



Review article

Nanoparticle-based therapeutics for the treatment of skin infections in animals: A comprehensive literature review

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Abstract

Animal skin infections pose significant challenges in veterinary dermatology, necessitating effective and targeted treatment modalities. This review explores the current landscape of skin infection treatments, emphasizing the potential of nanoparticles (NPs) as innovative therapeutic agents. The primary objectives are to comprehensively evaluate existing treatment modalities for skin infections in animals, highlight the advantages of NPs over conventional drugs, and discuss recent advances in NP-based therapies. To achieve this, a systematic review of the literature was conducted, encompassing studies published in peer-reviewed journals. The analysis focuses on current treatment approaches, recent developments in NP technology, and their applications in managing animal skin infections. While conventional treatments—such as antibiotics, antifungals, topical agents, and systemic medications—have proven effective, challenges such as antibiotic resistance (AR) and adverse side effects underscore the need for alternative approaches. NPs offer enhanced penetration, antimicrobial properties, reduced side effects, sustained drug release, and the ability to overcome AR, making them promising candidates for improved therapeutic outcomes. In conclusion, this review underscores the pressing need for innovative therapeutic approaches in veterinary dermatology. NPs represent a paradigm shift in treating animal skin infections, offering a multifaceted approach to overcoming current limitations. Harnessing their potential could significantly enhance the management of skin infections in veterinary practice, paving the way for more effective and sustainable treatment solutions.

Keywords: Nanoparticles, Veterinary dermatology, Antibiotic resistance, Antimicrobial activity, Treatment strategies

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Introduction

Skin infections in animals pose significant challenges to veterinary health and welfare, necessitating effective therapeutic strategies to ensure the well-being of the animals under care (Arvidsson et al., 2022). The prevalence of skin infections caused by various pathogens,

including bacteria, fungi, and parasites, underscores the urgency of developing innovative and effective treatment modalities (Tiwari et al., 2023). These infections manifest in various forms, each presenting unique clinical features and requiring tailored therapeutic interventions.

Understanding the types and nature of these skin infections is essential for developing effective treatment strategies that address the underlying causes (Masters et al., 2022). Conventional approaches predominantly rely on antibiotics, antifungals, and topical agents. However, the increasing prevalence of antibiotic resistance (AR), potential side effects, and incomplete efficacy pose significant hurdles to successfully managing these infections (Chinemerem et al., 2022).

Recently, interest in exploring nanotechnology as a novel avenue for tackling animal skin infections has increased (Nasr-Eldahan et al., 2021). Owing to their unique physical and chemical properties, nanoparticles (NPs) are promising alternatives to conventional drugs (Khan et al., 2019). The small size of the NPs allows for enhanced penetration through the skin barrier, facilitating targeted drug delivery to the infection site. This targeted approach minimizes systemic exposure, potentially reducing the risk of adverse effects associated with traditional drugs (Yusuf et al., 2023).

The limitations of existing treatments highlight the need for an evolution in veterinary dermatology, prompting a paradigm shift toward nanotechnology-based therapeutics. This literature review aims to comprehensively explore the current landscape of treatments for skin infections in animals and subsequently focuses on the potential applications of NPs in revolutionizing this field. By elucidating the advantages of NP-based therapeutics, this review aims to contribute to the ongoing discourse in veterinary medicine, thereby fostering a deeper understanding of the potential benefits that nanotechnology can bring to treating skin infections in animals. As we navigate the intricate web of challenges posed by animal skin infections, exploring NP-based interventions holds promise in offering new dimensions of efficacy, safety, and sustainability in veterinary dermatological care.

Overview of skin infections in animals

Skin infections in animals can be broadly categorized into bacterial, fungal, parasitic, and viral infections, with numerous specific conditions falling under each category (Mala et al., 2021). Bacterial infections, often caused by *Staphylococcus* spp. and *Streptococcus* spp., can lead to pyoderma, cellulitis, and abscess formation (Del Giudice, 2020). Fungal infections,

such as dermatophytosis caused by *Microsporum* spp., *Trichophyton* spp., and *Malassezia pachydermatis*, are common, especially in companion animals. Parasitic infestations, including mange caused by mites and dermatitis caused by fleas, ticks, and lice, contribute significantly to the spectrum of animal skin diseases. Viral infections, such as canine papillomatosis, feline herpesvirus dermatitis, and caprine contagious ecthyma, further complicate the clinical landscape (Martinez-Rossi et al., 2021). Skin infections in animals can result from various factors, typically involving a combination of microbial, environmental, and host-related influences (Flowers and Grice, 2020). Microbial causes include the proliferation of bacteria, fungi, parasites, and viruses on the skin surface or within the epidermal layers (Byrd et al., 2018). Environmental factors, such as humidity, temperature, and exposure to allergens or irritants, can contribute to the development and persistence of skin infections. Host-related factors, including an animal's immune status, breed predispositions, and underlying health conditions, play crucial roles in susceptibility to skin infections (Murrison et al., 2019).

Skin infections not only compromise the health and well-being of animals but also pose challenges in veterinary practice, including diagnostic complexities and the need for prolonged treatment regimens (Caneschi et al., 2023). Chronic and recurrent skin infections can lead to discomfort, pain, and secondary complications, impacting the quality of life for animals and the satisfaction of pet owners (McDonald et al., 2022). Livestock skin infections can cause significant economic losses for farmers and animal owners. Damaged hides in cattle can reduce market value, while sheep might produce less wool, and dairy animals may yield less milk with higher somatic cell counts. Infected horses may also perform poorly, contributing to financial setbacks (Limon et al., 2020). Certain animal skin infections, such as staphylococcal infections (including methicillin-resistant *Staphylococcus aureus* (MRSA) and rare dermatophilus, pose zoonotic risks, making their management important for public health. The frequent use of systemic antimicrobials for treating these infections in dogs and cats highlights the need for responsible antibiotic stewardship (Mala et al., 2021). Furthermore, the emergence of antibiotic-resistant strains and the

limitations of current treatment modalities underscore the need to explore innovative therapeutic approaches for effectively and sustainably managing animal skin infections (Chinemerem et al., 2022).

