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REVIEW

Nanoparticles as a novel and promising antiviral platform in veterinary medicine

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Abstract

Traditional veterinary virus vaccines, such as inactivated and live-attenuated vaccines, have achieved tremendous success in controlling many viral diseases of livestock and chickens worldwide. However, many recent viral outbreaks caused by different emerging and re-emerging viruses continue to be reported annually worldwide. It is therefore necessary to develop new control regimens. Nanoparticle research has received considerable attention in the last two decades as a promising platform with significant success in veterinary medicine, replacing traditional viral vector vaccines. However, the field of nanoparticle applications is still in its initial phase of growth. Here, we discuss various preparation methods, characteristics, physical properties, antiviral effects, and pharmacokinetics of well-developed nanoparticles and the potential of nanoparticles or nano-vaccines as a promising antiviral platform for veterinary medicine.

Introduction

Nanotechnology is a rapidly growing field that dates back to 1974 and has led to the development of many novel nanoparticles with average diameters ranging from 1 to 100 nanometers (nm) [77, 79]. The prefix nano is derived from the Latin word “nanus” which means "very small", as 1 nm corresponds to 10^{-9} meter (m) [77]. Currently, nanotechnology is being applied in different fields, including agriculture, infection control [80], and biomedicine [10, 69]. Nanoparticles have several physical and biological characteristics, such as a large surface area, improved reactive properties, an enormous size-to-volume ratio, durability, bioactivity, bioavailability, regulated particle length, managed pharmaceutical release, site-specific targeting, and regulated delivery of medications [49]. Moreover, nanoparticles can penetrate cells, tissues, and organs, making them effective drug delivery tools [18]. Different medicinal products can also be attached to the surface of nanoparticles [57, 69]. In order to overcome difficult problems, traditional treatments may not be sufficient, and novel approaches need to be considered, which can inform future findings and criteria for existing problems [88]. The economies of many countries rely on animal-based industries, and with the emergence of many viral diseases, novel disease control and prevention regimens are urgently needed [67]. Nanotechnology has shown incredible potential for enhancing the delivery of medicines and vaccines in the field of veterinary medicine [10]. The increasing growth of the nanoparticle field will lead to the development of new therapeutics to cure viral or bacterial infections, as well as to enhance the healing of deep wounds. In addition, these newly developed nanoparticles could successfully transfer medicines to different cells to treat diseases [15, 50]. Another amazing development in nanotechnology is nano-theranostics, a medical technique that integrates medicines and diagnostics with the aim of improving the effectiveness of currently used medicines. Furthermore, this integration provides a great opportunity to improve and design these agents, which enable therapeutic

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delivery as well as a method of detection before and during the treatment process [47, 66]. One of the most encouraging and positive sectors of nanotechnology is nanopharmaceutical products, which have several advantages in veterinary medicine [59, 100].

Additionally, nanomaterials have been used as antiviral agents in many studies, with about 27% of total publications relating to nanoparticle applications in medical and health sciences, according to the dimensions database http://www.dimensions.ai/. Due to the importance of nanoparticles, this review aims to address the topic of antiviral nanoparticles as novel and promising treatments in veterinary medicine.

Classification of nanoparticles

Nanoparticles are classified into one-dimensional nanoparticles, two-dimensional nanoparticles, and three-dimensional nanoparticles [27, 77]. The differences between these types are summarized in Table 1.

One-dimensional nanoparticles (1D-nanoparticles) are thin-film manufactured surfaces with sizes ranging from 1–100 nanometers (nm). They are commonly used in various technological applications such as solar cells, biological and chemical sensors, magneto-optic and optical information storage systems, and fiber optic systems [55].

Carbon nanotubes are an example of two-dimensional nanoparticles (2D-nanoparticles) that fold into a cylindrical shape. They have different properties, such as strength, hardness, and electrical conductivity [55]. They are made of either organic material, such as carbon, or inorganic material, such as metal oxide. However, metal oxide tubes are heavier and weaker than carbon tubes [2].

