoderma spp.* Using amphotericin B and fluconazole as positive controls, AgNPs showed significant antibacterial efficacy in *Candida* and *Trichophyton spp.* with 80% inhibitory concentrations (IC80) ranging from 1 to 7 μg/mL. Its antifungal efficacy was comparable to that of amphotericin B [IC80 (1-5 μg/mL)] and significantly higher than that of fluconazole [IC80 (10-30 μg/mL)][16].

Li et al[17] reduced silver nitrate (AgNO3) to AgNPs by adding $AgNO_3$ to a graphene oxide (GO) solution. AgNPs were attached to GO through oxygen-containing functional groups and surface defects, and GO-AgNPs complexes were prepared by microwave reduction method, exhibiting strong antifungal activity against clinically resistant strains of *Candida tropicalis* and *Candida albicans* in abdominal surgery, *Candida vaginitis*, and burn wounds. Copper oxide NPs (CuO-NPs) was synthesized by chemical method and evaluated their antifungal activity. CuO-NPs were found to provide good antifungal activity against *Trichophyton spp.* and *Trichophyton rubrum*, and morphological changes and mycelial lysis of *Trichophyton rubrum* could be observed under electron microscopy. The presence of carboxyl and amine groups on the surface of fungi provides a strong affinity for copper ions, which may be the main reason for the antifungal effect of CuO-NPs. CuO-NPs have a large surface area and can be absorbed into the blood by the skin at a size of less than 30 nm[18].

Ayatollahi Mousavi et al[19] found the strongest antibacterial activity of AgNPs against *Microsporum canis*, followed by *Trichoderma spp.* and *M. gypsum-like microsporidia*. It was found[19] that AgNPs coupled with monoclonal antibodies for combined treatment with Q-switched Nd: YAG and that they exhibited significant antibacterial activity even at a low concentration. The laser creates pits in the cell wall of the fungus, allowing for easier access of AgNPs into the cell. The thermal effect of the laser causes the electron excitation of AgNPs, which react with oxygen to produce superoxide radicals, and these radicals can produce reactive oxygen species with antifungal activity and reduce dermatophyte keratinase activity in co-administration. Of skin surface fungi, *Flocculent epidermidis* is the most sensitive

and *Trichophyton rubrum* is the most tolerant[19]. Characterization and improvement of the *in vitro* antifungal activity of ketoconazole-poly (lactic acid) against *Candida* and dermatophytes showed that ketoconazole-containing nanoparticles exhibited superior antifungal activity to free ketoconazole against all fungal strains tested and also achieved inhibition of yeast biofilm formation[20]. Ketoconazole-poly (lactic acid) nanoparticles enabled better antifungal activity of ketoconazole nanoparticles as free agents against dermatophytes and *Candida* species[21].

Biosynthetic Antifungal Metal Nanoparticles

Biosynthetic antifungal nanoparticles are another focus of research. Nitrate reductase in fungi converts nitrate to nitrite and transfers electrons to silver ions, generating nano-silver. The extracellular biosynthesis of AgNPs was performed by using the fungus *Xylella rickettsii* with an average diameter of 50 nm, which effectively inhibited the growth of *gypsum-like microsporidia*, *Trichoderma spp.* and *Penicillium wanzii* with a minimum inhibition range of 17-25 mm, significantly greater than amphotericin B[22]. Plant extracts can also be used as reducing agents to synthesize nano-silver. AgNPs with a diameter of 2 nm either alone or in combination with amphotericin B exhibited antifungal activity against dermatophytes of 1-2 mg/mL and 1-5 mg/mL. It was found that AgNPs could disrupt the lipid bilayer of cell membranes, leading to ion transfer, pore formation, and membrane potential attenuation, and showed the strongest antifungal activity against *flocculent S. epidermidis*, as well as disrupting the cell membrane of *Candida albicans* and increasing its permeability[23]. Antifungal drugs derived from natural plant extracts and oils are a viable approach to address fungal resistance. Furthermore, cinnamon, menthol, fennel, lemongrass, pepper, clove, and camphor extracts have been used in the preparation of antifungal drugs because of their potent antifungal properties[24]. However, the poor solubility, stability, and bioavailability of plant extracts may hinder the potential therapeutic effects[25]. In combination with nanocarriers, these natural antifungal chemicals feature different compositions, surface properties, and membrane fluidity to be efficiently transported in nanostructures[26]. Rónavári[27] investigated the ability of *Saccharomyces cerevisiae* and *Streptomyces sp.* to biosynthesize AgNPs and AuNPs, and the formation of NPs was associated with the presence of the potent antioxidant astaxanthin in the microorganisms. In the evaluation of the biological activity of NPs, AgNPs inhibited almost all of the pathogenic bacteria detected in the study. These AgNPs exhibited strong antifungal activity against the dermatophytes *Trichoderma spp.* and *Microsporum canis*, and no cytotoxicity of NPs was observed in HaCaT keratinocytes. Moreover, AuNPs have antifungal activity against *Cryptococcus novelis*, but at 10-30 μg/mL, dermatophytes are resistant to AuNPs[27].

