



# Nanotechnology: Changing the World of Animal Health and Veterinary Medicine

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## Abstract

Nanoparticles have long been used as diagnostic and therapeutic agents in human medicine, but their use in veterinary medicine and animal production is recent. Several laws and regulations have been implemented in response to growing concerns about antibiotic resistance, including a ban on feed-grade antibiotics in Europe. As a result of banning these antibiotics, the industry is searching for safe alternatives to fill the void left behind. The increasing global population, decreasing fertile land, increasing animal protein demand, and increasing income have further accelerated the demand for animal production. These conditions have created a dire need for technologies and substitutes that would increase the productivity and well-being of animals, improve drug delivery, and reduce the toxic effect of drugs. It appears that nanotechnology has great potential and future applications in the animal husbandry industry. According to numerous reports, nanoparticles make excellent anti-microbials, promoting animal growth and well-being. Nanotechnology research has the potential to offer revolutionary tools for improving animal health and production in the future. The purpose of this chapter is to describe the types of nano-materials used in animal sciences, as well as the unique technologies developed by nanoscience for improving animal health and production. Further, the toxicity of nano-materials and considerations for animal health and safety are also discussed.

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**Keywords**

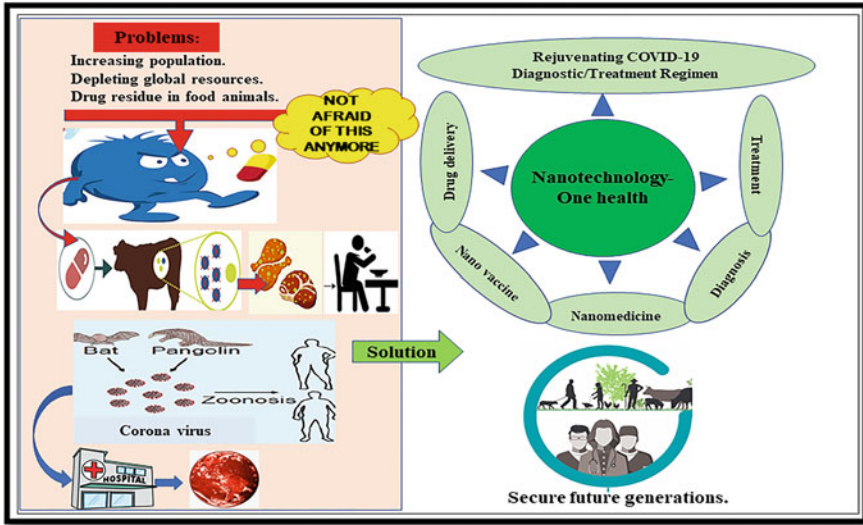
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## 7.1 Introduction

Nanotechnology or nanoscience refers to the study of the understanding and manipulation of the properties of nanoscale materials ranging between 1 and 100 nm in dimensions (Sim and Wong 2021). Using nanotechnology, we can design entirely new molecular structures and properties. Apart from being small, nanoparticles (NPs) have the advantage of having a large surface area-to-volume ratio, making them unique in drug delivery and anti-microbial action as well as more reproducible and reliable (Dawadi et al. 2021). Nanoparticles are finding increasing attention in improving catalytic activity, chemical stability, thermal conductivity, and non-linear optical performance (Laouini et al. 2021). By modifying their shape, surface properties, and sizes, various nanoparticles can be transformed into nano-systems that can be used in the diagnosis, imaging, and treatment of diseases, including cancer, cardiovascular, ocular, and central nervous system diseases. These functionalized nano-materials can deliver controlled-release therapy by providing drugs to specific sites or tissues (Khan et al. 2020). Most biological systems are nanoscale, making nano-materials ideal for biomedical devices. Research in alternative therapies has been driven by advances in nano-medicine and nano-devices as current methods cannot detect and treat early-stage diseases (Anjum et al. 2021).

Nanotechnology has found prospects in one health approach that encompasses animal and human health and the environment. However, several unknown probable health hazards overshadow these potential benefits, creating doubts about the successful application of technology by governments and the public worldwide. It is a delicate situation where uncertainty of behaviour of these designed nanoparticles or how their products function which restricts universal usage. As a result, it necessitates regulatory control to assure safe production processes and safe application to humans, requiring appropriate and balanced oversight (Jain et al. 2021). As the human population grows exponentially, so does the need for agricultural and animal food products, prioritizing new industry technologies to address the looming food shortage issues in the future. In attempts to increase animal production, antibiotics were used recklessly, which became a crucial factor in the evolution of cross-resistant microorganisms. By 2030, agriculture intensification will have contributed to a 67% rise in anti-microbial usage (Myers et al. 2022). Antibiotic usage climbed by over 36% in 71 countries, with the BRICS (Brazil, Russia, India, China, and South Africa) accounting for over 75% of this rise (Tiseo et al. 2020). However, measurement of anti-microbial use in animal production in low- and middle-income countries (LMICs) is difficult because of anti-microbials sold “over the counter” and of poorly enforced regulatory frameworks (Jibril et al. 2021). Nanotechnology can improve animal production qualitatively and quantitatively



**Fig. 7.1** Problems and solutions by nanotechnology

while providing many environmental, health, and economic benefits. Nanotechnology research and development are likely to facilitate and frame the next stage of development of genetically modified animal products, vaccines, precision animal feeds, and reproductive techniques (Fig. 7.1). Biosensors using nanotechnology can monitor animal health, safety, and fertility (Fesseha et al. 2020).

As the twentieth century rolled around, a pandemic seemed a long way off, despite experiencing plague and Spanish flu in the eighteenth and nineteenth centuries. However, in 2019, the entire world came to a standstill due to the COVID-19 pandemic, shattering our illusions of being invincible. The current coronavirus-associated acute respiratory disease is the third reported spillover of an animal coronavirus to humans in under two decades, resulting in an epidemic (Coronaviridae Study Group of the International Committee on Taxonomy of Viruses 2020). It has necessitated taking immediate steps to check disease screening and address new cutting-edge technologies in human therapeutics and animals as one health. It has become clear that animal and human health must be treated as one, with equal priorities, to avoid future pandemics and that new promising technologies, such as nanotechnology, which can transform diagnosis, treatment, and therapeutics in humans and animals, must be reviewed regularly. Nanomedicine and nanotechnology are emerging fields and provide excellent tools for overcoming the problem of drug resistance and dose reduction. Though nanotechnology is not a new subject but a technology with such promise for the future, it warrants periodic reviews and updates to inspire thinking and novel approaches. The primary types of nano-carriers to be used in the preparation of nano-medicines for the animal population are covered in this chapter. It will also go over toxicity

concerns, future potential, and novel approaches developed by nanotechnology for use in enhancing animal health and production.