As we embark on this comprehensive review, our focus extends beyond conventional treatments for skin infections in animals to explore the potential applications of nanoparticle (NP)- based therapeutics. By gaining a deeper understanding of the types, causes, and implications of skin infections in animals, we aim to provide a solid foundation for evaluating the role of NPs in revolutionizing veterinary dermatological care (Lee et al., 2019).

Current treatment modalities for skin infections in animals

Skin infections in animals are commonly treated through various conventional modalities, each with its advantages and limitations (Mala et al., 2021). These treatment approaches focus

primarily on combating microbial pathogens, including bacteria, fungi, and parasites, that contribute to the development of skin infections. While these methods have been the mainstay of veterinary dermatology, they are not without challenges (Mala et al., 2021).

Antibiotics. Antibiotics have been extensively used in veterinary medicine to combat bacterial skin infections in animals, and various antibiotic agents and classes have been licensed for use in treating these infections. Table 1 summarizes the commonly used antibiotics for skin infections, along with their classes and mechanisms of action. However, this technique helps combat skin infections in animals, however, the emergence of antibiotic-resistant strains poses a significant threat to the efficacy of these drugs. The overuse and misuse of antibiotics in veterinary practices contribute to the development of resistance, limiting the available options for effective treatment (Caneschi et al., 2023).

Table 1: Summary of common antibiotics used to treat skin infections in animals, along with their mechanism of action.

Antibiotic class	Antibiotic agents	Mechanisms of action	References
Beta-Lactam	Penicillin	▪ Inhibit the synthesis of the cell wall	Bush and Bradford (2016)
	Cephalosporin	▪ Interact with penicillin-binding proteins (PBPs) and transpeptidase, thereby blocking the transpeptidation reaction and compromising the structural integrity of the bacterial cell wall, ultimately leading to cell lysis and death	
	Amoxicillin		
Fluoroquinolones	Enrofloxacin	▪ Inhibit bacterial DNA gyrase, disrupting DNA replication and repair	Shariati et al. (2022)
Tetracyclines	Ciprofloxacin		Orylska-Ratynska et al. (2022)
	Doxycycline	▪ Inhibit protein synthesis by binding to the bacterial ribosome	
Macrolides	Minocycline		Vázquez-Laslop and Mankin, (2018)
	Azithromycin	▪ Inhibiting bacterial protein synthesis	
Sulphonamide	Erythromycin		Ovung and Bhattacharyya (2021)
	Sulphonamide	▪ Targeting the bacterial metabolic pathway by blocking the synthesis of folic acid. Folic acid is essential for bacterial cells to synthesize nucleic acids, including DNA and RNA. Blocking nucleic acid synthesis leads to inhibition of cell growth	

Antifungals. Fungal skin infections, such as dermatophytosis, are commonly treated with antifungal agents. While these drugs can be effective, they often require prolonged treatment courses, leading to issues of compliance and potential side effects. Additionally, resistance to antifungal medications is a concern, necessitating the development of alternative strategies (Hay, 2018). Among the commonly used antifungal agents are azoles, such as ketoconazole, itraconazole, and fluconazole, which inhibit the synthesis of ergosterol, a vital

component of fungal cell membranes. These agents are effective against various fungal infections, including dermatophytosis and yeast infections (Table 2). Polyene antifungals, exemplified by drugs such as nystatin and amphotericin B, act by binding to fungal cell membranes, disrupting their integrity. Nystatin is commonly used for animal cutaneous yeast infections (Haro-Reyes et al., 2022). Terbinafine, an allylamine antifungal agent, inhibits ergosterol synthesis and is particularly effective against dermatophytes, making it a commonly

used treatment for fungal skin infections in animals (Hammoudi et al., 2022). Griseofulvin, which disrupts fungal mitosis, was once widely used for treating dermatophyte infections but

has since been replaced mainly by newer antifungals for treating veterinary dermatological conditions (Aris et al., 2022).

Table 2: Summary of common antifungal agents used to treat skin infections in animals, along with their mechanisms of action.

Antifungal class/group	Antifungal agents	Mode of action	References
Azoles	Ketoconazole, Itraconazole, Fluconazole	Inhibit the synthesis of ergosterol, a crucial component of fungal cell membranes	Zhang et al. (2023)
Polyenes	Nystatin, Amphotericin B	Bind to fungal cell membranes, disrupting their integrity	Haro-Reyes et al. (2022)
Allylamines	Terbinafine	Inhibits the ergosterol synthesis	Hammoudi et al. (2022)
Griseofulvin	Griseofulvin	Interferes with fungal mitosis	Aris et al. (2022)