Pereira et al[28] synthesized AgNPs using a combination of biosynthesis and chemical synthesis and compared the efficacy of AgNPs with other antifungal drugs by reducing $AgNO_3$ in an aqueous solution of polyvinylpyrrolidone and glucose and chemically synthesizing AgNPs. A comparison of the antifungal activity of chemically synthesized AgNPs, as well as biosynthetic AgNPs against *Trichoderma reesei strains* using extracellular biosynthetic AgNPs from *Penicillium flavum-producing* and *Aspergillus oryzae*, revealed that chemically synthesized AgNPs showed a lower MIC than biosynthetic AgNPs and that the antimicrobial activity of chemically synthesized AgNPs with smaller diameter was correlated with a larger surface area/volume ratio[28]. The biosynthetic ZnO-NPs were found to demonstrate anti-dermal fungal activity and to enhance the antifungal activity of ketoconazole[29]. Currently, selenium sulfide NPs are also available biosynthetically, selenite, sodium sulfite, biosynthesized by *Saccharomyces cerevisiae*, and suppress pathogenic bacteria such as saprophytes and yeasts as well as dermatophytes[30].

Non-Metallic Antifungal Nanoparticles

A nanoemulsion called NB-002 has also been used against surface fungal infections and the cationic quaternary ammonium compound, which contributes to the antifungal activity and stability of the nanoemulsion droplets. Pannu et al[31] evaluated the antifungal activity of NB-002 against *Candida albicans*, dermatophytes, and other filamentous fungi with broad-spectrum antifungal activity and identified that this antifungal activity was directed against the pathogens of tinea cruris, tinea pedis, tinea capitis, tinea corporis, and nail fungus. Moreover, they compared the antibacteri-

al activity of NB-002 with that of oral antifungals such as terbinafine, ashwagandha, and itraconazole against *Microsporum canis*, *Trichophyton spp.* and *epidermophyton floccosum* and discovered significant heterogeneity in the antifungal activity of the oral drugs, demonstrating the antifungal activity of NB-002 against other filamentous genera and the resistance of these filamentous genera to a wide range of drugs. These fungi were isolated from immunodeficient patients. Furthermore, NB-002 showed strong activity against azo-resistant *Candida albicans* isolates, terbinafine-resistant *Trichoderma reesei* isolates, and multidrug-resistant mycobacteria, providing inactivation of both microconidia and mycelium, even in dormant fungal cells[31].

Nanoparticles as Carriers for Superficial Fungal Infections

Many nanocarriers have been used for topical delivery of antibiotics against skin fungi. Nanocarriers deliver antifungal drugs to the target site without causing damage to the liver through the bloodstream or rapid excretion from the kidneys. By controlling the release of antifungal drugs, nanocarriers contribute to prolonged drug damage counteracting and aiding wound healing.

Nanoparticles in Liposomal Drug Delivery Systems

Liposomes are one of the most widely used nanocarriers that can penetrate the stratum corneum, which is the part most exposed to skin fungal attack. Sudhakar et al[32] conducted *in vitro* experiments on rabbit skin and found that liposomes dispersed in carrageenan gels were more durable antibacterially in gels containing drug-laden liposomes *vs.* carrageenan-containing terbinafine hydrochloride without liposomes[32]. Elmoslemany compared the effect of transdermal administration of miconazole nitrate propylene glycol liposomes with conventional liposomes and reported that the MIC of miconazole nitrate propylene glycol liposomes was 1.46 μg/mL for *Candida albicans* and 2.93 μg/mL for conventional liposomes. In addition, the penetration and skin retention of miconazole nitrate liposomes in human skin is higher than that of miconazole nitrate suspensions and conventional liposomes[33].