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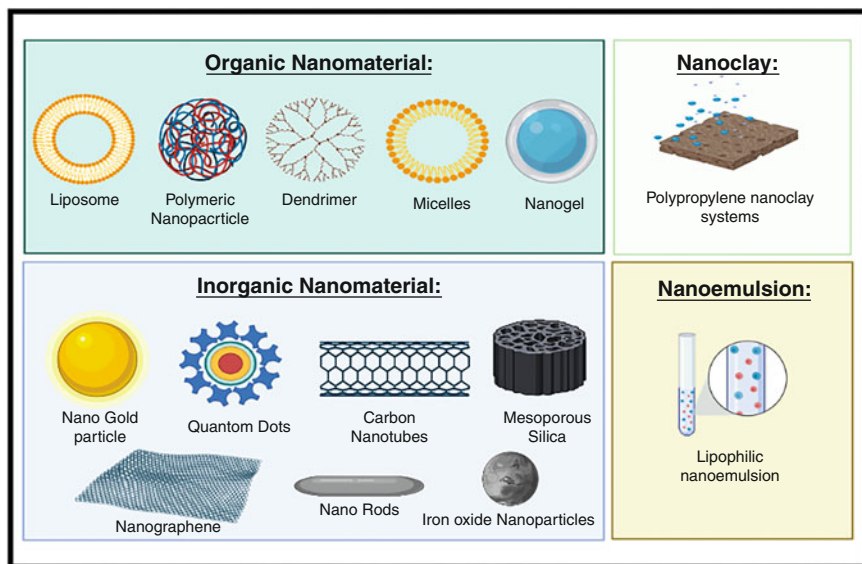
## 7.2 Nano-carriers

The term “nano-medicines” refers to medical products that are developed and produced using nano-carriers and/or nano-materials. Nano-vectors or nanocarriers are two names for nanoparticles (NPs) that are used to make nano-medicines. The NPs are defined as systems smaller than 1000 nm, which is an important parameter for clinical applications because it is directly related to physical and chemical interactions with biomolecules (Kreuter 2007). Drug release from nano-structured systems can have significant biopharmaceutical advantages over conventional systems because nano-compartmentalization enables modulation of the release profile of the therapeutic agent (time and site) and modifies its pharmacokinetics parameters without changing the therapeutic agent’s pharmacological properties (Suri et al. 2007). To deliver antibacterial, anti-fungal, antiviral, anaesthetic, anti-parasitic, vaccine, and anti-neoplastic drugs to the animal population as well as cosmetic items to enhance the appearance of pets, nano-carriers are ideal (Carvalho et al. 2018). The therapeutic agents in nano-carriers can also be attached to their surface, dispersed in a matrix, or included in a reservoir system. Nanoparticle surfaces can be functionalized to increase drug efficacy and safety as well as to target particular tissues, organs, or cells.

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## 7.3 Using Nano-carriers in Veterinary Sciences

Liposomes, nano-emulsions, micelles, lipidic, polymeric, mesoporous silica, metallic nanoparticles, and dendrimers are the main nano-carriers used to prepare nano-medicines for veterinary applications and are discussed in this study (Fig. 7.2) (Carvalho et al. 2020). In order to increase the bioavailability and decrease the toxicity of conventional dosage forms based on therapeutic agents with low solubility, nano-carriers are a good strategy. The primary goal of using nano-carriers in veterinary medicine is to be able to vectorize the release of the therapeutic agent with dose reduction, thereby minimizing serious adverse reactions and discomfort in long-term treatments. In general, the advantages of nano-carrier systems are extensive and include the following: (1) targeting the therapeutic agent through accumulation at the site of action; (2) lowering the required dose of the therapeutic agent, decreasing the dose-associated toxicity; (3) protecting the therapeutic agent by increasing its stability; (4) modulating the release profile of the therapeutic agent; (5) modifying the pharmacokinetic parameters of the therapeutic agent, increasing bioavailability; and (6) reduction of toxicity.



**Fig. 7.2** Nano-carriers in veterinary sciences

## 7.4 Classification of Noncarriers

### 7.4.1 Liposomes

Liposomes are phospholipid and cholesterol bilayer spherical vesicles that form at least one lipid bilayer around an aqueous core in water, allowing Van der Waals forces to encapsulate both hydrophilic and hydrophobic compounds immersed in the lamellae (Gonda et al. 2019). Liposomes have unique properties due to their nano sizes, such as biocompatibility and biodegradability. They can be used in nanomedicine, cosmetics, and the food industry (Panahi et al. 2017). Liposomal formulations are less toxic and have better pharmacological parameters than drugs alone. Although they appear to be the preferred drug delivery system for many diseases, more research into dose and time regimens is needed (Beltrán-Gracia et al. 2019).

### 7.4.2 Polymeric Nanoparticles

With the advances in polymer science and nanotechnology, a diverse range of polymer nanoparticles has been described. The potential applications of polymeric nanoparticles are determined by their unique properties or desirable characteristics (Chenthamara et al. 2019). Important properties of polymeric nanoparticles, like

biocompatibility and biodegradability, are frequently used in the drug delivery system. There are both synthetic and natural polymer nanoparticles available. Natural polymers have excelled because of inherent properties, like biodegradability, biocompatibility, and ease of modification. Chitosan, collagen, albumin, and gelatine have been extensively researched and applied. Formalized paraphrase complex modifications to synthetic polymers handle specific properties, such as improved specificity, biological availability, reduced toxicity, and desirable pharmacokinetics (Kakkar et al. 2017; Rezaei et al. 2019).

### 7.4.3 Quantum Dots

Quantum dots (QDs) are nanoscale semiconductor crystals discovered helpful in many fields, including biology. QDs have various applications, including biological imaging, diagnostics, stem cells, and cell tracking. Cells must be targeted from the injection site to their final destination to provide effective diagnosis and therapy. QDs are a popular type of cell tag that has received much attention. QDs are not toxic or immunogenic. QD labelling solved the tissue autofluorescence problem due to their emission properties (Kargozar et al. 2020). The usage of QDs with other methods, such as emission scanning microscopy, might aid in better detection and understanding of cellular interactions within the target tissue. Cryo-imaging can detect single-cell sensitivity cells, making it vital for stem and stromal cell therapies and regenerative medicine (Wuttisarnwattana et al. 2020).