Three-dimensional nanoparticles (3D-nanoparticles), such as dendrimers, quantum dots (QDs), and fullerenes, are three-dimensional and semi-conductive colloidal nanomaterials. They have a core and shell with diameters ranging from 2 to 10 nm. The physical and chemical properties of QDs depend mainly on their size. Moreover, QDs provide sufficient space for delivery of therapeutic agents in a variety of applications, such as simultaneous drug delivery and *in vivo* imaging and tissue engineering. Dendrimers are branched molecules that got their name from the Greek word "dendron", which means "tree" [77]. Dendrimers are used to deliver drugs and have average diameters ranging from 10 to100 nm, with multiple surface functional groups. They have various reactive groups (nanostructures) suitable for the conjugation of organic structures to their surface, such as DNA. They are regarded as essential tools for the large-format synthesis of inorganic and organic nanostructures with dimensions of 1-100 nm [77]. Dendrimers are used in the pharmaceutical industry to produce high-performance drug discovery products, such as non-steroidal anti-inflammatory formulas, antivirals, and antimicrobial medications [65]. However, dendrimers may damage cellular membranes due to their positively charged surface [63]. Fullerenes are carbon-based molecules made entirely of carbon atoms. They form a hollow ball that is sometimes called a "buckyball". Fullerenes are prepared by heating graphite in helium until evaporation. The atoms are finally arranged in an icosahedral shape similar to that of the football [52]. They may also be combined with a variety of medically useful products [9].

Characterization of nanoparticles

Characterization of nanoparticles depends on measuring parameters such as morphology, particle size, surface hydrophobicity, and surface charge. Advanced techniques, such as transmission electron microscopy (TEM), atomic force microscopy (AFM), and scanning electron microscopy (SEM), can be used for measurement of particle size, morphology, and particle size distribution, respectively. The common nanoparticle characterization methods are summarized and listed in Table 2. The surface charge of nanoparticles has a significant impact on the physical stability and efficiency of the polymer. Therefore, the zeta potential technique is widely used as a tool for indirect measurement of a nanoparticle's surface charge. It also can be used to evaluate the surface hydrophobicity and the nature of materials encapsulated inside nanocapsules or coated onto their surface [74]. On the other hand, several techniques have been used in the last decade to measure the surface hydrophobicity of nanoparticles, including hydrophobic interaction

Table 1 Classification of nanomaterials according to dimensions

Classification	Examples	Dimensions
0D nanomaterials	Spheres or clusters, which are considered point-like particles	All dimensions at the nanoscale
1D nanomaterials	Nanofibers, wires, rods	Two dimensions at the nanoscale One dimension at the macroscale
2D nanomaterials	Films, plates, multilayers, or networks	One dimension at the nanoscale Two dimensions at the macroscale
3D nanomaterials	Nanophase materials consisting of equiaxed nanometer-sized grains	No dimensions at the nanoscale All dimensions at the macroscale

Table 2 Examples of common characterization methods for nanoparticles

Nanoparticle	Method	Objective	Reference
Emeraldine base of polyaniline nanosensor	Fourier transform infrared spectroscopy (FTIR)	Data confirm the formation of the EB-PANI	(Omara et al.[76])
	TEM and SEM	Revealed the size and shape of the nanoscale EB-PANI	
	X-ray diffraction (XRD)	Showed that the obtained Nano EB-PANI has a partial crystalline nature	
Iron nanoparticles	X-ray diffraction (XRD)	Analysis indicates that magnetite (Fe3O4) is the most predominant phase	(Arenas-Alatorre et al.[6]; DEMİREZEN et al. [20]; VG and Prem, 2018)
	Scherrer's equation	Average particle size calculation	
	Electron microscopy techniques (SEM, TEM)	Regular shapes were identified	
Multi-walled carbon nanotubes/chitosan nanocomposite	Scanning electron microscopy (SEM),	Characterization of morphological properties	(Abbas et al. [1]; Salam et al. [90]; Sattler [91])
	Fourier transform infrared spectroscopy (FT-IR).	Data confirm the formation of the composite	
	Thermal gravimetric analysis (TGA).	To estimate the homogeneity of the MWC-NTs/CS nanocomposite and its thermal stability	
	Brunauer–Emmett–Teller (BET) equation	Calculated the specific surface area	
Synthesized carbon nanomaterials (CNMs)	Powder wettability instrument (GBX)	Surface hydrophobicity of CNMs	(Ruparelia et al. [87])
	X-ray diffraction (XRD)	Crystallinity and purity of CNMs	
	Scanning electron microscopy (SEM)	Surface morphology	
Molecularly imprinted polymer (MIP) particles loaded with Ag nanoparticles (AgNPs)	Fourier transform infrared spectroscopy (FTIR)	Data confirm the formation of the composite	(Hu et al. [53])
	X-ray diffraction (XRD)	Crystallinity and purity	
	Ultraviolet-visible (UV-vis) spectroscopy	The strongest adsorption peak at 408nm shows the surface plasmon resonance of silver nanoparticles	
Chitosan, chitosan nanoparticles, and copper-loaded nanoparticles	Atomic force microscopy (AFM)	Visualization of both the chitosan nanoparticles and copper-loaded nanoparticles	(Qi et al. [81])
	FTIR analysis	Data confirm formation of chitosan nanoparticles and copper-loaded nanoparticles	
	XRD pattern	Crystallinity and purity	
	Zetasizer	Particle size distribution and the zeta potential	

