Innovative Strategies for the Control of Zoonotic Diseases by using Nanotechnology

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ABSTRACT

This book chapter focuses on novel innovative strategies for the prevention and treatment of various types of zoonotic diseases like viral, bacterial, fungal, parasitic, mycoplasma, protozoal and chlamydial infections. The treatment and diagnosis of zoonotic infections are challenging due to drug resistance, genetic mutations and modification of target sites. Therefore, more effective and low-cost theranostics tools are needed to manage the emerging zoonotic infections. Nano-formulations have many advantages over conventional medicines which are used in the treatment of zoonotic infectious diseases by delivering targeted drug delivery, minimizing drug resistance, and causing less toxic effects. Enormous developments have been prepared in manufacturing innovative nano-formulations to control zoonotic diseases based on the usage of mannose-linked thiolated nanocarriers, arginine-based nanocarriers, mannosylated thiolated chitosan (MTC)-coated PM-loaded PLGA NPs, adjuvant pDNA hydrogel, poly (ethylenimine) conjugated nanomicelles and quantum dots to diagnose and treat a huge range of zoonotic infections for examples rabies, tuberculosis, zoonotic influenza, lyme diseases, salmonellosis, leishmaniasis, brucellosis, other emerging infections caused by coronaviruses (COVID-19, MERS, SARS) and West Nile virus in a specially targeted way. The controlled delivery and targeted antimicrobial drugs for treating and diagnosing zoonotic infections via binding to the overexpressed infectious macrophages are the revolutionized development in medicine by nanotechnology. Nano-vaccines and theranostic solicitations of nano-formulation have significant therapeutic potential to combat diverse microbial pathogens. Nanorobots and biocompatible nanoparticles are the nanoscale materials that are used in nanomedicine for the purposes of sensing, diagnosis and drug delivery in the living organism. This chapter reviewed innovative strategies to control zoonotic diseases and future perspectives by using nanotechnology.

Keywords: zoonotic infections, nano-formulations, resistance, targeted drug delivery

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1. INTRODUCTION

Zoonotic diseases are numerous infections that are transferred from animals to humans and diagnosis and treatment of these diseases are confusing due to drug resistance, genetic mutations and modification of target sites. Above 60% of the human pathogens have zoonotic in origin that includes various types of viruses, bacteria, protozoa, parasites or fungi and other pathogens. There are numerous factors that have significantly influenced on the zoonosis patterns, distribution, emergence and re-emergence like urbanization, tourism, travel and trade, climate change, vector biology, natural or anthropogenic factors and animal migration (Minakshi et al. 2022). The occurrence of zoonotic emerging and re-emerging infections are increasing day by day predominantly due to the heterogeneity of zoonotic pathogens among the different family. Regardless of their benefits, mostly molecular diagnostic methods have certain limits in terms of sensitivity and repeatability. To solve these disquiets, there is need to develop cost effective and an efficient diagnostic method. Enormous developments have been prepared in manufacturing innovative nano-formulations to control zoonotic diseases based on the usage of mannose linked thiolated nanocarriers, arginine-based nanocarriers, mannosylated thiolated chitosan (MTC)-coated PM-loaded PLGA NPs, adjuvanted pDNA hydrogel, poly (ethylenimine)-conjugated nanomicelles and quantum dots to diagnose and treat a huge range of zoonotic infections for examples rabies, tuberculosis, zoonotic influenza, lyme diseases, salmonellosis, leishmaniasis, brucellosis, other emerging infections caused by coronaviruses (COVID-19, MERS, SARS) and West Nile virus in a specially targeted way (Prasad et al. 2020). Recently established nanoformulations load anti-pathogens with hemocompatibility, biocompatibility and enhanced cellular uptake have shown their ability after oral administration to cross biological barriers. The controlled delivery and targeted antimicrobial drugs for treating and diagnosing zoonotic infections via binding to the overexpressed infectious macrophages are the revolutionized development in the medicine by nanotechnology. The nanoformulations have many advantages over the conventional medicines which are used in the treatment of zoonotic infectious diseases (Minakshi et al. 2022) as shown in Fig. 1. This chapter reviewed the innovative strategies to control the zoonotic diseases and future perspectives by using nanotechnology.