### 7.4.4 Nano-shells

Nano-shells are spherical nanoparticles with dielectric silica cores covered by thin metals, mainly gold. These shells may be conjugated with other biomolecules, such as antibodies, fluorophores, oligonucleotides, targeting ligands, polymers, therapeutic drugs, and radioisotopes for more effective and better diagnostic and therapeutic goals. The synthesis of gold nano-shells can be explained in three steps: the first step includes the surface amination of silica cores, the second step involves the deposition of gold nanoparticles (2–3 nm gold seed), and the last step concerns the re-growing of these seeds (Lermusiaux et al. 2021). Nano-shells find their application in gene delivery, target therapy, biomedical imaging, tissue welding, drug delivery systems, cancer imaging, and other therapeutic applications. They have a place in medicine for such applications because of their safety, stability, biocompatibility, bioavailability, as well as high ability to bind with different therapeutic agents (Ahmadi and Arami 2014).

### 7.4.5 Dendrimer

The term “dendrimer” is derived from two Greek words that mean “tree” and “parts”, respectively, and describes their branching form. Dendrimers are nano-metric molecules that are radially symmetrical, globular, monodispersed, and homogeneous (Sohail et al. 2020). Dendrimers have therapeutic potential because of their anti-fungal, antibacterial, and cytotoxic properties. They are helpful as drug and gene delivery vehicles, but studies have shown that some dendrimers have therapeutic potential due to their antifungal, antibacterial, and cytotoxic properties. Since their discovery, the biological utility of dendrimers has rapidly evolved, with over 100 families and thousands of chemical modifications documented. Dendrimers like Frechet-type polyether and Tomalia-type (poly)amidoamine are poly (amidoamine) dendrimers, which are widely used in biomedicine as protein, enzyme, and virus analogues (Tetteh-Quarshie et al. 2021).

### 7.4.6 Solid Lipid Nanoparticles

Solid lipid nanoparticles have a lipophilic centre, making them suitable for cancer treatment (Youssef et al. 2019). The outer hydrophilic shell of various hydrophilic medications or antibodies can be conjugated with them. The outer shell also improves the bio profitability of the drug. Cationic solid lipid nanoparticles can electrostatically link nucleic acid components, allowing quality control. Topical, oral, and subcutaneous injections are all options for administering this type of nanoparticle. They can pass through the blood-brain barrier, allowing them to deliver medications. They can cross the blood-brain border, allowing medicines to reach the central nervous system more efficiently (Elgqvist 2017).

### 7.4.7 Metallic Nanoparticles

Metallic nanoparticles made of gold, silver, manganese, and platinum have a metallic core surrounded by a protective coating. They contain antibodies and radionuclides, which can be chelated. Metallic nanoparticles, particularly bimetallic nanoparticles, have been used for disease therapy, including silver/gold nanoparticles, silver-selenium nanoparticles, and gold-platinum nanoparticles (Youssef et al. 2019).

### 7.4.8 Polymeric Micelles

Polymeric micelles have a hydrophobic core that facilitates the transport of hydrophobic drugs and are highly water soluble. According to their description, they were also made with amphiphilic polymers, like caprolactone or poly(lactic-co-glycolic

acid) (PLGA). Less water-soluble drugs, such as paclitaxel and amphotericin B, are commonly delivered using this method (El-Sayed and Kamel 2020).

### 7.4.9 Polymeric Nano-spheres

Biodegradable or non-biodegradable polymers with less than a micron create uniform circular frameworks. Polymer-based drug-encapsulated nanospheres have been described for effective cancer or antigen-presenting cell (APC) targeting, and this is an exciting area of research because it allows for the controlled release of drugs in a cell- or tissue-specific manner (DeFrates et al. 2018).

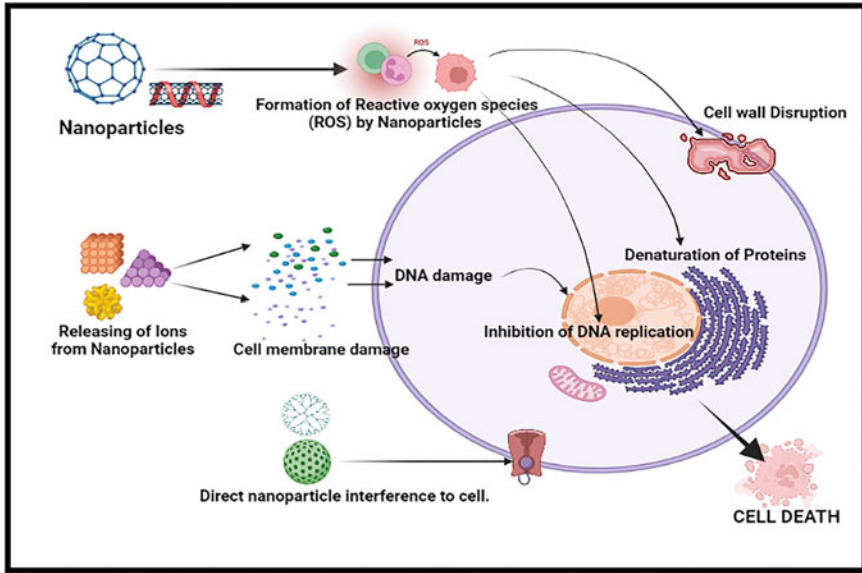
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## 7.5 Mechanism of Action of Nanoparticles Against Microorganisms

Small-sized NPs between 5 and 17 nm exhibit high anti-microbial activities (Slavin et al. 2017). There has been considerable research into various mechanisms for promoting contact between NP and bacteria, such as Van der Waals forces, electrostatic forces, and ligand-receptor and hydrophobic interactions. When NPs contact microbes, they can disrupt metabolic pathways and affect membrane shape and function. Inside a bacterial cell, NPs interact with cellular mechanisms to inhibit enzymes, inactivate proteins, alter gene expression, generate free radicals, and cause electrolyte imbalance (Hamida et al. 2021). The antibacterial activity of NPs is most commonly attributed to reactive oxygen species (ROS). While oxygen enters in its unwanted reduced states, it has more tendency to transform into free radicals, peroxides, and superoxides rather than to get converted into water. As the concentration of nanoparticles increases, free radicals are produced, resulting in ROS increase and cell death (Fig. 7.3) (Canaparo et al. 2021). Superoxide radical, singlet oxygen, hydroxyl radical, and hydrogen peroxide are the four types of ROS produced (Sharma et al. 2019).