Topical agents. Topical treatments, including creams, ointments, and shampoos, are frequently employed to manage localized skin infections in animals (Rabindranathnambi and Abid, 2021). While these methods can relieve specific conditions, their effectiveness may be limited by factors such as poor penetration through the skin barrier and the need for frequent applications (Parekh et al., 2021). Among the common topical agents used to treat animal skin infections is chlorhexidine, a broad-spectrum antiseptic utilized in veterinary dermatology (Hoang et al., 2021). It exhibits antimicrobial activity against bacteria and fungi. Chlorhexidine solutions or wipes are often employed to cleanse affected skin areas (Rafferty et al., 2019). Povidone-iodine, known for its antiseptic properties, is used to clean and disinfect skin wounds and infections. It has broad-spectrum activity against bacteria, fungi, and viruses (Lepelletier et al., 2020). Also, medicated shampoos containing antibacterial or antifungal agents are frequently used to treat dermatological conditions in animals (Saeed et al., 2024). Examples include shampoos containing chlorhexidine, ketoconazole, or miconazole (Loeffler et al., 2011). These shampoos offer topical treatment and help manage skin infections (Guillot and Bond, 2020). Oatmeal-based shampoos and lotions are often used to soothe and moisturize the skin. They can be beneficial in dry or irritated skin associated with infections. Oatmeal is anti-inflammatory, contributing to skin comfort (Criquet et al., 2012). Creams containing antifungal agents such as miconazole or clotrimazole are used for the localized treatment of fungal infections, including yeast infections and dermatophytosis (ringworm) (Bandyopadhyay, 2021).

Antiparasitic. Several antiparasitic agents are commonly used for treating skin infections in animals caused by parasites (Campbell and Soman-Faulkner, 2025). Among them are macrocyclic lactones such as ivermectin, which treat parasitic conditions, including certain mites. It disrupts parasites' nervous system (Failoc-Rojas et al., 2023).

Immunomodulatory agents. In cases where skin infections are linked to underlying immunosuppression or autoimmune conditions, immunomodulatory therapies may be employed (Varghese et al., 2023). These include corticosteroids and other immunosuppressive agents, which alleviate inflammatory responses (Zhang et al., 2021). However, their use necessitates careful monitoring due to potential side effects, and their efficacy in managing infections depends on a nuanced understanding of the underlying immunopathology (Mettelman et al., 2022). Corticosteroids are potent anti-inflammatory agents that suppress the immune response. They are commonly used to manage allergic skin conditions, immune-mediated diseases, and severe inflammatory reactions associated with skin infections (Noreen et al., 2021).

Dexamethasone, a potent corticosteroid, may be used in severe cases requiring more substantial immunosuppression. It is administered orally or by injection to control inflammatory responses rapidly (Noreen et al., 2021). Ciclosporin is an immunosuppressive medication that inhibits the activation of T cells. It is often used to manage immune-mediated skin diseases, including atopic dermatitis, where allergies contribute to skin inflammation (Rajagopalan et al., 2022).

Oclacitinib is a Janus kinase (JAK) inhibitor that modulates the immune response by targeting cytokine signaling. It is designed to treat allergic skin conditions, including atopic dermatitis, and has shown efficacy in reducing pruritus and inflammation (Jasiecka-Mikołajczyk et al., 2021). Interferon-alpha is an immunomodulatory protein that can be used to manage certain viral skin infections. It enhances the antiviral response and can be beneficial in cases of feline herpesvirus-associated dermatitis (Mertowska et al., 2023).

Nanoparticle-based therapeutics for skin infections in animals

In recent years, NPs have emerged as promising candidates for treating animal skin infections, offering unique advantages over traditional drugs (Hetta et al., 2023).

Physicochemical properties of the NPs. Owing to their small size and unique physicochemical properties, NPs exhibit enhanced penetration through the skin barrier (Ghasemiyeh and Mohammadi-Samani, 2020). This characteristic enables the targeted delivery of therapeutic agents to the site of infection, thereby minimizing systemic exposure and maximizing drug concentration at the desired location (Soliman et al., 2022). Studies have shown that NPs, such as silver nanoparticles (AgNPs) and lipid-based nanoparticles (LNPs), can effectively penetrate the skin layers, reaching the deeper dermal layers where pathogens may reside (Yusuf et al., 2023). Compared with traditional drug formulations, NPs can traverse various layers of the skin more effectively. This enhanced penetration enables the efficient delivery of therapeutic agents to deeper dermal layers, where pathogens may reside (Liu et al., 2023). Silver nanoparticles, for example, have been shown to penetrate the skin more effectively than larger particles, thereby ensuring a better distribution of antimicrobial agents (Bruna et al., 2021). A study conducted by Ong and Nyam (2022) investigated the penetration of silver NPs into porcine skin. The results indicated that silver NPs with a mean diameter of 23 nm had significantly greater skin penetration than larger particles (88 nm) (Tawfik et al., 2016). These findings emphasize the size-dependent penetration capabilities of NPs, which can be harnessed for targeted drug delivery (Ong and

Nyam, 2022).

NPs can be engineered to exhibit targeting properties, allowing them to accumulate specifically at the infection site (Orellano et al., 2019). The functionalization of NPs with ligands that recognize specific microbial markers or receptors on the skin can increase their specificity. Lipid-based NPs, for example, can target fungal infections by incorporating ligands that selectively bind to fungal cell walls, ensuring more precise drug delivery (Mitchell et al., 2021). Lipid-based NPs functionalized with a peptide targeting fungal cell walls demonstrated enhanced antifungal efficacy. Compared with their nontargeted counterparts, the targeted NPs exhibited superior adherence to fungal cells, emphasizing the potential for precise drug delivery in the context of skin infections (Almawash, 2023). One of the key advantages of enhanced penetration and targeting is the ability to minimize systemic exposure to therapeutic agents, reducing the risk of systemic side effects (Ibne Shoukani et al., 2024). By delivering drugs directly to the infection site, NPs can achieve therapeutic concentrations locally without requiring high systemic doses (Ezike et al., 2023). This targeted approach is crucial in veterinary medicine, where minimizing adverse effects is essential for ensuring animal welfare (Hiestand, 2022). A study investigated the penetration and distribution of silver NPs in rat skin. The results demonstrated that silver NPs penetrated the skin efficiently and were retained predominantly in the epidermal and dermal layers, minimizing systemic exposure (Ferdous and Nemmar, 2020). These findings support the potential of NPs to achieve localized therapeutic effects while reducing systemic impact (Peng et al., 2024).