2. TYPES OF ZOONOTIC INFECTIONS

Zoonotic infections are caused by a wide range of pathogens and classified into various types on the basis of etiology like viral zoonoses (avian influenza, rabies, Ebola and acquired immune deficiency syndrome-AIDS), bacterial zoonoses (plague, anthrax, brucellosis, salmonellosis, Lyme disease and tuberculosis), fungal zoonoses (ring worm), parasitic zoonoses (malaria, trichinosis, echinococcosis, toxoplasmosis, giardiasis and trematodosis), protozoan zoonoses, rickettsial zoonoses (Q-fever), mycoplasma zoonoses (*Mycoplasma pneumoniae* infection), chlamydial zoonoses (psittacosis) and acellular non-viral pathogenic zoonosis (Mad cow disease and transmissible spongiform encephalopathy (Chomel 2009). Fig. 2 illustrates the different types of zoonotic diseases with examples.

3. APPLICATION OF NANOMEDICINE IN ZOONOTIC BACTERIAL INFECTIONS

According to World Health Organization (WHO), mainly seven groups of bacteria caused 85–90% infectious diseases and half of the clinical diseases are due to *Staphylococcus aureus* and *Escherichia coli*. Although, due to improvement in diagnostic, prophylactic and therapeutic strategies the number of death due to infectious diseases is expected to reduced but the global emergence of resistant microbial populations and rapid transmission of both anthropozoonotic (zoonotic) and zooanthroponotic (reverse zoonotic) microorganisms are demanding solution of these question mark over this enthusiastic situation (Minakshi et al. 2022). In this perspective nanomedicine can be an effective alternative for manipulating efficient diagnostic, prophylactic and therapeutic approaches to fight the transmissible diseases in a low-cost effective way during the condition of microbial resistance. The uses of nanoparticles (NPs) have illustrated effective bactericidal properties due to distinctive physicochemical properties of numerous nanoformulations. In addition nano-vaccines and theranostic solicitations of nano-formulation have significant therapeutic potential to combat the diverse microbial pathogens. Nanorobots and biocompatible nanoparticles are the nanoscale materials that are used in the nanomedicine for the purpose of actuation or sensing, diagnosis and drug delivery in the living organism (Pati et al. 2018). The recent nanotechnology solicitations in vaccine development against prominent anthropozoonotic and zooanthroponotic bacterial infections have been depicted in Table 1.