Alcohol plasmas are nanocarriers of phospholipid-based vesicles with a good ethanol concentration to dissolve the lipids in the stratum corneum and allow the vesicles to penetrate the skin. The diameter of the alcohol plasmid is controllable by changing the ratio of ethanol and phospholipid, and the more ethanol, the smaller the size of the nanocarrier. Jarratt et al[34] found that luliconazole cream 1% applied once daily for either 2 or 4 weeks is safe and effective for treatment of tinea pedis. More importantly, the antifungal effects of luliconazole persist for several weeks, resulting in increased rates of mycological cure. Terbinafine is a commonly used drug for topical fungal infections with limited solubility in water and skin permeability[35]. The results of the 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2-H-tetrazolium bromide, Thiazolyl Blue Tetrazolium Bromide (MTT) study showed that terbinafine liposomes were not cytotoxic and had a lower MIC than terbinafine in anti-*Trichoderma*, *Fusarium,* and *Trichoderma* effects[36]. Besides, the nanoprecipitation method was used[36] to compound terbinafine-loaded nanoparticles.

Application of Nanoparticles in Fibrous Drug Delivery Systems

Electrospinning technology is an efficient and low-consumption technique for the preparation of nanofibers, and the combination of polyhexanoate/gelatin nanofibers prepared with terbinafine hydrochloride can deliver antifungal drugs to the surface infection site and allow continuous and stable drug release, which can successfully inhibit the growth of *Trichoderma spp.* and *Aspergillus fumigatus*. Nanofiber carrier eugenol prepared using polyacrylonitrile nanofibers as a delivery system for eugenol (a phenolic component of clove oil with antifungal effects) can effectively inhibit the growth of *Candida albicans* and is of interest in the treatment of superficial *Candida albicans* infections[37]. Mofidfar prepared nanofibrous polymeric carriers of clotrimazole by first co-extracting with poly(ethylene oxide) containing polycaprolactone clotrimazole and then removing the poly(ethylene oxide) to obtain polycaprolactone clotrimazole fibers. Compared with the electrospinning technique, this formulation of clotrimazole provided a longer duration of activity retention[38]. Zhang et al[39] prepared ketoconazole-lecithin-zebrahin nanoparticles (KLZ-NPs) and used the Franz diffusion cell method for *in vitro* penetration and

retention ability of ketoconazole in rat and pig skin. The *in vitro* permeation assay confirmed that the ketoconazole concentration was significantly higher in the stratum corneum and deep KLZ-NPs groups (2.98-fold and 1.51-fold higher than free ketoconazole, respectively). Moreover, the hair follicle closure technique indicated a significant enhancement in the entry of formed nanoparticles into the skin through the hair follicle route, suggesting that KLZ-NPs facilitate enhanced drug retention in different skin layers, thereby increasing the concentration of ketoconazole in the skin and allowing sustained release to extend the dosing interval. In addition, KLZ-NPs demonstrated advantages in reducing hepatic drug accumulation and toxicity[39]. Na et al[40] prepared econazole-loaded nanostructured lipid carrier hybrid film-forming systems to enhance antifungal activity against dermatophytes, which could form transparent, uniform, and difficult-to-remove films after topical application. The drug allows sustained release and prolonged antifungal activity, enabling continuous exposure to the infection site and reducing the frequency of single-dose applications.

Direct potassium hydroxide (KOH) microscopy and fungal culture are considered the gold standard for the diagnosis of dermatophytosis. However, direct KOH microscopy and other available direct microscopy-based techniques require proper sampling as well as skills in identifying microorganisms[41]. Direct antigen-antibody interactions have been employed to prepare antigen-antibody-gold NPs-pAbs complexes for the detection of dermatophyte antigens present in hair, nail, and skin debris samples, and results can be obtained within 3 to 7 minutes after sample collection[42]. However, additional studies are required for confirmation.