Antimicrobial properties of the NPs. Various NPs possess inherent antimicrobial properties, making them effective against a broad spectrum of pathogens (Figure 1). In particular, silver NPs (AgNPs) have demonstrated potent antibacterial and antifungal activity (Mondal et al., 2024; Sharmin et al., 2021; Do et al., 2025). Additionally, polymeric NPs (PNPs) loaded with antimicrobial agents have shown efficacy in combating resistant strains, addressing the challenge of AR in veterinary dermatology (Murugaiyan et al., 2022).

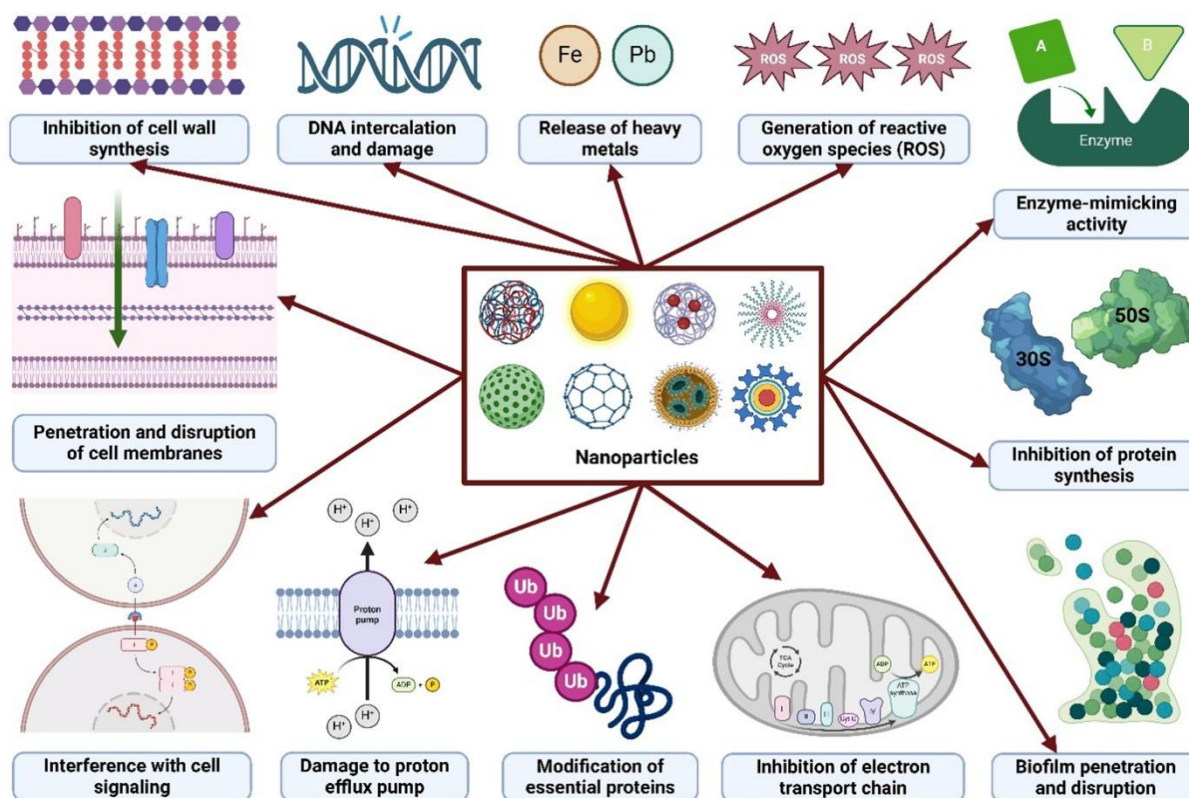


Figure 1: Different antimicrobial mechanisms of nanoparticle-based therapeutics. The figure was created with BioRender.com.

Anti-biofilm properties of NPs. NPs have emerged as a promising therapeutic strategy for treating biofilm-associated skin infections in animals, owing to their unique ability to penetrate and disrupt biofilm structures (Youssef et al., 2023). The efficacy of nanoparticles against biofilms—known for their resistance to traditional antibiotics—largely depends on their ability to penetrate (Yan et al., 2024; Lawal et al., 2025). Different types of nanoparticles have exhibited the capacity to infiltrate biofilms associated with skin infections (Do et al., 2024). For example, AgNPs have shown substantial antibiofilm properties against *S. pseudintermedius*, a prevalent pathogen in canine otitis externa. AgNPs can penetrate biofilm matrices and significantly reduce their formation at concentrations as low as 10-20 µg/mL (Seo et al., 2021). This penetration enables AgNPs to directly interact with bacterial cells within the biofilm, leading to structural disruption and inhibition of further bacterial growth. Similarly, ZnO NPs have demonstrated the penetration abilities against biofilms (Hu et al., 2022). Research focusing on multidrug-resistant *S. aureus* has demonstrated that ZnO NPs can effectively disrupt biofilms and inhibit

their formation by affecting the growth of planktonic bacteria (Nikpasand and Parvizi, 2019). The small size of ZnO NPs facilitates their movement through the extracellular polymeric substances (EPSs) of biofilms, enabling direct contact with bacterial cells and enhancing their antibacterial activity (Yusof et al., 2021). CSNPs also promise to penetrate and disrupt biofilm structures in animal dermatological infections. CSNPs can penetrate cell walls and membranes, particularly those of low molecular weight, thereby creating an impermeable barrier on microbial surfaces that restricts nutrient uptake (Teo et al., 2021). These advantages, including penetration capability, biocompatibility, and biodegradability, positioned CSNPs as a viable option for treating biofilm-associated infections in veterinary settings (Dowaidar, 2024).