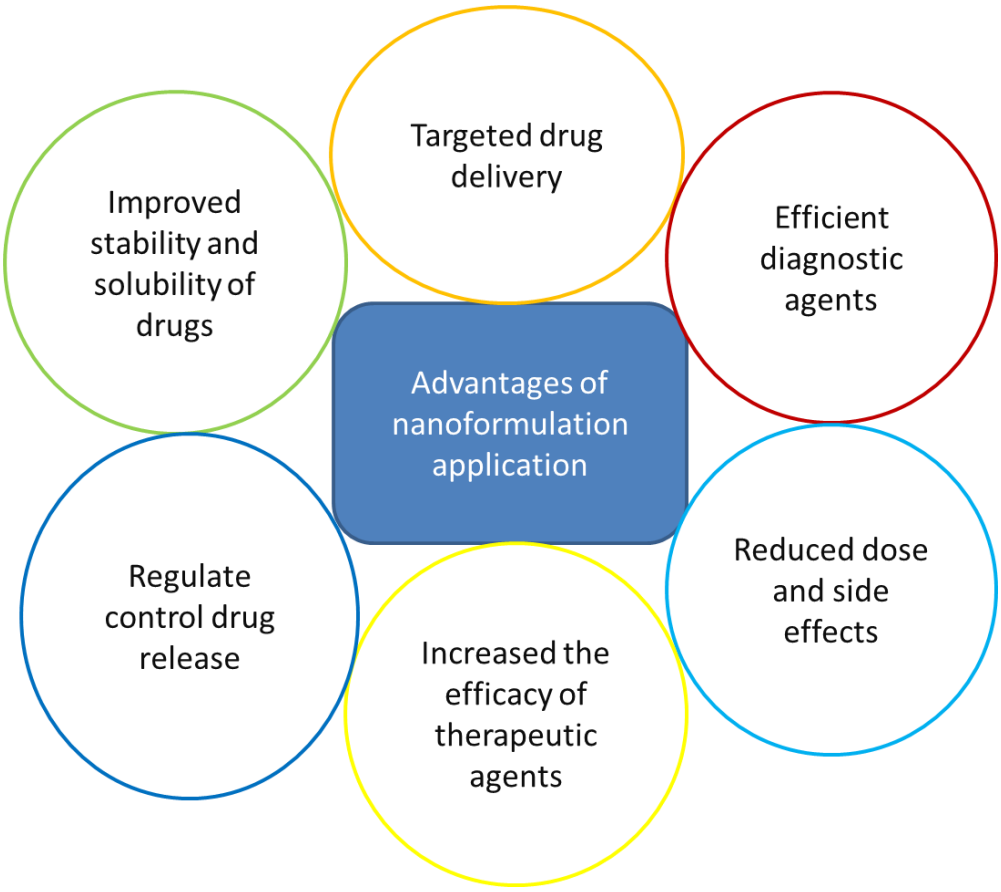

Fig. 1: Advantages of nanomedicines over the conventional medicines for the control of zoonotic diseases

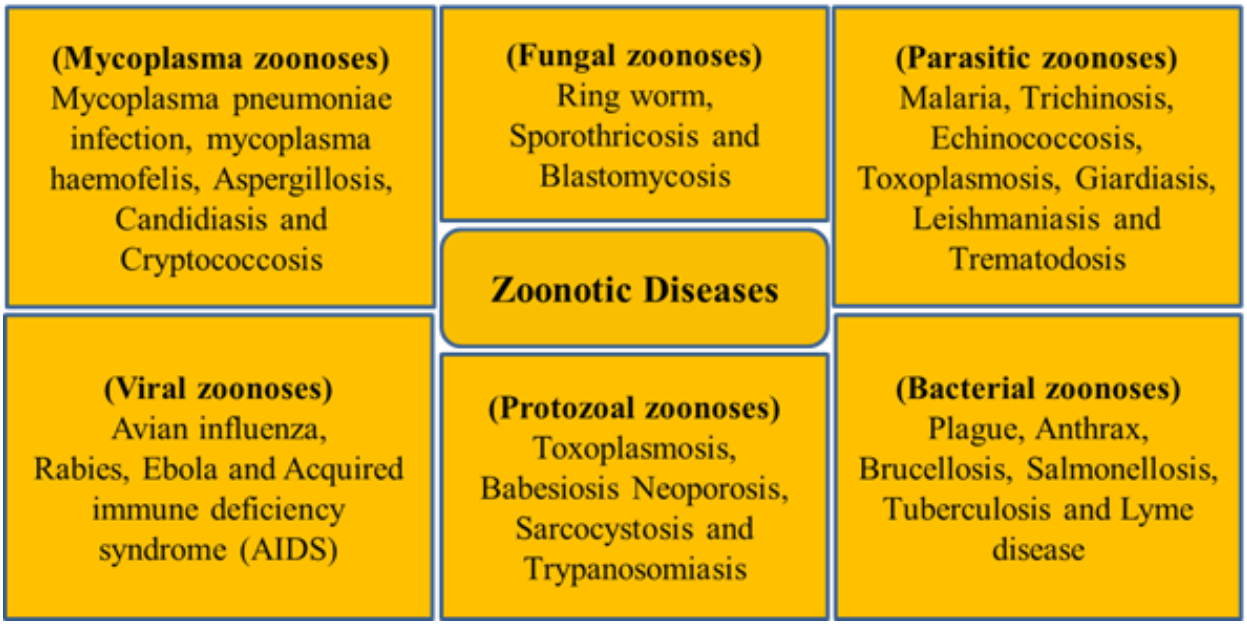

Fig. 2: Classification of different types of zoonotic infections

4. APPLICATION OF NANOMEDICINE IN ZOONOTIC VIRAL INFECTIONS

In the current scenario emerging zoonotic viral infections are major problems with their limitation in prophylactic, diagnostic and therapeutic methods. Mostly viral diseases have wildlife origin and due to deprived knowledge their outbreaks are unpredictable. Therefore, substitute management approaches are needed to improve prophylactic vaccines, rapid diagnostics, efficient drug delivery system and targeted therapeutics. Nanomedicines have been used with promising benefits as adjuvant targeted drug delivery systems, efficient diagnostics, enhancing immunogenicity, specific site therapeutics and reducing the anti-viral drugs side effects (Pelaz et al. 2017). The innovative applications of nanomedicines are enlisted in Table 2 which is used to eradicate the major viral zoonotic diseases to overcome the conventional methodologies limitations.