Conclusions

The difficulties in the treatment of SFIs lie in the resistance of topical drugs and recurrent adverse effects such as hepatotoxicity of oral treatment. NGs are a novel field of drugs for the treatment of fungal infections, offering better antifungal efficacy alone or in combination with other antibiotics. NGs can provide a good drug delivery system to deliver antifungal drugs to the target tissue. Liposomal nanocomposites and other liposomal products, due to their lipophilic nature, easily pass through the surface layer to target the drug to the pathogenic fungus. Fibrous drug delivery systems enable direct drug delivery to target tissues, gradual release, and shortened treatment time through direct contact with pathogenic microorganisms. Nanotechnology offers viable and more effective solutions for the management of SFIs, especially for patients with cancer, autoimmune diseases, and immunosuppressive drugs. Nevertheless, its clinical application requires further promotion and popularization.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Authors' Contributions

M.-Y. Ren: methodology, investigation, writing original draft, writing-reviewing, and editing. X.-H. Tao: conceptualization and supervision. Y.-J. Shi: literature research. Y. Ding, W. Lu, S.-S. Fan: investigation, supervision, and methodology. All authors contributed to the article and approved the submitted version.

Funding

This study was funded by The Young Talents Project of Zhejiang Medicine and Health Science and Technology Project (Grant number: 2022KY049) and Zhejiang Province Public Welfare Technology Research Project (Grant number: LGF20H110003).

Ethics Approval and Informed Consent

Not applicable.

ORCID ID

Xiaohua Tao: 0000-0003-3527-2914
Mingyang Ren: 0000-0003-4428-831X

References

1) Strickland AB, Shi M. Mechanisms of fungal dissemination. Cell Mol Life Sci 2021; 78: 3219-3238.
2) Pihet M, Le Govic Y. Reappraisal of Conventional Diagnosis for Dermatophytes. Mycopathologia 2017; 182: 169-180.
3) Shen JJ, Jemec G, Arendrup MC, Saunte D. Photodynamic therapy treatment of superficial fungal infections: A systematic review. Photodiagnosis Photodyn Ther 2020; 31: 101774.
4) Salehi Z, Shams-Ghahfarokhi M, Razzaghi-Abyaneh M. Antifungal drug susceptibility profile of

clinically important dermatophytes and determination of point mutations in terbinafine-resistant isolates. Eur J Clin Microbiol Infect Dis 2018; 37: 1841-1846.