The penetration characteristics of nanoparticles are affected by various factors, including particle size, surface charge, and surface chemical makeup (Pangprasit et al., 2023). Optimal penetration requires that nanoparticles be smaller than the dimensions of the water-filled channels within biofilms (Guo et al., 2023). Furthermore, surface modifications can further enhance their penetration efficacy.

For instance, dextran-coated nanoparticles have demonstrated improved biofilm penetration compared to their uncoated counterparts, owing to the inherent affinity of dextran for biofilm components (Liu et al., 2023).

The enhanced penetration capabilities of nanoparticles facilitate direct interactions with bacterial cells and the effective delivery of antimicrobial agents deep within the biofilm structure (Ding et al., 2019). This characteristic is crucial for managing persistent infections, as conventional antibiotics often struggle to reach bacteria embedded within the biofilm matrix (Shree et al., 2023). A notable example is ciprofloxacin-loaded PEG-coated ZnO nanoparticles, which have demonstrated increased antibiofilm activity against skin infections, likely due to their enhanced penetration and drug delivery properties (Ibne Shoukani et al., 2024).

Silver nanoparticles (AgNPs). AgNPs have garnered significant attention for their potent antimicrobial activity against bacteria and fungi (Feng et al., 2021). The unique physicochemical properties of AgNPs enable them to interact with microbial cell membranes, leading to structural damage and disruption of essential cellular functions (Bruna et al., 2021; Sulaiman et al., 2024). In a seminal study, Bruna et al. (2021) investigated the bactericidal effect of AgNPs. The NPs were found to induce structural damage to bacterial cell membranes, leading to cell death. This study provides the foundation for understanding the antimicrobial mechanisms of AgNPs (Bruna et al., 2021). Further highlighted the broad-spectrum bioactivities of AgNPs. This study emphasized the ability of AgNPs to inhibit the growth of various bacteria and fungi, underscoring their potential as versatile antimicrobial agents (Rizwana et al., 2021). The unique mechanisms of action of AgNPs, involving membrane disruption and interference with cellular processes, contribute to their effectiveness against diverse pathogens (Wahab et al., 2023).

Zinc oxide nanoparticles (ZnO NPs). NPs have shown significant potential for treating animal skin infections. These NPs exhibit robust antimicrobial properties against various pathogens, including bacteria, fungi, and viruses (Rahman et al., 2022). Research findings suggest that ZnO NPs effectively reduce bacterial load and inflammation in infected skin, improving

tissue architecture (Pati et al., 2014). For instance, the intradermal administration of ZnO NPs has been linked to substantial decreases in skin infections, bacterial counts, and inflammation in mice models (Rahman et al., 2022; Pati et al., 2014). In veterinary medicine, ZnO NPs are emerging as a promising option for managing subclinical mastitis in dairy cattle and treating chronic diabetic wounds (Asif et al., 2023). The antimicrobial efficacy of ZnO NPs can be attributed to various mechanisms, including the generation of reactive oxygen species, the release of Zn²⁺ ions, and direct interactions with bacterial cell membranes (Asif et al., 2023). Furthermore, ZnO NPs have shown effectiveness against antibiotic-resistant strains, such as MRSA, presenting a viable alternative to traditional antibiotics (Mahmoud et al., 2021). The biocompatibility and biodegradability of ZnO NPs make them particularly attractive for topical applications in veterinary dermatology (Youssef et al., 2024).

Chitosan nanoparticles (CSNPs). CSNPs represent a promising alternative for the antimicrobial treatment of skin infections in animals (Orellano et al., 2019). These CSNPs are characterized by their natural origin, biodegradability, and broad-spectrum effectiveness against various bacterial and fungal pathogens (Mala et al., 2021). CSNPs exhibit significant antibacterial activity against both Gram-positive and Gram-negative bacteria, with particular efficacy observed against Gram-negative strains, such as *Escherichia coli* and *Pseudomonas aeruginosa* (Orellano et al., 2019). Evidence suggests that CSNPs can significantly reduce bacterial loads and associated inflammation within infected skin, thereby improving the structural integrity of damaged tissue (Orellano et al., 2019). Specifically, studies have documented reductions in viable bacteria by as much as 4 logs over several days, particularly against clinically relevant strains, such as *Staphylococcus epidermidis* (Al-Zahrani et al., 2021). Concerning antifungal efficacy, CSNPs exhibit considerable activity against numerous pathogenic fungi, including *Candida albicans*, *Aspergillus* spp., and *Fusarium* spp. (Arafa et al., 2018). They have been shown to inhibit fungal development at various stages, such as mycelial growth, spore formation, and spore viability. The mechanisms underlying antifungal activity include the disruption of the fungal cell membrane and interference with

membrane-associated enzymes (Orellano et al., 2019). The antimicrobial efficacy of CSNPs can be attributed to several key mechanisms. The elevated density of positively charged amino groups on the surface of the NPs facilitates enhanced binding to negatively charged microbial surfaces (Guarnieri et al., 2022). Furthermore, CSNPs, especially those of lower molecular weight, can penetrate cellular membranes and form an impermeable barrier on the microbial surface, thereby obstructing nutrient uptake.