Even so, as NPs concentrations rise, the cell prefers oxidation via excessive ROS production (oxidative stress), resulting in cell component damage. As a result, the cell membrane's permeability changes, resulting in cell membrane damage. Some nanoparticles have been biofunctionalized to replace chemicals like mannose, which attract bacteria via mannose receptor sites (Bondarenko et al. 2018). Carbon nanoparticles enter bacterial cells and prevent multiplying and dying, causing cell lysis. The antibacterial activity of carbon nanoparticles may be due to the electrostatic repulsion of Gram-negative microorganisms and carbon surfaces, where microbes bind to carbon particles via solid Van der Waals forces, and Gram-positive bacteria change the positive charge on the carbon surface (Quek et al. 2022). Silver nanoparticles destroy biomacromolecules by deactivating enzymes, changing protein expression, and disrupting the respiratory chain. Nanoparticles can damage or burst bacterial cell membranes by interacting with their hydrophobic chains of various lengths. Because their cationic surfaces interact strongly with bacterial





**Fig. 7.3** General anti-microbial action of nanoparticles

cells, polymeric nanoparticles kill germs when they make contact them (Jiang et al. 2022).

## 7.6 Nanotechnology in Animal Science

### 7.6.1 Nano-medicine

Nano-delivery systems and nano-medicine are emerging nanoscience techniques essential in veterinary medicine. Even though such systems are relatively new, they are swiftly developing where a wide range of nanoscale biological and non-biological materials are used to serve as diagnostic tools or to deliver therapeutic agents to target sites in a regulated manner (Tewabe et al. 2021). Nano-medicine is a branch of medicine that employs nanotechnology to prevent and cure diseases using different nanoscale materials (Josyula et al. 2021). The nanoscale materials used in nano-medicine include biocompatible nanoparticles and nano-robots. Nano-medicine has various applications, like disease diagnosis, drug delivery, and sensory and actuation purposes in organisms (McNamara and Tofail 2015).

Innovative drug delivery systems can deliver therapeutic agents as small sealed packages with high efficacy to the specified target in an animal's body. Microscale and nano-mechanical systems are smart drug deliveries that make use of smaller quantities of antibiotic. These advanced drug delivery systems also possess chemical detection and decision-making capability for self-regulated drug delivery or nutrient

**Table 7.1** Various types of biomaterials used to coat nano-materials

S. No.	Biomaterials	Reference
1.	Erythrocyte cell membranes	Wang et al. (2019)
2.	Neutrophil cell membranes	Zhang et al. (2018)
3.	Natural killer cell membranes	Pitchaimani et al. (2019)
4.	Macrophage cell membranes	Gong et al. (2020)
5.	Platelet cell membranes	Wang et al. (2019)
6.	Extracellular vesicle cell membranes	Kao and Papoutsakis (2019)
7.	Natural proteins	Iqbal et al. (2021)
8.	Viral capsids	Kines et al. (2021)
9.	Aptamers	Huang et al. (2021)

treatment as required. This system has the advantage of minimizing antibiotic use and, ultimately, medication expenses as well. They can also monitor the delivery effects of nutraceuticals, pharmaceuticals, nutrients, bioactive compounds, food supplements, chemicals, probiotics, and vaccines (Tewabe et al. 2021).

Although nanotechnology has provided alternative therapeutic opportunities, there are still challenges that emerge with nanoparticles. While travelling from the injection site to the target site, nanoparticles encounter various physiological and cellular barriers that recognize and eliminate foreign bodies (Chen et al. 2021). Nanoparticles are usually modified with synthetic polymers like polyethylene glycol or poly(lactic-co-glycolic acid) to extend circulation in blood. The surface of targeting ligands is grafted to bind selectively only to the specified target while preventing non-specific interactions with healthy tissues (Zhao et al. 2020). Optimizing synthetic nanoparticles has been implemented for effective targeted delivery with minimum side effects (Ryu et al. 2020). Many efforts have been made towards bioinspired nanotechnology, in which design cues are taken from the organism for effective delivery.

Biomimetic nanoparticles are an emerging class of nanoparticles whose surface is fabricated or integrated with biomaterials or other synthetic materials, able to mimic the biological functions and characteristics of native cells. Because of this property, biomimetic nanoparticles possess enhanced biocompatibility, have a long retention time and high target specificity, and induce minimal immune responses (Chen et al. 2019). Different types of biomaterials are used to embed nanoparticles to enhance their stability and efficacy, which are enlisted in Table 7.1.

## 7.6.2 Diagnosis and Treatment of Disease

Nanotechnology exhibits activity at the same size as that of the pathogen and therefore has an excellent capability for early diagnosis and treatment. Nanotechnology has been described as an effective technique in critical clinical diagnoses. The application of nanotechnology in diagnostic tools is remarkable, owing to enhanced specificity, sensitivity, and functionality (Zhang et al. 2019). Biomarker detection,

**Table 7.2** Various nano-structured materials with application in the health sector

S. No.	Nano-structured material	Application in healthcare	Potential risks	Reference
1.	Carbon nano-tubes	Glucose monitoring	Pulmonary toxicity	Yan et al. (2015)
2.	Graphene	Biosensing, imaging	Graphene-induced toxicity, inflammatory response	Nagraik et al. (2021)
3.	Quantum dots	Optoelectronic application, detection of bio-macromolecules like proteins, enzymes, and neurotransmitters; substitute to fluorophores; cancer diagnosis	Skin penetration	Henna and Pramod (2020)
4.	Chitosan	Used in bioanalytical device biosensors and lab-on-chip devices	Chitosan toxicity	Nagraik et al. (2021)
5.	Dendrimers	Used in various diagnostic sensors, such as those based on fluorescence, electrochemistry, impedimetric, Raman scattering or SPR transfection, drug delivery, and biocatalysis	Haemolytic toxicity, cytotoxicity, and haematological toxicity	Mahmoudpour et al. (2021)

which involves significant waiting times and high costs and requires sophisticated analyzers, needs to be replaced with more economical, faster, and more robust diagnostic tools. Nano-structured materials are promising in the advancement of diagnostics. Nanotechnology combined with proteomics, genomics, and molecular machine systems can help develop reliable, effective, and fast medical diagnostics.

Nanotechnology primarily focuses on improving conventional diagnostic methods by increasing process efficiencies and enhancing the reusability of nano-materials, therefore reducing the overall cost of diagnosis. Biomedical applications, like tissue scaffolds, drug delivery, implantable materials, or nano-devices such as biosensors, have widely used various nano-material structures. Due to its performance and sensitivity, nanotechnology plays a significant role in the development of biosensors. Biosensors that combine mechanical, biological, and physico-chemical properties of transducers have tremendous applications in healthcare and biodefence systems. Nano-structured materials in biosensors play a vital role in disease detection and diagnosis. Some commonly used nano-structured materials (Table 7.2) in biosensors are nanoparticles, carbon nano-tubes, graphene dots, quantum dots, nano-wires, and metallic sheets (Nagraik et al. 2021).