5. APPLICATION OF NANOMEDICINE IN ZOONOTIC PARASITIC INFECTIONS

There are 3 major groups of parasites including helminths, protozoa and ectoparasites dispersed worldwide. The high prevalence of parasitic infections is due to lack of research in pharmaceutical sciences and appropriate treatment alternatives (Rokkas et al. 2021). Mostly chemotherapeutic anthelmintic, anti-ectoparasitic agents and antiprotozoal drugs are used to treat these parasitic infections but due to overuse of these drugs, resistance has developed with the passage of time. Previously, massive advancement has made in vaccines preparation to regulate these zoonotic diseases. Mostly in vaccine preparation those pathogens are selected which caused the disease outbreaks throughout the world (Pritt 2020). The numerous mechanisms have developed in the parasites that assist them to defend from immune system after exposure of vaccine preparations. Although immune system is involved against parasites but during immunogenic response due to the enormous antigenic variation, the hosts are re-attacks by parasites with antigenic mimicry and antigenic shift that created a big challenge to develop effective vaccine against parasitic infections (Versteeg et al. 2019). In this consequence, nanoparticles are demonstrating a significant and innovative role in the management and

Table 1: Application of nanoformulation against zoonotic bacterial diseases

Sr. No.	Nanoformulation	Bacterial species	Applications	Model	References
1	Gentamycin-AgNPs	*Pasteurella Multocida*	Antimicroibal activity against bacteria resistant to coilstin, gentamicin and amoxicillin	*In-vitro*	(Smekalova et al. 2016)
2	PLGA-gentamycin	*Brucella melitensis*	Activate oxidative burst and significant direction into the mononuclear phagocytic system	Cell culture	(Lecároz et al. 2006)
3	Albumin nanoparticles-gamma interferon	*Brucella abortus*	Enhanced efficacy and bactericidal effect	Mice, *In-vitro*	(Shilpa et al. 2012)
4	Ceftazidine-silver nanoparticles (AgNPs)	*Burkholderia Pseudomallei*	Decrease dose and minimum cytotoxic effect in RBC	*In-vitro*	(Hongsing et al. 2015)
5	ZnONPs-Carvacrol	*Campylobacter jejuni*	100-fold reduction in cell count	*In-vitro*	(Windiasti 2016)
6	Stabilized silver Nanoparticles Glutathione (Ag NPs-GSH)	Multidrug resistant (MDR) *Campylobacter* Strains	Dose dependent cytotoxic effect	*In-vitro*	(Silvan et al. 2018)
7	Silver nanoparticles with nickel or iron	*E. coli*	Bacterial load reduction	Culture	(Abeylatha et al. 2008)
8	Amoxicillin-AgNPs	*E. coli*	Synergistic effects	*In-vitro*	(Li et al. 2005)
9	Ampicillin-AuNPs	*E. coli, Salmonella aureus*	Antibacterial potential against *Micrococcus luteus, Salmonella aureus* and *E. coli,*	*In-vitro*	(Saha et al. 2007)
10	Cinnamon bark Extract-PLGA	*Listeria* (*L.*) *monocytogenes* and *Salmonella typhimurium*	Effective inhibitors, better retention time up to 24 and 72 hours at concentrations ranging from 224.42 to 549.23 (g/mL)	*In-vitro*	(Hill et al. 2013).
11	PLGA-Quercetin	*L. monocytogenes, S. aureus*	Antibacterial activity against Gram +ve bacteria by reducing the bacterial integrity	*In-vitro*	(Arasoglu et al. 2017)
12	Gold nanoparticles-outer membrane proteins	*Salmonella gallinarum*	Synergistic effect to induce immune responses	Chicken	(Anwar et al. 2021)
13	Liposomes-Kanamycin	*Mycobacterium Intracellulare*	Increased antibacterial activity	Mice	(Cosma et al. 2003)
14	Liposome-Rifabutin	Tuberculosis	Improved drug penetration in alveolar epithelium	Wister Rat	(Narayanasamy et al. 2015)
15	Chitosan dexteran sulfate-cefteriaxon or ciprofloxacin	*Salmonella*	Reduces MIC, enhanced retention time and drug delivery, damage the intracellular pathogen	BALB/cmice	(Gnanadhas et al. 2013)
16	Essential oil-silver nanoparticles	*S. epidermidis* and *S. aureus*	Observed additive effects and 62.5 (µg/ml) MIC value was calculated for *S. epidermidis* and *S. aureus*	*In-vitro*	(Ahmadi Ashtiani et al. 2016)
17	Penicillin or oxacillin or amampicillin-Selenium nanoparticles	*S. aureus*	Have synergistic effect	*In-vitro*	(Cihalova et al. 2015)
18	AgNPs-leaf extracts of acalyphaindica	*E. coli , Vibrio cholera*	Reduced MIC value	*In-vitro*	(Krishnaraj et al. 2010)
19	PLGA- Monosialotetra Hexosylganglioside	*Vibrio cholera*	Bind selectively and neutralize the toxin of cholera	Mice and cell culture	(Das et al. 2018)
20	Silica nanoparticles-Chlorhexidine	*Enterococccus faecalis, Streptococcus sobrinus, Streptococcus mutans*	Potent antimicrobial activity, prevent dental caries and decrease biofilm formation	*In-vitro*	(Seneviratne et al. 2014)