Additionally, CSNPs can induce oxidative stress within microbial cells (Guarnieri et al., 2022; Orellano et al., 2019). CSNPs offer numerous benefits for managing skin infections in veterinary applications, including their biocompatibility and biodegradability, which help minimize the risk of adverse side effects (Orellano et al., 2019). They also enable sustained release of antimicrobial agents, thus providing extended protection against infections. Moreover, CSNPs can be synergistically combined with other antimicrobial agents to enhance their overall effectiveness, while their muco-adhesive properties contribute to improved retention on skin and mucosal surfaces (Al-Zahrani et al., 2021). In veterinary medicine, the potential applications of CSNPs are vast, particularly in treating wound infections, where they can promote faster healing and reduce inflammation. They are also promising for managing skin infections in pets caused by *Staphylococcus* spp. and treating fungal skin infections (Seo et al., 2021). As ongoing research unfolds, CSNPs may serve as a significant alternative to traditional antibiotics, addressing the pressing issue of AMR within veterinary practice (Orellano et al., 2019; Al-Zahrani et al., 2021).

Gold nanoparticles (AuNPs). AuNPs have gained recognition as an innovative approach for treating animal skin infections, presenting distinct advantages in antimicrobial therapy (Kumalasari et al., 2024). These AuNPs demonstrate a broad-spectrum antibacterial effect against Gram-positive and Gram-negative bacteria, including strains resistant to antibiotics (Naderi et al., 2018). The mechanisms by which AuNPs exert their antimicrobial activity include the disruption of bacterial cell membranes, interference with bacterial respiratory pathways, and the production of reactive oxygen species (Naderi et al., 2018). AuNPs have shown notable potential in promoting wound healing and

facilitating the regeneration of damaged collagen tissue (Soliman et al., 2022). For instance, research involving rabbits with onychomycosis revealed that applying AuNPs in conjunction with light stimulation resulted in a recovery rate of up to 96%, significantly surpassing the efficacy of conventional treatment methods (Tawfik et al., 2016).

Furthermore, the photothermal properties of AuNPs render them suitable for targeted antibacterial therapies, as they can be activated by light to eliminate bacterial infections (Naderi et al., 2018). They can also be modified or combined with other antimicrobial agents to enhance their effectiveness against resistant bacterial strains (Naderi et al., 2018). Regarding wound healing, AuNPs have been demonstrated to accelerate healing rates and diminish inflammation in infected wounds (Soliman et al., 2022). Their adaptability in drug delivery systems and their capacity to be integrated into various formulations, such as gels and ointments, further underscores their promising potential in veterinary dermatology (Arafa et al., 2018).

Lipid-based nanoparticles (LNPs). LNPs, including liposomes and lipid nanocarriers, have demonstrated antimicrobial properties and potential for targeted drug delivery (Liu et al., 2023). These nanoparticles can encapsulate antimicrobial agents, facilitating their controlled release at the site of infection (Hu et al., 2019). Ferreira et al. (2021) investigated the antimicrobial activity of LNPs against *S. aureus*. Researchers have formulated liposomes loaded with antimicrobial agents, observing sustained drug release and prolonged antimicrobial effects (Guo et al., 2023). This study highlighted the potential of LNPs for their intrinsic antimicrobial properties and their ability to serve as carriers for controlled drug release. Alfutaimani et al. (2024) explored the antimicrobial efficacy of lipid nanocarriers against fungal infections. The lipid nanocarriers were loaded with antifungal agents, which enhanced activity against fungal strains (Nosratabadi et al., 2024). This highlights the potential of LNPs for achieving sustained drug release, which can be adapted for antimicrobial agents in the context of skin infections in animals (Zhang et al., 2023).

Polymeric nanoparticles (PNPs). PNPs represent another class of nanoparticles with inherent antimicrobial properties. The physicochemical characteristics of PNPs enable

interactions with microbial cell walls, resulting in membrane disruption and the inhibition of vital cellular functions. [Spirescu et al. \(2021\)](#) investigated the antimicrobial activity of PNPs against multidrug-resistant (MDR) bacterial strains. The study demonstrated that PNPs exhibited broad-spectrum antimicrobial effects, suggesting their potential to overcome antibiotic resistance ([Moradi et al., 2023](#)). The unique mechanisms of action of PNPs make them promising candidates for developing alternative antimicrobial strategies. [Zhang et al. \(2019\)](#) investigated the application of PNPs for treating fungal infections. Researchers have formulated nanoparticles loaded with antifungal agents and observed enhanced efficacy against fungal strains ([Limon et al., 2020](#)). This study highlighted the potential of PNPs to deliver sustained antifungal effects, providing a novel approach to addressing the challenges associated with conventional antifungal treatments ([Moradi et al., 2023](#)). PNPs can be engineered to achieve sustained drug release by controlling the release kinetics due to their versatile formulation capabilities. This property is particularly valuable in treating chronic or persistent skin infections, where prolonged exposure to antimicrobial agents is beneficial ([Nunes et al., 2022](#)). [Nunes et al. \(2022\)](#) explored the sustained release of antimicrobial agents from PNPs. The study demonstrated that PNPs provided prolonged release of the encapsulated drug, ensuring sustained antimicrobial effects ([Spirescu et al., 2021](#)). This sustained release profile can be advantageous in addressing the challenges associated with conventional topical treatments for skin infections in animals. [Mishra et al. \(2022\)](#) investigated the potential use of PNPs against MDR bacterial strains. This study highlighted the sustained release of antimicrobial agents from PNPs, leading to prolonged inhibitory effects on bacterial growth ([Zhu et al., 2022](#)). This sustained-release property is crucial for optimizing therapeutic outcomes and overcoming challenges associated with conventional treatments ([Spirescu et al., 2021](#)).