Nanotechnology offers solutions to a number of serious diseases, like tuberculosis, foot and mouth disease, methicillin-resistant *Staphylococcus aureus* (MRSA),

brucellosis, and other infections due to intracellular or blood pathogens (El-Sayed and Kamel 2020), respiratory infectious diseases, melanoma, and other types of cancers. Fluorescent nanoparticles with photophysical characteristics have demonstrated excellent performance in *in vivo* imaging. In addition, nanoparticles have unique optical contrast agents in image-guided tumour surgeries. Nanotheranostics is another remarkable progress in nanotechnology, a medical technique that combines medicine and diagnostics to enhance the effectiveness of currently used medicines (Fawzy et al. 2021).

### 7.6.3 COVID-19 and Nanotechnology: Rejuvenating Diagnostic Regimen

Coronaviruses (CoVs) are a group of enveloped single-stranded ribonucleic acid (RNA) viruses that infect mammals and birds, causing respiratory and gastrointestinal diseases (Li et al. 2020). Alpha coronavirus (prevalent in mammals and pigs as animal hosts), beta coronavirus (prevalent in mammals and bats, mice, and cows as animal hosts), delta coronavirus (dominant in pigs and birds, with pigs as animal hosts), and gamma coronavirus (prevalent in whales and birds, with chicken and turkey as animal hosts) are the four genera of *Coronavirinae* (Krishnan et al. 2021). Before December 2019, which marked the outbreak of COVID-19, four beta coronavirus strains caused severe human diseases: HKU1, MERS-CoV, OC43, and SARS-CoV. Once again, the spillover came from the beta coronavirus strain COVID-19 in Wuhan, Hubei, Central China (Zhou et al. 2020).

At present, Omicron has accumulated over 30 mutations on its spike protein, resulting in its immune evasiveness. Omicron cannot utilize TMPRSS2-expressing cells, primarily found in the lower respiratory, explaining its alleged mildness. The matter of concern is, what if, under selection pressure, it overcomes its inability to infect TMPRSS2-expressing cells, as it has done for human angiotensin-converting enzyme-2 (ACE2)? A catastrophe like this will be beyond the capabilities of any nation. Therefore, we must review and analyze all the advanced technologies that can make a breakthrough in this area of research, and nanotechnology stands out as a promising option.

Nanotechnology has aided in developing a new generation of vaccines that are critical for the global control of the COVID-19 epidemic and the return to normalcy. Nanotechnology investments have benefited vaccine development, research, and innovation. Vaccine development has primarily taken place in countries in the northern hemisphere. South Africa, as an important emerging country, has made significant investments in nanotechnology and bioinformatics and the skills and resources needed to develop and manufacture vaccines (Dube et al. 2021). Bioinformatics tools have also aided in developing quick and cost-effective vaccines and provided recommendations for future research and development. Using an opto-electro-magnetic nano, scientists used a biosensing technique to identify the SARS-CoV-2 virus during the current COVID-19 pandemic. Viruses can be detected by using electrical, optical, or magnetic biosensors based on gene sensing and immune

sensing. Paliwal et al. (2020), in their study, selectively detected the SARS-CoV-2 virus at a shallow level by using biosensors.

These efficient biosensors can be controlled with a smartphone and marketed for clinical use in COVID-19 infection diagnosis at an early stage. Furthermore, the successful integration of these SARS-CoV-2 viral sensors with artificial intelligence (AI) and the Internet of Medical Things (IoMT), effectively helped in virus detection at the point of care while also sharing bioinformatics with the medical centre for quick therapeutic decisions. This method can also manage COVID-19 infection based on patient infection profiles and keep track of chores. In addition, researchers developed stimuli-responsive nanotechnology to trap and eliminate viruses when stimulated externally to prevent human-to-human transmission of the SARS-CoV-2 virus (Kaushik 2021).

Nanotechnology, for example, could enable photo-sensitive viral destruction. Several types of clothing containing nanoparticles have been successfully used to demonstrate SARS-CoV-2 virus entrapment and eradication. The increased production and distribution of these masks for general use, on the other hand, will necessitate a significant amount of effort. One of the documented advancements in this field is microneedle-based vaccine administration to treat COVID-19 infection. Early results are encouraging, but there is still much work to be done regarding animal-model-based experiments and Food and Drug Administration (FDA) approval, both of which are required before clinical implications can be suggested (Kaushik et al. 2020).

#### **7.6.4 Nanotechnology-Based Therapeutic Agents Against Animal Coronaviruses**

Nanotechnology is crucial in combating emerging diseases, including coronaviruses like SARS-CoV-2. The similarity in the molecular sizes of nanoparticles and coronavirus enables better interactions and the potential for future applications (Medhi et al. 2020). Further biomedical properties of nanoparticles favour the development of therapeutic formulations that can have higher efficacy against viruses. Nanoparticles also have antiviral properties. Improved drug pharmacokinetic properties by applying nanoparticles with antiviral drugs have further made nanotherapeutics beneficial and effective (Chakravarty and Vora 2021). Both metallic nanoparticles and lipid-based nanoparticles have been explored against antiviral applications (Sharmin et al. 2021). Antiviral drugs such as zidovudine, maraviroc, ritonavir, and a few other pharmaceuticals are developed using multiple types of lipids for optimal cellular absorption and targeted drug delivery. Nano-formulations, which use multifunctional nanoparticles to optimize gene transport, protect cargo from nuclease degradation, and improve the targeting mechanism, are also used in non-viral gene therapy (Lin et al. 2018).

Nano-formulations outperform traditional antiviral drugs by preventing virus replication in mammals in multiple ways. First, nanoparticles can directly inactivate viruses by interacting with virus surface proteins or the viral genome, preventing

replication. Gold, silver, and copper nanoparticles act as antiviral agents by preventing viral entry into host cells. These nanoparticles prevent viral replication by adhering to viruses and rendering them inactive, as well as interfering with virus-host cell interactions. Finally, virucidal zinc (Zn) nanoparticles interfere with viral DNA polymerase and block virus growth inside host cells (Jampilek and Králová 2019).