Table 2: Application of nanoformulation against zoonotic viral diseases

Sr. No.	Nanoformulation	Viral species	Applications	Model	References
1	Inter-bilayer crosslinked Multilamellar vesicles (ICMVs) with recombinant EBOV antigen (rGP)	Ebola virus	Robust neutralizing antibody response and greater formation of both T cells (poly-functional) and B cells (germinal)	Mice	(Bazzill et al. 2018)
2	Selenium nanoparticles-Ribavirin	Influenza virus	Better antiviral activity and less side effects	Mice, Canine kidney cells	(Lin et al. 2018)
3	Nano beads polystyrene-synthetic peptides	Foot and mouth disease virus (FMDV)	Boosted cell interceded immune response identified by various type of cytokine assays method	Sheep	(Greenwood et al. 2008)
4	Poly-2-hydroxyethyl methacrylate (PHEMA) nanoparticles with whole clone gene in pCAG	Avian Influenza	Immune responses augmented by nanoparticles but frequency of virus shedding from cloaca is significantly not reduced	Hy-line Chicken	(Shan et al. 2010)
5	Chitosan or PLGA with attenuated whole viral antigen (RV-Ag)	Rabies	Minor toxic effect, and enhanced immune responses	*In-viro*	(Nivedh et al. 2016)
6	Silver nanoparticles with inactivated rabies virus	Rabies	Enhanced antibodies that neutralize rabies virus with cell viability adverse effects	Mice	(Asgary et al. 2014)
7	Lipid nanoparticles (LNP)-mRNA vaccine	Rabies/ Influenza virus	Initiation of pro-inflammatory chemokine or cytokines and activation of the immune system (Innate or inherent)	Primates	(Lutz et al. 2017)
8	Polypeptide nanoparticles with B-cell epitope from the virus spike protein	Severe acute respiratory syndrome (SARS) by Corona virus	*In-vitro* infection inhibition assay demonstrated its neutralization activity	Mice or BALB/c	(Pimentel et al. 2009)
9	Protein nanoparticles-Purified coronavirus spike adjuvant	Severe acute respiratory syndrome coronavirus or Middle east respiratory syndrome coronavirus	Improved antibody titer by neutralization	Mice or BALB/c	(Coleman et al. 2014)
10	PLGA nanoparticles-DENV2-E protein	Dengue virus (DENV)	Potent DENV2-specific neutralizing antibody response compared to sRecE protein alone and Nanoparticle induced higher IgG titers without any adjuvant after adsorbed sRecE	Mice or BALB/c	(Metz et al. 2018)
11	VLPs vaccine using prM and E Proteins	Dengue virus	High levels of IL-10 and TNF-α were estimated which stimulated neutralizing antibodies against serotype	Mice	(Liu et al. 2014)
12	Fungal chitosan Nanoparticles with FMDV	Foot and mouth Disease virus (FMD)	CS-FMDv nanoparticles enthused mucosal and humoral immunity and greater serum titers were determined with these nano-formulation as compared to fluid vaccine administered intraperitoneally or with free virus	Guinea pigs	(Tajdini et al. 2014)
13	Gold nanoparticles (GNP) conjugates with pFMDV	Foot and mouth Disease virus (FMD)	8–17 nm size GNPs produced maximal antibody binding that is size-dependent antibody response	Mice and BALB/c	(Chen et al. 2010)
14	DNA vaccines-chitosan nanoparticles	Newcastle disease virus (ND)	Systemic and mucosal immune responses enhanced	Chicken	(Zhao et al. 2018)
15	Virus like particle (VLP) vaccine based on LASV Z, NP proteins and GPC	Lassa virus	Significant production of IgG antibody responses to individual viral proteins after immunization	Mice	(Branco et al. 2010)