chromatography. Modern techniques such as X-ray photon correlation spectroscopy allow the identification of specific chemical groups on the surface of nanoparticles, as well as the determination of the hydrophobicity of nanoparticles [101].

In addition, several techniques have been used to determine drug loading and drug release, such as high-performance liquid chromatography (HPLC) or ultraviolet (UV) spectroscopy. The HPLC method is used to measure the loading capacity of the nanoparticle conjugated drug, which can be expressed as moles of drug per mg of polymer, mg of drug per mg of polymer, or as a percentage relative to the polymer [25, 48, 77].

Preparation of nanoparticles

Preparation of nanoparticles is usually based on the chemical and physical characteristics of the drug and the polymer. Nanoparticles can be made from a variety of materials, including synthetic polymers, polysaccharides, and proteins. However, several factors should be considered during the selection of polymers to be used for drug delivery, such as toxicity, nanoparticle size, antigenicity of the final product, surface charge, hydrophobicity, biocompatibility, and biodegradability [5, 83]. As discussed below, nanoparticles are usually prepared by emulsion, ionic gelation, and polymerization methods.

Emulsion method

The dispersion of a synthetic polymer with the drug under investigation is the basis of this process [17]. The size of the nanoparticles is affected by the polymer concentration, the type and concentration of stabilizers, and the stirring speed during the preparation process [93]. This method can be used for preparing lipophilic drugs with the flexibility to be combined with different modification methods to prepare them. This method can be modified to alter the properties of the nanoparticles or to create suitable conditions for hydrophilic drugs [4]. These different modification methods can include spontaneous emulsification to form an oil-in-water-in-oil emulsion [35] or double emulsion combined with evaporation methods [58]. Another method, known as salting-out, involves dissolving the drug and the polymer in an aqueous miscible solvent. This procedure can be carried out at room temperature and is particularly useful for the preparation of heat-sensitive materials.

Ionic gelation or coacervation method

This method is based on the preparation of nanoparticles by mixing oppositely charged particles [99]. It is also suitable for hydrophilic polymer-based nanoparticle preparation. Moreover, strong electrostatic interactions between the two aqueous phases contribute to creating coacervates using this method [72].

Polymerization method

In this method, nanoparticle molecules are generated chemically in the presence of an aqueous medium. The candidate drug is then added to the polymerization medium or adsorbed onto the nanoparticles after completion of the polymerization process. The polymerization process uses various stabilizers and surfactants, which are usually removed in an ultracentrifugation step, followed by resuspension of particles in a surfactant-free medium. The desired nanocapsule sizes can be achieved by optimizing the surfactant concentration and stabilizers [33, 96].

Nano-vaccines and antiviral nanoparticles in veterinary medicine

Efficacy of nanoparticles against livestock viruses

Foot-and-mouth disease virus (FMDV)

Foot-and-mouth disease (FMD) is a highly contagious viral disease caused by foot-and-mouth disease virus (FMDV), a positive-sense RNA virus that belongs to the family *Picornaviridae*. FMDV causes illness in cows, sheep, goats, pigs, deer, and other animals with divided hooves [11, 24, 43, 68, 70]. Inactivated FMDV vaccines have been shown to be part of the best practices for prevention and control since the 1990s. However, a possible escape of the virus from manufacturing facilities could cause unanticipated spread of the disease [86].