5) Razzaghi-Abyaneh M, Chen ZY, Shams-Ghahfarokhi M, Rai M. Editorial: Research Efforts, Challenges, and Opportunities in Mitigating Aflatoxins in Food and Agricultural Crops and Its Global Health Impacts. Front Microbiol 2022; 13: 881858.
6) Verma S, Utreja P. Vesicular nanocarrier based treatment of skin fungal infections: Potential and emerging trends in nanoscale pharmacotherapy. Asian J Pharm Sci 2019; 14: 117-129.
7) Nivoix Y, Ledoux MP, Herbrecht R. Antifungal Therapy: New and Evolving Therapies. Semin Respir Crit Care Med 2020; 41: 158-174.
8) Kenechukwu FC, Attama AA, Ibezim EC, Nnamani PO, Umeyor CE, Uronnachi EM, Momoh MA, Akpa PA, Ozioko AC. Novel Intravaginal Drug Delivery System Based on Molecularly PEGylated Lipid Matrices for Improved Antifungal Activity of Miconazole Nitrate. Biomed Res Int 2018; 2018: 3714329.
9) Qurt MS, Esentürk İ, Birteksöz Tan S, Erdal MS, Araman A, Güngör S. Voriconazole and sertaconazole loaded colloidal nano-carriers for enhanced skin deposition and improved topical fungal treatment. JDDST 2018; 48: 215-222.
10) El-Zaafarany GM, Nasr M. Insightful exploring of advanced nanocarriers for the topical/transdermal treatment of skin diseases. Pharm Dev Technol 2021; 26: 1136-1157.
11) Asadi P, Mehravaran A, Soltanloo N, Abastabar M, Akhtari J. Nanoliposome-loaded antifungal drugs for dermal administration: A review. Curr Med Mycol 2021; 7: 71-78.
12) Rai M, Yadav A, Gade A. Silver nanoparticles as a new generation of antimicrobials. Biotechnol Adv 2009; 27: 76-83.
13) Šebesta M, Vojtková H, Cyprichová V, Ingle AP, Urík M, Kolenčík M. Mycosynthesis of Metal-Containing Nanoparticles-Fungal Metal Resistance and Mechanisms of Synthesis. Int J Mol Sci 2022; 23.
14) Siddiqi KS, Husen A, Rao R. A review on biosynthesis of silver nanoparticles and their biocidal properties. J Nanobiotechnology 2018; 16: 14.
15) Różalska B, Sadowska B, Budzyńska A, Bernat P, Różalska S. Biogenic nanosilver synthesized in Metarhizium robertsii waste mycelium extract - As a modulator of Candida albicans morphogenesis, membrane lipidome and biofilm. PLoS One 2018; 13: e0194254.
16) Kim KJ, Sung WS, Moon SK, Choi JS, Kim JG, Lee DG. Antifungal effect of silver nanoparticles on dermatophytes. J Microbiol Biotechnol 2008; 18: 1482-1484.
17) Li C, Wang X, Chen F, Zhang C, Zhi X, Wang K, Cui D. The antifungal activity of graphene oxide-silver nanocomposites. Biomaterials 2013; 34: 3882-3890.
18) Sit NW, Chan YS, Lai SC, Lim LN, Looi GT, Tay PL, Tee YT, Woon YY, Khoo KS, Ong HC. In vitro antidermatophytic activity and cytotoxicity of extracts derived from medicinal plants and marine algae. J Mycol Med 2018; 28: 561-567.
19) Ayatollahi Mousavi SA, Salari S, Hadizadeh S. Evaluation of Antifungal Effect of Silver Nanoparticles Against Microsporum canis, Trichophyton mentagrophytes and Microsporum gypseum. Iran J Biotechnol 2015; 13: 38-42.
20) Endo EH, Makimori RY, Companhoni M, Ueda-Nakamura T, Nakamura CV, Dias Filho BP. Ketoconazole-loaded poly-(lactic acid) nanoparticles: Characterization and improvement of antifungal efficacy in vitro against Candida and dermatophytes. J Mycol Med 2020; 30: 101003.
21) de Oliveira D, Silva LB, da Silva BV, Borges TC, Marques BC, Dos Santos MB, de Oliveira LF, Bolzani VS, Rodrigues A, Regasini LO, Andrade AA. A new acridone with antifungal properties against Candida spp. and dermatophytes, and antibiofilm activity against C. albicans. J Appl Microbiol 2019; 127: 1362-1372.
22) Guilger-Casagrande M, Germano-Costa T, Pasquoto-Stigliani T, Fraceto LF, Lima R. Biosynthesis of silver nanoparticles employing Trichoderma harzianum with enzymatic stimulation for the control of Sclerotinia sclerotiorum. Sci Rep 2019; 9: 14351.
23) Gholami-Shabani M, Imani A, Shams-Ghahfarokhi M, Gholami-Shabani Z, Pazooki A, Akbarzadeh A, Riazi G, Razzaghi-Abyaneh M. Bioinspired synthesis, characterization and antifungal activity of enzyme-mediated gold nanoparticles using a fungal oxidoreductase. J Iran Chem Soc 2016; 13: 2059-2068.
24) Kokoska L, Kloucek P, Leuner O, Novy P. Plant-Derived Products as Antibacterial and Antifungal Agents in Human Health Care. Curr Med Chem 2019; 26: 5501-5541.
25) Barbosa MS, da Silva Souza B, Silva Sales AC, de Sousa J, da Silva F, Araújo Mendes MG, da Costa K, de Oliveira TM, Daboit TC, de Oliveira JS. Antifungal Proteins from Plant Latex. Curr Protein Pept Sci 2020; 21: 497-506.
26) Mutlu-Ingok A, Devecioglu D, Dikmetas DN, Karbancioglu-Guler F, Capanoglu E. Antibacterial, Antifungal, Antimycotoxigenic, and Antioxidant Activities of Essential Oils: An Updated Review. Molecules 2020; 25.
27) Rónavári A, Igaz N, Gopisetty MK, Szerencsés B, Kovács D, Papp C, Vágvölgyi C, Boros IM, Kónya Z, Kiricsi M, Pfeiffer I. Biosynthesized silver and gold nanoparticles are potent antimycotics against opportunistic pathogenic yeasts and dermatophytes. Int J Nanomedicine 2018; 13: 695-703.
28) Pereira L, Dias N, Carvalho J, Fernandes S, Santos C, Lima N. Synthesis, characterization and antifungal activity of chemically and fungal-produced silver nanoparticles against Trichophyton rubrum. J Appl Microbiol 2014; 117: 1601-1613.