control of zoonotic parasitic diseases. During the last decade, in the field of nanomedicine enormous development has made for control of parasitic infections. The nanoparticles of silver and gold have presented encouraging facts in the cures of numerous parasitic diseases. The several molecular and conventional methods are used to synthesize the nanoparticles that have shown great efficacy. There are several mechanisms of action by which these nanoparticles work against parasites like inhibition of protein synthesis, damaging the parasite membrane, disruption of Deoxyribonucleic acid (DNA) and free radical formation (Sousa et al. 2020).

The various other nanoparticles like platinum, nickel and zinc have also presented better outcomes in the control and cure of zoonotic parasitic diseases as enlisted in the Table 3. The intracellular parasites can also be treated effectively by these agents as well. The several research studies have proved the potential of nanoparticles (NPs) used in the cure of many viral, parasitic, bacterial and fungal infections (Aderibigbe 2017; Lin et al. 2018; Chandra et al. 2020; Anwar et al. 2021). It has proved that after reducing to nano-size, various materials undergo wide changes in their properties. These nanoparticles (NPs) have distinct optical, mechanical and chemical properties. The nanoparticles also have cytotoxic effects which vary with form, size, charge, stability and nano-materials purity. The various types of nano-sized particles have been used widely for the effective diagnostic purposes, control and cure of various parasitic infections with outstanding results (Khezerlou et al. 2018; Nafari et al. 2020).

6. APPLICATION OF NANOMEDICINE IN ZOONOTIC FUNGAL INFECTIONS

Fungal infections come in a variety of forms, ranging from superficial infections that affect the skin to systemic infections that invade internal organs (Rai et al. 2017). Every year, millions of individuals around the world are affected by fungus. Of these, over 1.5 million involve offensive fungal zoonotic diseases that necessitate hospitalization and extensive care. Aspergillus, Candida, pneumocystis and Cryptococcus species that are the causative agents of aspergillosis, candidiasis, pneumocystis pneumonia and cryptococcosis

Table 3: Application of nanoformulation against zoonotic parasitic diseases

Sr. No.	Nanoformulation	Parasitic infections	Application	References
1	Iron oxide nanoparticles	Helminth	Induces oxidative stress	(Swargiary et al. 2019)
2	Zinc oxide nanoparticles	Helminth infection	Inhibits the contractile movement of the parasite and adenosine triphosphate (ATP) production	(Chandra et al. 2020)
3	Silver nanoparticles	Leishmaniasis, Helminth infections, Malaria	Improved antihelminthic potential against worms, Better *in-vivo* and *In-vitro* antileishmanial activity, Inhibition of proliferation and metabolic activity of promastigotes. Inhibition of the growth of *Plasmodium* (*P.*) *falciparum*	(Panneerselvam et al. 2015)
4	Gold nanoparticles	Helminth Infections, Malaria	Moderate anti-plasmodial activity against *P. falciparum* which alter physiological functioning of parasite by causing paralysis and leading to death, Moderate to delayed rise in parasitemia	(Pissuwan et al. 2020)
5	Some metal oxides (MO) (Fe3O4, MgO, ZrO2, Al2O3 and CeO2)	Leishmaniasis, Malaria	Induction of apoptosis by enhanced cytotoxic effects on promastigotes of Leishmania	(Chikkanna et al. 2019; Tong et al. 2019; Chandra et al. 2020).
6	Albendazole- Solid lipid nanoparticles	*Toxocara canis* infection	Enhanced *In-vitro* activity of albendazole	(Kudtarkar et al. 2017)

respectively, account for the majority of these disseminated infections (Pianalto and Alspaugh 2016). Possibly while they do not usually pose a life-threatening, superficial fungal infections can extent to other parts of the skin and may widespread. They can also spread to other organs and result in secondary bacterial skin infections, which lower a person's quality of life. Dermatophytosis, yeast infections, and mould infections are the three categories into which skin mycoses are usually divided based on the type of fungi that cause these infections (Dantas et al. 2021).