Many studies have shown that gold nanoparticles can be an excellent adjuvant when conjugated with current FMDV vaccines because they can stimulate both the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) signaling pathway and the production of cytokines and specific cytotoxic T cells [98]. According to a recent study, the combination of synthetic gold-star nanoparticles (AuSNs) with FMDV-like particles (VLPs) resulted in the formation of a VLP-AuSNs complex that was not toxic in various cell lines tested. Moreover, a detailed mechanistic analysis showed that AuSNs can effectively promote the entry of FMDV VLPs into cells and improve macrophage activation when compared to FMD VLPs alone [98]. Furthermore, the protection rate in an AuSN-adjuvanted group was found to be significantly higher post-virus-challenge than that in a group adjuvanted with traditional mineral oil (ISA206). This is very promising, as we may in the future

be able to use lower doses of nanovaccines against FMDV, thus lowering production costs and facilitating rapid and broad distribution to different countries.

Another group reported that injection of gold nanoparticles conjugated to a synthetic peptide VP1 corresponding to the capsid protein of FMDV with complete Freund's adjuvant resulted in maximum production of antibodies in guinea pigs, increased gamma interferon (IFN-γ) production, and enhanced the activity of peritoneal macrophages. Interestingly, in the same study, the use of gold nanoparticles as a hapten carrier augmented the immune response even when complete Freund's adjuvant was not used [26].

Rift Valley fever virus (RVFV)

Rift Valley fever virus (RVFV) is a mosquito-borne virus that causes devastating disease in ruminants and can be transmitted to humans. In humans, RVFV induces an influenza-like illness, but it can also lead to a more complicated scenario with elevated morbidity and mortality [44]. Currently, there is no licensed RVFV vaccine available for human use. Therefore, effective therapeutics are urgently needed. Silver nanoparticles have long been reported to have potent antiviral activity against many viruses belonging to different families [82].

A recent report showed a potential application of silver nanoparticles to control RVFV in which silver nanoparticles were formulated as Argovit™ [13]. The antiviral activity of Argovit was evaluated in two ways: *in vitro* on Vero cells and *in vivo* in type-I-interferon-receptor-deficient mice. First, different concentrations of Argovit were added to previously RVFV-infected-cells or given to animals infected with a lethal dose of RVFV. Second, RVFV was pre-incubated with different concentrations of Argovit before inoculation of mice and/or Vero cells. The ability of Argovit to control the RVFV infection was limited. However, incubation of the virus with Argovit before infection resulted in a significant reduction in RVFV infectivity in both *in vivo* and *in vitro* experiments [13].

Bovine herpesviruses

Infectious bovine rhinotracheitis/infectious pustular balanoposthitis (IBR/IPB) is a highly contagious viral disease caused by bovine herpesvirus type 1 (BoHV-1), a double-strand DNA virus that belongs to the family *Herpesviridae*. The virus infects cattle and buffaloes worldwide, resulting in significant economic losses [56]. A recent study showed that silver nanoparticles (Ag-NPs) at a dose of 24 µg/mL in medium inhibited virus infection in MDBK cells [28].

Peste des petits ruminants virus (PPRV)

Peste des petits ruminants (PPR) is a highly contagious transboundary viral disease that mainly affects sheep and goats. PPR is endemic in Egypt, causing major economic losses and high morbidity and mortality (up to 100%) in the affected flocks [30]. The disease is caused by PPRV, a negative-sense single-stranded RNA virus that belongs to the genus *Morbillivirus*, subfamily *Orthoparamyxovirinae*, family *Paramyxoviridae* [85]. The current PPRV vaccine on the market is a live-attenuated cell culture vaccine that did not show success in the control of the disease worldwide due to insufficient coverage, vaccine instability (especially in subtropical countries), low protection during epidemics, and poor cross-protection between circulating PPRV strains in the field and vaccine strains [64]. A study reported *in vitro* activity of silver nanoparticles (SNPs) on PPRV infection in Vero cells, where SNPs significantly inhibited virus entry at a minimum inhibitory concentration of 11.11 µg/ml by interacting with the virion surface and core, but they did not have a direct viricidal effect on cell-free virions. The SNPs showed greater stability after storage at 37°C for seven days [61].