Overcoming antibiotic resistance (AR)

The broad-spectrum antimicrobial activity of nanoparticles can potentially overcome challenges associated with AR ([Makabenta et al., 2021](#)). NPs can act through multiple mechanisms, making it difficult for pathogens to develop resistance. This is particularly important

in addressing the evolving landscape of microbial resistance in veterinary medicine ([Hetta et al., 2023](#)).

Combating multidrug-resistant (MDR) bacteria. MDR bacteria pose a significant challenge in veterinary medicine, limiting the efficacy of conventional antibiotics. NPs, particularly AgNPs, have demonstrated efficacy against MDR strains, suggesting an alternative approach for combating bacterial skin infections ([Hetta et al., 2023](#)). [Bruna et al. \(2021\)](#) investigated the potential of AgNPs against MDR bacterial strains. This study highlighted the broad-spectrum activity of AgNPs, including their effectiveness against antibiotic-resistant strains ([Bruna et al., 2021](#)). The ability of nanoparticles to target multiple mechanisms can help overcome the challenges posed by antibiotic-resistant bacteria, offering a promising avenue for treating skin infections in animals ([Makabenta et al., 2021](#)). [Makabenta et al. \(2021\)](#) discussed the broad-spectrum bioactivities of AgNPs. This review emphasized the potential of AgNPs to combat AR by disrupting bacterial cell membranes and interfering with cellular processes. The versatility of AgNPs in overcoming resistance mechanisms makes them valuable tools for addressing the evolving landscape of AMR ([Wahab et al., 2023](#)).

Synergistic effects with antibiotics. NPs can act synergistically with antibiotics, enhancing antimicrobial effects and potentially overcoming resistance ([Anand et al., 2022](#)). This synergy is particularly valuable in combination therapy, where NPs can potentiate the activity of existing antibiotics, allowing for lower antibiotic concentrations and reducing the risk of resistance development ([Malawong et al., 2021](#)). [Spirescu et al. \(2021\)](#) investigated the synergistic effects of antimicrobial agents combined with polymeric nanoparticles. This study demonstrated that polymeric NPs enhanced the efficacy of antimicrobial agents against bacterial strains ([Mahmoud et al., 2021](#)). The synergistic effects observed in this study suggest that NP-based formulations can be utilized to optimize the therapeutic outcomes of antibiotic treatments. [Subhan et al. \(2023\)](#) investigated the synergistic effects of lipid nanocarriers with small interfering RNA (siRNA) for treating skin cancer. This study highlights the potential of lipid nanocarriers to enhance the therapeutic effects of siRNAs. While this study focused on cancer treatment, NP-mediated synergy with therapeutic

agents can be extrapolated to treating bacterial skin infections, where overcoming AR is crucial (Chang et al., 2023).

Targeting resistant mechanisms. NPs can be designed to target specific resistance mechanisms employed by bacteria, addressing the root causes of AR (Makabenta et al., 2021). This targeted approach involves tailoring NP formulations to disrupt resistance mechanisms, potentially restoring the sensitivity of bacteria to conventional antibiotics (Makabenta et al., 2021). Wahab et al. (2023) discussed the potential use of AgNPs to target bacterial resistance mechanisms. This study highlighted the multifaceted effects of AgNPs, including their ability to disrupt bacterial cell membranes and interfere with cellular processes. By targeting these fundamental resistance mechanisms, NPs can contribute to overcoming AR and restoring the efficacy of conventional treatments (Makabenta et al., 2021). More et al. (2023) emphasized the importance of understanding the mechanisms of action of NPs against antibiotic-resistant bacteria. This review highlighted that NPs can circumvent specific resistance mechanisms by acting on multiple targets, offering a comprehensive approach to combating resistance (Shelke et al., 2024). This knowledge-driven strategy can pave the way for developing NP-based therapies tailored to address specific challenges posed by antibiotic-resistant strains (Gupta et al., 2019).

Accelerated wound healing

NPs have demonstrated significant potential in accelerating wound healing and treating skin infections in animals. Various types of NPs, including AgNPs, ZnO NPs, and titanium dioxide (TiO₂ NPs), have shown promising results in preclinical studies. These NPs exhibit potent antimicrobial properties against various pathogens, including antibiotic-resistant strains, while promoting wound closure and tissue regeneration (Nikpasand and Parvizi, 2019; Pangprasit et al., 2023). For instance, AgNPs have been found to reduce bacterial load, decrease inflammation, and enhance re-epithelialization in animal models (Naderi et al., 2018). ZnO NPs have demonstrated efficacy in managing subclinical mastitis in dairy cattle and promoting wound healing in chronic wounds (Feng et al., 2021). TiO₂ NPs have demonstrated the ability to enhance cell migration, collagen formation, and wound contraction in both *in vitro*

and *in vivo* conditions (Pangprasit et al., 2023). The multifaceted approach of NPs in wound healing, combining antimicrobial activity with the promotion of tissue repair processes, makes them a promising avenue for developing advanced wound management strategies in veterinary medicine.

Considering the safety of NPs

Reduced side effects. The precise targeting of nanoparticles to the infection site reduces systemic exposure, minimizing the risk of systemic side effects associated with conventional drugs (Yusuf et al., 2023). This targeted approach is crucial in veterinary medicine, where minimizing adverse effects is essential for ensuring animal welfare (Guarnieri et al., 2022). Studies have reported nanoparticle formulations' safety and reduced toxicity, emphasizing their potential for enhancing the safety profile of skin infection treatments (Hetta et al., 2023).