Nano-structured materials are used to make adjuvant-based nano-vaccines for animals to protect them from infections caused by the animal coronavirus. In recent years, there has been much interest in incorporating virus entities into the production of nano-vaccines with adjuvants. Due to improved antigen-processing pathways, nano-vaccines provide benefits such as a controlled immune response and activated B-cell immunity (Singh 2021). However, conventional vaccinations have drawbacks, such as low immunogenicity and insufficient protection. Furthermore, following the recent coronavirus disease-19 (COVID-19) pandemic, which may have started in bats (primary reservoir) and was caused by the lethal coronavirus SARS-CoV-2, it is critical to use nanotechnology to prevent viral infections from spreading to other species.

### **7.6.5 Anti-microbial Resistance**

The emergence of anti-microbial resistance is a serious concern that has drawn attention worldwide. The issue can be aggravated by the irrational use of anti-microbial drugs, insufficient surveillance, and the inadequately controlled regulation of antibiotic use in the medication and livestock industry. Furthermore, because of the emergence of multidrug-resistant microorganisms and the scarcity of new antibiotics, there is a dire need for new anti-infectious strategies. Some of the new strategies and their action are summarized in Table 7.3.

### **7.6.6 Nano-vaccines**

Vaccines comprise adjuvants and antigens, which trigger the defense mechanism or long-lasting protective antibody response. Live and dead organisms were used in the production of vaccines earlier. Later, the production of safe synthetic and recombinant vaccines came into vogue. These new vaccines are highly sensitive to degradation and require optimized adjuvant with good stability to augmented immunogenicity. The regulation of conventional adjuvants is complex, but advanced antigen-delivery strategies are being developed with the evolution of nanotechnology.

The immunity of vaccines is increased with nanoparticle adjuvants by imitating molecular models relating to pathogens, regulating co-stimulatory molecules on cells with antigens, maintenance of the immune system, and long-time delivery of antigens. Nanoparticles can produce virus-like particles with morphological similarity to virus capsids and can stimulate immune responses that do not cause infection

**Table 7.3** Nanotechnology strategies against anti-microbial resistance

No.	Strategy	Action	Reference
1.	Use of silver nanoparticles	Antibacterial effect against pathogenic species of Gram-positive bacteria ( <i>Bacillus licheniformis</i> , <i>Bacillus cereus</i> ) and Gram-negative bacteria ( <i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i> )	Basera et al. (2019)
		Inhibitory action against <i>Acidovorax oryzae</i> strain RS-2	Masum et al. (2019)
		Post-surgical treatment for <i>Corynebacterium pseudotuberculosis</i> infection	Santos et al. (2019)
2.	Phyto-fabrication of selenium nanoparticles	Anti-microbial, antioxidant, and biocompatibility	Gunti et al. (2019)
3.	Bio-fabrication of zinc oxide nanoparticles	Limiting the growth and mycotoxins of <i>Fusarium graminearum</i>	Lakshmeesha et al. (2019)
4.	Bio-mimetization of hydroxyapatite with <i>Azadirachta indica</i>	Therapeutic anti-inflammatory and antibacterial action	Nagaraj and Samiappan (2019)
5.	Nano-composites of nano-crystals doped with silver and silver oxide nano-crystals	Inhibition of biofilms formation	Fonseca et al. (2019)
6.	Magnetic nano-conjugated teicoplanin	Targeting of the bacterial infection site	Armenia et al. (2018)
7.	Vancomycin-loaded nanoparticles	Enhance antibacterial efficacy and sporicidal for <i>Clostridium difficile</i> infection	Chen et al. (2019)
8.	Pullulan nanoparticles	Enhance the antibacterial properties of <i>Lactobacillus plantarum</i>	Hong et al. (2019)
9.	Anti-microbial peptides and bacteriophages nano-encapsulated in liposomes	Prolonged delivery	Zambom et al. (2019)

(Ravi et al. 2021). In recent years, nanotechnology research has received massive attention for the potential to replace conventional viral vector vaccines (Fawzy et al. 2021). Various nanoparticles are used as adjuvants in nano-vaccines against live-stock viral diseases (Table 7.4).

### 7.6.7 Feed Technology

Engineered nanoparticles could help facilitate dietary supplementation to weaned animals and boost growth rates by increasing the bioavailability and efficacy of nutrient cargoes (Hill and Li 2017). However, while developing a carrier nanoparticle for the oral administration of nutrients, certain things need to be considered. For

**Table 7.4** Nanoparticle adjuvants effective against various viruses

S. No.	Virus	Potential adjuvant	Action	Reference
1.	Foot and mouth disease virus	Gold nanoparticles	Improved macrophage activation	Teng et al. (2021)
2.	Rift Valley fever virus	Silver nanoparticles	Reduction in virus infectivity	Borrego et al. (2016)
3.	Infectious bovine rhinotracheitis virus	Silver nanoparticles	Inhibited virus infection	El-Mohamady et al. (2018)
4.	Peste des petits ruminants virus	Silver nanoparticles	Inhibited virus entry	Khandelwal et al. (2014)
5.	Avian influenza virus	Silver nanoparticles	Increased protective level of antibodies	Yu et al. (2013)
		Polyanhydride nanoparticles	Prolonged release of encapsulated antigens	Kingstad-Bakke et al. (2019)
6.	Newcastle disease virus	Polyrhodanine nanoparticles	In ovo anti-Newcastle disease activity	Nazaktabar et al. (2017)
		Microalgae-mediated silver nanoparticles	In vivo anti-Newcastle disease activity	Khalid et al. (2017)
7.	Infectious bursal disease virus	PLGA nanoparticle	Increased cellular and humoral immune responses	Al-Rubaei et al. (2019)
		Silver nanoparticle-anchored graphene-oxide sheets	Antiviral activity against non-enveloped IBD virus	Chen et al. (2016)

example, it includes the challenges of resisting the action of enzymes and the pH of the gastrointestinal tract of animals.

Nanoparticles must be capable of surmounting these obstacles to supply their nutritional elements at the specified location (Ban et al. 2015). Nanoparticles developed from canola protein cruciferin are able to encapsulate both hydrophilic and hydrophobic bioactive elements, protect them from degradation in the stomach, and release them in the intestinal lumen to get absorbed and function as if they originated from the feed. Being small sized, nanoparticles gain an increased level of bioavailability in comparison to microparticles, especially in the digestive tract, as nanoparticles can pass readily through the intestinal mucosa (Akbari and Wu 2016).

Copper nanoparticles pass through intestinal mucosa more quickly than microforms, helping better absorption (Gonzales-Eguia et al. 2009). The quality and stability of livestock feed and water can be improved by the addition of nanomaterials. In a study conducted by Zha et al. (2009) on broilers, it was demonstrated that the addition of chromium nanoparticles to poultry feed increases the average daily gain, feed efficiency, thigh, and breast muscle protein content but lowers cholesterol levels. However, a comprehensive study of nanoparticle activity must be carried out to test the potency and any undesirable biological consequences.