Efficacy of nanoparticles against avian viruses

Avian influenza virus

Avian influenza virus (AIV) is a highly contagious virus that causes substantial morbidity and mortality in poultry populations, and some strains pose a possible pandemic threat to humans [34, 94]. Despite the wide use of several inactivated AIV vaccines, they have proven ineffective, necessitating the development of new technology to improve their immunogenicity and enhance their effectiveness. A recent study showed that H5 mosaic (H5M) vaccine antigen conjugated with polyanhydride nanoparticles (PAN) provided continued release of the encapsulated antigens [62]. Moreover, this vaccine candidate was immunogenic when encapsulated in PAN and/or delivered using the modified vaccinia Ankara (MVA) vector. Interestingly, both platforms (MVA vector and PAN encapsulation) elicited humoral and cellular immunity in specific-pathogen-free (SPF) and commercial chicks. In addition, protective levels of antibodies were elicited against highly pathogenic avian influenza (HPAI) caused by the homologous H5N1 and heterologous H5N2 strains. However, little is known about the toxicology profiles of silver nanoparticles *in vivo*, either in avian species and/or livestock. The biological effects may vary depending on the animal species studied, age, gender, and other factors, including the physical properties of the silver nanoparticles administered, but also the dosage, route, and time of delivery [7, 103].

Newcastle disease virus (NDV)

Newcastle disease (ND) is one of the most important viral diseases of poultry in terms of global distribution and devastating economic losses. ND is caused by NDV, which belongs to the genus *Orthoavulavirus*, subfamily *Avulavirinae*, and family *Paramyxoviridae* [85]. An intensive NDV vaccination programs in Egypt using traditional inactivated and live-attenuated NDV vaccines, has not been successful, and outbreaks continue to be reported, caused by velogenic and emergent virulent virus strains [45].

One earlier report showed that polyrhodanine nanoparticles have potent anti-NDV activity *in ovo*, suggesting that this non-toxic material could be used in the control of NDV in chickens, as it reduced the egg infective dose 50 (EID_{50}) of the NDV strains isolated from outbreaks in Tehran, Iran, in 2009 [75]. Interestingly, egg embryos inoculated with 0.1, 1, 10, and 100 parts per million (ppm) of polyrhodanine had no pathological tissue lesions, abnormalities, or deformities, and there were also no changes in blood serum biochemical parameters [75].

Another interesting study showed that microalgae-mediated silver nanoparticles (AgNPs) had significant *in vitro* antiviral activity against NDV infection in Huh7 cells [60]. Moreover, microalgae extracts had significant activity against NDV with an unclear mode of action, but it appears to be through inhibition of virus penetration into the infected cells, as AgNPs interacted directly with the NDV envelope glycoprotein. In another study, nanoparticles and polymer-adjuvanted mucosal inactivated vaccines were developed for ND and avian influenza (H9N2), which were administered to SPF chickens either by spray or by the intranasal route. These vaccines induced a significant increase in the phagocytic index, interleukin-6 (IL-6) levels, and IFN-γ responses, and they protected chickens against challenge with both viruses. The authors recommended mass application of such vaccines in vaccination strategies against avian influenza subtype H9N2 and NDV [29].

Since mucosal immunity plays a key role in protection against NDV [105, 106], a DNA vaccine that contained the NDV fusion (F) gene encapsulated in either Ag@SiO2 hollow nanoparticles (pFDNA-Ag@SiO2-NPs) or chitosan-coated polymeric (PLGA) nanoparticles showed low toxicity and high stability and did not destroy the bioactivity of the plasmid DNA *in vitro*. Moreover, intranasal vaccination of chickens with pFDNA-Ag@SiO2-NPs elicited higher anti-NDV IgG and serum IgA levels, enhanced lymphocyte proliferation, and promoted IL-2, IL-4, and IFN-γ expression [108]. Further studies are required to develop NDV mucosal vaccines incorporated in nanoparticles, as they are considered safe and effective carriers for the NDV-DNA vaccine.

In other studies, the efficacy, stability, and safety of live NDV vaccine (LaSota strain) encapsulated in chitosan nanoparticles has been evaluated [19, 104]. The encapsulated vaccine was found to be safe and highly stable, and after virus challenge, vaccinated chickens that received oral and/or intranasal immunization with the nanoparticle vaccine were completely protected, whereas only partial protection was observed in chickens vaccinated with live LaSota or inactivated NDV vaccine alone [19, 104]. Moreover, a comparison of commercially combined NDV and IBV live-attenuated vaccines to NDV-IBV live-attenuated vaccines encapsulated in two types of chitosan nanoparticles revealed that the chitosan-adjuvanted vaccines had higher safety, stability, and efficacy and elicited robust cellular and mucosal immune responses that protected the chickens against challenge with virulent NDV and IBV [107]. This is very promising, because the majority of currently approved NDV and IBV vaccines elicit partial protection due to an inadequate cellular immune response. Inadequate protection could facilitate the emergence of new viral variants causing many outbreaks, subsequently leading to a shortage in the animal protein supply. Using these newly developed nano-vaccines could help in minimizing the emergence of new viral variants and lowering the cost of animal protein production.