Minimizing systemic exposure. Nanoparticles allow targeted drug delivery, reducing the need for high systemic doses (Yusuf et al., 2023). This targeted approach ensures that the therapeutic agents are explicitly delivered to the infection site, minimizing systemic exposure (Yusuf et al., 2023). This is particularly crucial in veterinary medicine, where reducing systemic exposure helps mitigate the risk of adverse effects on internal organs and tissues (Youssef et al., 2019). In another study by Ferdous and Nemmar (2020), the penetration and distribution of AgNPs in rat skin were investigated. The results indicated that AgNPs predominantly accumulated in the epidermal and dermal layers, with minimal systemic absorption. This finding supports the potential of nanoparticles to achieve localized therapeutic effects while minimizing systemic exposure, consequently reducing the risk of systemic side effects. Muhamad et al. (2022) conducted a study on the mechanism of toxicity of AgNPs in porcine lung epithelial cells. Researchers have reported that the toxic effects depend on the dose and exposure time, emphasizing the importance of optimizing nanoparticle formulations to ensure efficacy while minimizing adverse effects (Borgert et al., 2021). This study highlighted the potential of nanoparticles to balance therapeutic effectiveness and reduce toxicity (Muhamad et al., 2022).

Size-dependent Effects. The size of

nanoparticles plays a crucial role in their biodistribution and potential toxicity. Compared with larger particles, smaller nanoparticles often exhibit enhanced penetration but may have different interactions with cells (Mitchell et al., 2021). Understanding the size-dependent effects of nanoparticles is essential for tailoring formulations that optimize therapeutic efficacy while minimizing side effects (Elumalai et al., 2024). Elumalai et al. (2024) demonstrated the size-dependent cytotoxicity of AgNPs in human lung cells. The study revealed that smaller nanoparticles induced more significant cytotoxic effects than larger ones, suggesting that the size of nanoparticles can influence their safety profile (Egbuna et al., 2021). This highlights the importance of careful consideration in designing and optimizing nanoparticle formulations for specific therapeutic applications. Harish et al. (2022) discussed the size-dependent penetration of nanoparticles through the skin. This review emphasized that smaller nanoparticles penetrate more effectively than larger ones, enabling targeted delivery. However, the potential for size-dependent effects on cellular interactions underscores the need for a nuanced approach in nanoparticle design to achieve optimal therapeutic outcomes with reduced side effects.

Engineering for safety

Advances in nanoparticle engineering have allowed the formulation of nanoparticles with enhanced safety profiles (Mitchell et al., 2021). Surface modifications, such as coating nanoparticles with biocompatible materials, can reduce potential interactions with biological tissues and improve safety (Yusuf et al., 2023). Chehelgerdi et al. (2023) demonstrated nanoparticles' safety and reduced toxicity by engineering responsive colloids for enhanced sampling of biomolecular-free energy landscapes (Yu et al., 2021). This study highlights the potential for careful engineering to enhance the safety profile of nanoparticles, ensuring their suitability for therapeutic applications (Mitchell et al., 2021).

Challenges and future perspective

Despite the array of treatment options available, challenges persist in achieving optimal outcomes. These challenges include the rising threat of AMR, potential side effects associated with prolonged use of medications, and the need for accurate diagnosis to tailor treatments

effectively (Lee and Kim, 2023). Veterinary practitioners are faced with the imperative to balance therapeutic efficacy with minimizing adverse effects while considering the individual characteristics of the animal patient (Chinemerem et al., 2022). Antibiotics and antifungals (oral, injectable, or topical) have been instrumental in treating bacterial and fungal infections; however, their use is challenging, particularly in the context of skin infections in animals (Sulowska-Ziaja et al., 2023). The prolonged and indiscriminate use of antibiotics has led to the emergence of antibiotic- and antifungal-resistant strains of pathogens (Ahmed et al., 2024). This poses a significant challenge in veterinary dermatology, as resistant bacteria and fungi may not respond to conventional antibiotics or antifungal treatments (Caneschi et al., 2023). These antimicrobial agents can sometimes cause adverse effects in animals, ranging from mild gastrointestinal damage to severe allergic reactions. Monitoring for side effects is crucial during antibiotic and antifungal therapy (Mohsen et al., 2020). Inadequate completion of prescribed antimicrobial courses can contribute to developing antibiotic and antifungal resistance. Following the recommended treatment duration is essential to ensure complete eradication of the infection (Velazquez-Meza et al., 2022).

Some antibiotics have a narrow spectrum of activity and may not effectively target certain bacterial species. This limitation necessitates accurate identification of the causative bacteria for optimal treatment selection (Uddin et al., 2021). Topical treatments may require regular application, and compliance can sometimes be challenging (Pati et al., 2014). Pet owners must be educated on proper application techniques and encouraged to follow the prescribed treatment plan (Ti et al., 2024). Furthermore, topical agents are generally effective for treating superficial skin infections but may not be effective against deep-seated infections. Systemic treatments may be necessary (Valentine, 2019). Some animals may be sensitive or allergic to specific topical agents. Careful monitoring for adverse reactions is essential during treatment (Holbert et al., 2020).

While advances in NP-based treatments for animal skin infections are promising, further research is needed to optimize formulations, assess long-term safety, and evaluate the scalability of production. Regulatory considerations and economic feasibility must

also be addressed for successful translation into veterinary practice.

Conclusion

In conclusion, the application of NPs in treating skin infections represents a transformative approach with the potential to revolutionize veterinary dermatology. The unique properties of NPs, including enhanced penetration, antimicrobial efficacy, reduced side effects, sustained drug release, and the ability to overcome AR, make them promising avenues for the future of skin infection therapeutics in animals. Continued interdisciplinary research efforts are crucial to unlocking the full potential of NP-based treatments and paving the way for their integration into veterinary clinical practice.

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