According to their mechanism of action, there are four main types of currently used medicines for treating invasive fungal infections including polyenes, azoles, allylamines, and echinocandins (Nami et al. 2019). They all have disadvantages in terms of drug interactions, pharmacokinetics and pharmacodynamics, resistance mechanisms, and the toxicity of the compounds themselves, in addition to limitations in their range of activity. Additionally, there are some restrictions on clinical efficacy and efficiency, primarily as a result of their physico-chemical characteristics like its low solubility in water due to hydrophobic nature and selectivity issues resulting from the similarity between human cells and fungi (Chang et al. 2017; Souza and Amaral 2017). The nanoparticles have potential to enhance and change the pharmacodynamics and pharmacokinetic features of the medications that make them ideal to use in pharmaceutical formulations. These also have potential to improve the stability and solubility of the drugs, regulate drug control release and show biocompatible with cells and tissues that lead to enhancement in the efficacy of therapeutic agents (Bhatt et al. 2017). Additionally, subcellular size of nanoparticles and high surface area adaptable to modification become the use of nanoparticles in specific target drug release, better therapeutic effects and reducing systemic side effects by lowering the frequency and dose of the administered therapeutic agents (Jinhyun 2015). By conjugating target ligands with peptides on the surface of the transporters and antibodies, it is possible to integrate target ligands at the nanomolecular level, allowing a preferential binding of specific cell types (Rangari 2015; Goyal et al. 2016). In order to increase the therapeutic effectiveness, safety, and compliance of current antifungal medications, it is wise to develop innovative biopharmaceutical systems, particularly nanoparticulate carriers (Sousa et al. 2020).

7. NANOTECHNOLOGY AND MYCOLOGY

The link between mycology and nanotechnology has developed in both directions throughout time. The word "myconanotechnology" was coined as a result of the dynamic interplay between mycology and nanotechnology. With encouraging *in-vitro* and *in-vivo* results, nanotechnology has emerged as an intriguing method to improve the effectiveness and potency of conservative antifungals drugs, to permit a decline in cost and toxicity, to evade an expected degradation and to improve distribution of drug by increasing circulation time and enhancing drug targeting and pharmacokinetics. Furthermore, a variety of synthesized nanoelemental particles and numerous metallic nanoparticles have been utilized against pathogenic plant and human fungi due to their natural antifungal activity (Mashitah et al. 2016).

The metallic nanoparticles have been employed to remove fungi that are pathogenic to plants and humans because nanoparticles have natural antibacterial action and antifungal properties. There are main three pathways including (a) damage of cell wall/cell membrane through accumulation (b) nanoparticles direct uptake (c) reactive oxygen species (ROS) production by indirect activity of nanoparticles. The precise mechanisms through which this activity occurs are only hypothesized. According to Slavin et al. (2017), it is quite likely that the interaction of these multiple mechanisms causes antimicrobial activity. The nanoparticles can dissolve due to their electrochemical potential that causes nanoparticles to discrete into ions in the microbial fluid and culture medium. Additionally, these ions build up in the exterior or interior that inhibits microtubules. Nanoparticle buildup outside of

microtubules results in the development of layers that break down the microtubules by blocking the cellular respiratory chain (Qidway et al. 2018).