Infectious bursal disease virus (IBDV)

Infectious bursal disease (IBD) is a highly contagious immunosuppressive viral disease affecting 3- to 6-week old chicks with significant economic impact worldwide [89]. The disease is caused by IBDV, a non-enveloped, double-stranded RNA virus that belongs to the genus *Avibirnavirus* of the family *Birnaviridae* [84]. The current commercial IBDV vaccines are either inactivated or live attenuated and cause some side effects. On the other hand, IBDV peptide and subunit vaccines are extremely safe but poorly immunogenic [92]. Therefore, there is an urgent need to develop new, more-potent vaccines to control IBDV infection. Interestingly, a research group recorded a significant increase in both humoral and cellular immune responses in broiler chickens vaccinated with a PLGA nanoparticle vaccine when compared to chickens vaccinated with the traditional IBDV vaccine [3]. Another study showed that graphene oxide (GO) sheets and silver nanoparticle-anchored graphene oxide (GO-Ag) sheets have antiviral effects against non-enveloped IBDV and enveloped feline coronavirus (FCoV) [16]. Interestingly, they found that while GO had no antiviral activity against IBDV, it did reduce FCoV infection by 16%, whereas GO-Ag inhibited IBDV and FCoV infection by 23% and 25%, respectively [16].

Another study also showed that AgNPs had a preventive and therapeutic effect on IBDV *in vivo* using an enzyme-linked immunosorbent assay (ELISA) [78]. The study tested the preventive effect of AgNPs against IBDV by mixing IBDV with AgNPs two hours before inoculating the mixture into

embryonated eggs, whereas for testing the therapeutic effect, AgNPs were injected 48 hours after virus inoculation into embryonated eggs. Interestingly, AgNPs, especially at a concentration of 20 ppm, were effective against IBDV using both methods, with no significant differences [78].

Other veterinary viruses

Feline coronavirus (FCoV) is the causative agent of feline infectious peritonitis (FIP), and there is currently no effective vaccine. Diphyllin (a nanoparticulate vacuolar ATPase blocker) was previously tested as an antiviral agent against FCoV type II. Interestingly, diphyllin interfered with FCoV replication in fcwf-4 cells by inhibiting endosomal acidification. Diphyllin also showed *in vivo* efficacy against FCoV when administrated intravenously (I/V) to mice and demonstrated a high safety profile [53]. Another interesting study showed the antiviral effects of both CulNPs and AgNPs on feline calicivirus (FCV), a surrogate for human norovirus [12, 95]. In addition, polymeric nanoparticles such as PLGA stimulated significant IgA secretion in dairy calves when compared to the commercial modified live bovine parainfluenza 3 virus (BPI3V) virus vaccine [14, 71].

Several studies have shown that aluminum-magnesium silicate (AMS) nanoparticles have high *in vitro* antiviral activity against PPRV [36], canine parvovirus [41], AIV [39], NDV [40], egg drop syndrome 76 virus [38], IBDV [37], and fowlpox virus (FPV). In the last case, no hemagglutination activity was observed after treatment of the virus with AMS NPs [42]. Several other nano-vaccines have been developed successfully against different veterinary viruses, including a polyanhydride-NP-enclosed mucosal vaccine against bovine respiratory syncytial virus (BRSV) [73] and swine influenza virus vaccine encapsulated in polyanhydride NPs for intranasal vaccination of pigs [21], PLGA NPs [22], or CS-polymer-based NPs [23] that enhanced both the humoral and cellular immune responses and protected vaccinated pigs from swine influenza virus challenge. Furthermore, pseudorabies virus (a herpesvirus of swine) has also been shown to be inhibited by several nanoparticles [8, 46, 102]. Further studies are needed to evaluate the efficacy of previously described antiviral nanoparticles against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was first described in December 2019 in the city of Wuhan, Hubei province, China. As of 16 May 2021, over 136 million cases and 3.38 million deaths have been reported in more than 220 countries and territories worldwide [31, 32, 51, 97].

Conclusion

Previous studies regarding the development and use of nanoparticles and nano-vaccines in veterinary medicine have shown significant success in the last decade when compared to traditional vaccines. However, further field studies are needed to investigate the effect of nano-vaccines on immunosuppressed animals, and to determine the optimum application for different animal species.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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