### 7.6.8 Animal Breeding and Reproduction

Timely oestrus detection in dairy animals is one of the biggest challenges in dairy farming. Nano-tubes provide an effective solution for tracking oestrus in animals through real-time measurement of estradiol level changes in the blood. In addition, nano-tubes can be used to detect the oestrus period by binding to estradiol antibodies during oestrus through near-infrared fluorescence (Mekonnen 2021). Artificial insemination techniques can be advanced by incorporating nano-techniques such as nano-purification, non-invasive bioimaging of gametes, and protectants in cryo-preservation (Hill and Li 2017).

Quantum dots can help provide a better understanding of oocyte movement, mammalian spermatozoon, and their physiological interaction. These nanoparticles are of great interest to theriogenologists because of being biocompatible and photostable and due to their ability to produce more signal intensity compared to other organic fluorescent molecules, which have been used previously for imaging gametes and other types of cells *in vivo*. These engineered nanoparticles help visualize cellular and molecular events during fertilization, like fluorescent proteins, but at greater tissue depths (Feugang et al. 2015). The nano-purification of semen is a technique that can separate damaged sperms from healthy ones. One such technique is coating magnetic nanoparticles with antibodies against ubiquitin (a surface marker of defective spermatozoa) for a protein-based removal strategy. Another lectin-based strategy coats magnetic nanoparticles with lectins, which bind glycans exposed at the sperm surface. In a study (Odhiambo et al. 2014) on the nano-purification of bull spermatozoa, nano-purified spermatozoa achieved equal conception rates as un-purified ones. Therefore, it was concluded that more females could get inseminated from one nano-purified diluted ejaculate sample. The cryo-preservation of sperm can be enhanced by the addition of nano-protectant additives in extenders. Anti-microbial nanoparticles may also replace extender antibiotics since some antibiotics inhibit sperm motility and viability. Nanoparticles may also be used to incorporate other natural products in semen extenders to modify the properties of semen, such as to increase sperm motility (Bryła and Trzcińska 2015).

The integration of nanoparticles in molecular biology procedures may lead to further advancement in reproductive biotechnology. One such technique is the mediation of gene transfer through sperm, in which mesoporous silica nanoparticles are loaded with deoxyribonucleic acid (DNA) molecules and proteins of interest and delivered to oocytes at fertilization (Barkalina et al. 2014). Transfections with polymeric nanoparticles, like chitosan, poly(2-(dimethylamino)ethyl methacrylate (PDMAEMA), and polyethyleneimine, are reported to have more advantages over conventional viral approaches if polymers are used in low concentrations. The molecular weight of nano-polymers influences transfection efficacy and toxicity. Nanoparticles can also play a vital role in animal reproduction. However, some nanoparticles are spermatotoxic, which can have serious consequences. For example, in a study, it was reported that zinc oxide (ZnO) and titanium oxide nanoparticles reduce *in vitro* sperm viability (Poddar and Kishore 2022).

### 7.6.9 Food and Feed Safety

The meat and food industries are currently utilizing nano-material applications, such as using them as carriers for food ingredients or additives, which are added to food directly, or as a component of food packaging. Additionally, this can enhance flavour; decrease the use of fat, salt, sugar, and preservatives; and improve the ability of fat-soluble additives to disperse in food products. This can prevent hypertension and cardiovascular disease in both humans and animals. Zn NPs were once only used as a feed additive, but today, there are many uses for metal nano-materials in veterinary medicine (Rahman et al. 2022). Nevertheless, they are poisonous to microorganisms and are employed as anti-microbial agents, and their addition to cow feeds led to a marked increase in milk production. Additionally, they can be utilized in catalysis, sensors, environmental remediation, and human and animal personal care products (Reda et al. 2021).

Nutritive substances can resist protease enzymes and other desaturating agents, thanks to nano-carriers. Additionally, it might be improving its capacity to cross the intestinal membrane into blood. Additionally, nano-carriers improved the dispersion of nutrients in aqueous systems and controlled the release of nutrients in water-insoluble food ingredients (Xia et al. 2022). Nano-materials can create new tools for the rapid detection of food-borne pathogens, such as gold and iron oxide nanoparticles and nano-materials loaded with anti-*S. aureus* antibodies (Sheikhzadeh et al. 2021). The science of biomedicine, food systems, food system security, and disease treatment delivery could all benefit from the use of nanotechnology. Today, a wide range of nano-materials and nano-sensors are used as food safety additives and have significant value in all fields of animal science. Nanotechnology will soon make it possible to produce “interactive” poultry meat that alters its colour, flavour, or nutrients (Akter et al. 2022).

## 7.7 Toxicity Risk of Nanoparticles

The primary justification for restricting the use of biosensors in human and animal science is their toxicity risk to animals and the environment, despite the advancement and value of these tools in animal science (Hassan et al. 2020). Several aspects of biomedicine use nanotechnology, but there are also potential toxicity risks for the environment and users. Affected tissue fibres or secondary mutations cause oxidative stress and inflammation. Nanoparticle size, the health of humans and animals, administered doses, and exposure time all generally affect the toxicity of nano-materials. Additionally, the particle size and shape, crystalline form, functionalization, and purity of nanoparticles must be taken into account for an effective assessment of their risk of toxicity (Abedin et al. 2021). When sperm is exposed to certain nanoparticles in excess or for an extended period of time, such as zinc oxide and titanium oxide, it loses viability in vitro. Sperm cells that were incubated with concentrations of 100–500 g/mL of Zn NPs died within a short period of time. When buffalo sperm was incubated with 100 g/mL of titanium oxide

nanoparticles, Pawar and Kaul (2014) found that the viability of the sperm was decreased. According to a number of studies, metal nanoparticles can easily enter the skin, lungs, and brain, where they can have a negative impact on biological processes.

Before using Zn NPs as feed additives, it is important to understand their short-term environmental and animal toxicity. Therefore, it is necessary to measure the effective nontoxic doses of metal nanoparticles in laboratory animal models to determine whether their field application is appropriate. There have not been any toxicological effects of nanoparticles on health to date (El-Fatah et al. 2017). To fully understand the toxicological aspects of nano-materials, more ongoing research is therefore necessary.