29) Arciniegas-Grijalba PA, Patiño-Portela MC, Mosquera-Sánchez LP, Guerrero-Vargas JA, Rodríguez-Páez JE. ZnO nanoparticles (ZnO-NPs) and their antifungal activity against coffee fungus Erythricium salmonicolor. Applied Nanoscience 2017; 7: 225-241.

30) Asghari-Paskiabi F, Imani M, Rafii-Tabar H, Razzaghi-Abyaneh M. Physicochemical properties, antifungal activity and cytotoxicity of selenium sulfide nanoparticles green synthesized by Saccharomyces cerevisiae. Biochem Biophys Res Commun 2019; 516: 1078-1084.

31) Pannu J, McCarthy A, Martin A, Hamouda T, Ciotti S, Fothergill A, Sutcliffe J. NB-002, a novel nanoemulsion with broad antifungal activity against dermatophytes, other filamentous fungi, and Candida albicans. Antimicrob Agents Chemother 2009; 53: 3273-3279.

32) Sudhakar B, Varma JN, Murthy KV. Formulation, characterization and ex vivo studies of terbinafine HCl liposomes for cutaneous delivery. Curr Drug Deliv 2014; 11: 521-530.

33) Elmoslemany RM, Abdallah OY, El-Khordagui LK, Khalafallah NM. Propylene glycol liposomes as a topical delivery system for miconazole nitrate: comparison with conventional liposomes. AAPS PharmSciTech 2012; 13: 723-731.

34) Jarratt M, Jones T, Kempers S, Rich P, Morton K, Nakamura N, Tavakkol A. Luliconazole for the treatment of interdigital tinea pedis: A double-blind, vehicle-controlled study. Cutis 2013; 91: 203-210.

35) Tundisi LL, Mostaço GB, Carricondo PC, Petri D. Hydroxypropyl methylcellulose: Physicochemical properties and ocular drug delivery formulations. Eur J Pharm Sci 2021; 159: 105736.

36) Morteza-Semnani K, Saeedi M, Akbari J, Hedayati S, Hashemi S, Rahimnia SM, Babaei A, Ghazanfari M, Haghani I, Hedayati MT. Green formulation, characterization, antifungal and biological safety evaluation of terbinafine HCl niosomes and niosomal gels manufactured by eco-friendly green method. J Biomater Sci Polym Ed 2022; 33: 2325-2352.

37) Paskiabi FA, Bonakdar S, Shokrgozar MA, Imani M, Jahanshiri Z, Shams-Ghahfarokhi M, Razzaghi-Abyaneh M. Terbinafine-loaded wound dressing for chronic superficial fungal infections. Mater Sci Eng C Mater Biol Appl 2017; 73: 130-136.

38) Mofidfar M, Wang J, Long L, Hager CL, Vareechon C, Pearlman E, Baer E, Ghannoum M, Wnek GE. Polymeric Nanofiber/Antifungal Formulations Using a Novel Co-extrusion Approach. AAPS PharmSciTech 2017; 18: 1917-1924.

39) Zhang S, Song W, Wu H, Wang J, Wang Y, Zhang Z, Lv H. Lecithins-Zein nanoparticles for antifungal treatment: Enhancement and prolongation of drug retention in skin with reduced toxicity. Int J Pharm 2020; 590: 119894.

40) Na YG, Huh HW, Kim MK, Byeon JJ, Han MG, Lee HK, Cho CW. Development and evaluation of a film-forming system hybridized with econazole-loaded nanostructured lipid carriers for enhanced antifungal activity against dermatophytes. Acta Biomater 2020; 101: 507-518.

41) Aboul-Ella H, Hamed R, Abo-Elyazeed H. Recent trends in rapid diagnostic techniques for dermatophytosis. Int J Vet Sci Med 2020; 8: 115-123.

42) Aboul-Ella H, Sayed RH, Abo-Elyazeed HS. Development, preparation, and evaluation of a novel dotted lateral flow immunochromatographic kit for rapid diagnosis of dermatophytosis. Sci Rep 2023; 13: 248.