The interaction that takes place between the medicine and nanoparticle are depends on its electrical charge. The electrostatic mechanism explains why silver nanoparticles were the first to be shown to have antibacterial action. Since the positively charged nanoparticles membranes and negatively charged bacteria cellular membranes are electrostatically attracted to one another, it is commonly acknowledged that for the antimicrobial activity of the nanoparticles there is compulsory need of positive charge silver ion. Adenosine triphosphate (ATP) production is decoupled by Ag+ because of its strong affinity for the thiol groups in the cysteine of respiratory chain enzymes. Additionally, Ag+ binds to respiratory chain transport proteins, which results the breakdown of the proton motive force and proton leakage. It also prevents phosphate from being absorbed, which encourages the outflow of intracellular phosphate. The concentrations of silver nanoparticles against *Candida albicans* are ranging from 1 to 7 mg/mL and minimum inhibitory concentration (MIC) of 25 mg/ml. The silver nanoparticles show strong antifungal activity against ATCC strains of *Trichophyton mentagrophytes* and clinical isolates (Zhang et al. 2016). Simvastatin increases the antifungal effect in an additive and synergistic manner, possibly because as an inhibitor of ergosterol synthesis it causes disruption of cell membrane of fungi that allow the nanoparticles entry (Bocate et al. 2018). The nanoparticles of silver also show greater antifungal activity against *Aspergillus niger* by preventing biofilm formation and inhibiting spore germination (Bocate et al. 2018).

Chitosan and its derivatives have been used as building blocks in drug delivery system due to their biocompatibility, biodegradability, and mucoadhesive chemical properties. These materials have some advantages due to their potential to prolong the release of low molecular weight compounds to macromolecular drugs and *in-situ* gelling performance. It has been demonstrated that chitosan nanoparticles have excellent antibacterial action against Candida infections. According to published research and literature, the negatively charged lipopolysaccharides on the surface of microbial cells and proteins and positively charge amino groups interrelate with each other that lead to disintegration of cell membrane. The ability of nanoparticles to attach with DNA molecules may inhibit the formation of protein and mRNA (Calvo et al. 2019).

Table 4: Application of nanoformulation against zoonotic fungal/mycotic diseases

Sr. No.	Nanoformulation	Fungal infection	Applications	References
1	Amphotericin B-Zinc oxide nanoparticles	Leishmaniasis and Fungal Infections	Decrease dose, less nephrotoxic effects, potent *In-vitro* antifungal activity	(Adler-Moore et al. 2002; Stone et al. 2016; Lanza et al. 2019)
2	Liposomal Amphotericin B	Severe fungal infections	Less nephrotoxic	(Minodier et al. 2003)
3	Amphotericin B lipid complex	Invasive mycoses	Safer than amphotericin B alone, little nephrotoxicity	(Lister 1996)
4	Nanocrystal based Griseofulvin	Ringworm infection	Enhanced bioavailability	(Aoyagi et al. 1982)
5	Zinc oxide nanoparticles	*Microsporum canis, Candida albicans, Trichophyton mentagrophyte* and *Aspergillus fumigatus*	Antifungal activity	(Eman et al. 2013)

Chitosan specifically inhibits the spore germination and sporulation in case of fungal infection by interfering with the action of the enzymes that promote growth (Kucharska et al. 2020). The antifungal activity of zinc oxide nanoparticles (ZnONPs) has been demonstrated against pathogenic fungi like

Candida and Aspergillus species and other skin infections. In the meantime, it was assessed that ZnONPs have synergistic antifungal activity in conjunction with conventional antifungal drugs. The inhibitory efficacy of the antifungal drugs was not only augmented with ZnONPs combination but also reduced it toxicity (Sun et al. 2018). Additionally, these nanoparticles may offer an intriguing and exciting replacement for current preservatives in cosmetics (Singh and Nanda 2013). Dendrimers exhibit antifungal activity in addition to the aforementioned nanoparticles, opening the door to complex therapies in which dendrimers assist as an adjuvant component of the dose form and drug carrier (Winnicka et al. 2012). Table 4 represents the application of nanoformulation which are used for the control of fungal zoonotic diseases.

8. CONCLUSION

The majority of infectious diseases that affect people are animal-borne. Due to the emergence and re-emergence of numerous zoonotic diseases because of strong interrelatedness among humans and animals, research concentrating on one health approach to manage devastating zoonotic infections. Nanotechnology is the most recent technique in medical and pharmaceutics that has brought vast benefits over conventional medicines for the treatment and control of infectious diseases by delivering targeted drug delivery, minimizing drug resistance, and causing less toxic effects. It is certain that nanotechnology will advance medical science in the future by improving existing therapies and presenting novel treatment with significant clinical advancements.

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