Ingestion is the primary method of exposure for both humans and animals when it comes to nano-materials. The liver and spleen quickly eliminate the nano-materials after ingestion, after which they enter the gastrointestinal tract and reach the intestines. The ingestion is primarily caused by the presence of nanoparticles in food as a result of direct contact between food and nano-packaging (Baltić et al. 2013). The circulatory system distributes the nanoparticles to the liver and spleen (Baltić et al. 2013). Other routes of nanoparticle toxicity include inhalation and skin contact, which are mostly found in laboratories and industrial workers in factories that produce nano-materials. According to a different study, magnesium oxide nanoparticles can enter the central nervous system and nerve cells through skin contact and inhalation.

In other studies, the Zn NPs detected the presence of skin tissue that had been penetrated, and they have cancer-causing effects, like asbestos-caused lung fibrosis. The possibility of lung cancer development also exists when high doses of nano-TiO<sub>2</sub> are inhaled (Aschberger and Christensen 2011). Additionally, just as with the inhalation of ambient ultrafine particles, the entry of nanoparticles via the bloodstream may have negative effects on the cardiovascular system, blood vessel function, and blood clot formation. Similar microvascular dysfunction was seen in rats exposed to low concentrations of nano-sized titanium dioxide, as well as platelet aggregation and vascular thrombosis following exposure to single-walled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes MWCNTs (Kan et al. 2018). According to some studies, nano-materials can enter the bloodstream, where they are distributed throughout body organ cell tissues and occasionally pass from the mother to the foetus through the blood supply (Baltić et al. 2013). More advanced nano-biomedical research and accessibility are required in the near future to enhance animal health. Many issues with animal disease diagnosis, animal production, reproduction, and good hygienic practices when raising and maintaining food animals could be resolved. Regarding livestock, the potential uses of the technology are almost unbelievable. However, there is still a lot of research that must be done before nanotechnology applications are used in veterinary and animal sciences, especially regarding toxicity risks.

## 7.8 Challenges and Strategies

Nano-materials with potential health benefits are used as feed additives in animal nutrition, but research on its validity is limited to livestock species. Extensive investigation is needed to arrive at a safe dosage for nano-feed additives because of the delicate balance between safe and toxic levels. The interaction of nanoparticles with various biological components due to large surface free energy should be well reviewed by conducting a meta-analysis to arrive at final dosages. Swain et al. (2016) reported that the actual bioavailability of a few mineral-based nanoparticles, such as ZnO nanoparticles, is still to be specified accurately. Reduced particle size with increased surface area in nano-forms makes them more toxic than their macro counterparts. Several approaches have been tried to minimize toxicity concerns of nano-materials without a change in intrinsic properties, like encapsulating inorganic nanoparticles with organic molecules like lipids, polymers, and biomolecules and coating them with silica (Yan et al. 2019). Using these surface-decorated approaches, the biocompatibility and utility of a wide range of nano-materials have been improved for several biomedical applications. Among different available mineral nanoparticles, only limited nanoparticles, like ZnO NPs, selenium (Se) NPs, and copper oxide (CuO) NPs, are studied in the context of nutritional aspects in livestock. Reports on other nano-materials as feed supplements are yet to be explored (Bhagat and Singh 2022). So there is a need for the product to provide multiple nano-minerals mainly chelated with organic elements for improved absorption and bioavailability of encapsulated minerals.

The present quantification techniques of nanoparticles in animal systems, like inductively coupled plasma mass spectroscopy (ICP-MS), atomic absorbance spectroscopy (AAS), inductively coupled plasma optical emission spectroscopy (ICP-OES), electron microscopy, histology, fluorescence microscopy, liquid scintillation counting, in vivo optical imaging, computed tomography (CT) scan, magnetic resonance imaging (MRI), positron emission tomography (PET), and single-photon emission computed tomography (SPECT) (Sarparanta and Airaksinen 2021), are limited only to small animals, such as lab animals, pigs, small ruminants, chicken, etc.

Many regulatory bodies, such as the European Union's Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH); the United States Environmental Protection Agency; FDA's Environmental Protection Agency (EPA); the International Organization for Standardization; the Occupational Health and Safety Administration (OSHA); the Organisation for Economic Cooperation and Development; the European Food Safety Authority (EFSA); India's Food Safety and Standards Authority (FSSAI); Food Standards Australia New Zealand (FSANZ); Japan's Ministry of Education, Culture, Sports, Science, and Technology (MEXT); Ministry of Economic, Trade, and Industries (METI); Ministry of Health, Labor, and Welfare (MHLW); and Ministry of the Environment (MOE); China's National Center for Nanoscience and Technology (NCNST), etc., have issued certain guidelines on the potential risks posed by nano-feed additives in food animals. Even at minimal dosages, metal-based nanoparticles are known to accumulate in

body tissues. The chronic ingestion of silver compounds may accumulate in the eyes, skin, and other vital organs, such as the liver (Burduşel et al. 2018). Hence, the length of the feeding period is also an essential factor to be considered before promoting any nanotechnology-based feed additive. The anti-microbial effects of nanoparticles on beneficial bacteria are uncertain and have to be tested before employing them as feed additives. Researchers have been developing nano-packaging technologies in the food industry. However, Priyadarshi et al. (2021) raised a negative concern over the usage of nano-composites for food-packaging applications. They reported that nanoparticles would migrate into the food from the outer packaging, consequently resulting in unintentional consumer exposure to lipid peroxidation and DNA damage. These concerns led to a low public acceptance of nanotechnology-based products among consumers. Efforts need to be put in by manufacturers and food safety authorities to improve the acceptance of food nanotechnology by the public. Other bigger challenges related to nanotechnologies are environmental risks due to the release of nanoparticles into the environment.

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## 7.9 Future Prospectus

The range of applications for nanotechnology in the animal production sector will grow as it advances and attracts more attention. It is likely possible in the near future to regularly add nano-supplements to livestock feed to improve it; however, it will take more time before nanoparticles completely replace antibiotics in feed because many biocidal candidates still need to be tested *in vivo* before going through clinical trials and food safety tests in accordance with government regulations. Nanoparticles have already been used outside of animal products, such as in antiseptic wound dressings, and more will come. It is crucial to look into nanoparticle cytotoxicity in both cancer cell lines and normal, healthy cell lines for studies interested in nanoparticles with anti-cancer properties.

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## 7.10 Conclusion

This chapter highlights the numerous applications of nanoparticles in animal science and production as well as their future potential in other application areas. Nanoparticles are already on the market, and their properties will be fine-tuned for a wider range of applications with additional research and development. The use of nanotechnology in veterinary science and animal husbandry is still in its infancy, but encouraging results from nutrition, medicine, diagnostic tool, and reproductive studies are driving further investigation.

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