Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

CHAPTER

24 Nanomaterials and nanocomposite applications in veterinary medicine

Atef A. Hassan[a,*], Mogda K. Mansour[b], Ahmed M. El Hamaky[a], Rasha M. Sayed El Ahl[a], Noha H. Oraby[a]

[a]*Department of Mycology and Mycotoxins, Animal Health Research Institute, Agriculture Research Center, Cairo, Egypt* [b]*Department of Biochemistry, Animal Health Research Institute, Agriculture Research Center, Cairo, Egypt*

24.1 Introduction

Nowadays, nanotechnology potentiates the synthesis of novel materials and tools that help in the improvement of animal health and production (Bai et al., 2018). Several applications of nanoparticle material in animal science include the improvement of disease diagnosis, treatment, drug delivery, animal nutrition, breeding and reproduction, and food safety for human and animal health. Additional benefits of nanotechnology include biomedicine, tumor detection, tumor vaccines, tissue engineering, MRI contrast enhancement, sensor development, and the detection of biological molecules (Li et al., 2013; Saini et al., 2010). However, nanomedicine has elevated the efficacy of drug delivery and cancer thereby (Da Silva et al., 2016; Duncan and Gaspar, 2011). They added that several functionalized and conjugated nanoparticles could be used as drug delivery vehicles and act as cytotoxic and bioimaging agents. In addition, the nano-sized materials enable efficient encapsulation and delivery of drugs (Farokhzad and Langer, 2009) as well as imaging, measuring, modeling, manipulating the matter of diagnosis (National Nanotechnology Initiative, 2006), and the treatment of cancer cells (Dilbaghi et al., 2013a). Currently, the progressive advances in drug delivery by nanomaterial have overcome the side effects of the old traditional drugs and improved its efficacy in therapy (Davis et al., 2008; Hu and Zhang, 2010; Peer et al., 2007). On the other hand, nanotechnology has elevated the efficacy of food system security, the food industry, and safety (Chen et al., 2006) and has been used in industry, medicine, and therapeutics (Gajjar et al., 2009). In developing countries, animals are of

*Corresponding author

Multifunctional Hybrid Nanomaterials for Sustainable Agri-food and Ecosystems. https://doi.org/10.1016/B978-0-12-821354-4.00024-8

significant economic importance for the security of farmers (Thornton, 2010) whereas the products of these animals such as milk, meat, hides, and leather are essential for human populations (Patel et al., 2010). Nowadays, microbial infections cause several health hazards to humans and animals. Despite progressive advances in diagnosis and therapeutic technologies, microbial spoilage still has a major economic impact on the world's food supplies and is considered the main source of outbreaks of human and animal diseases (Taylor and Rodwell, 2001). In the ongoing race between the emergence of drug resistance and the development of novel antimicrobial agents, microbes appear to be the targets of several studies (Hassan et al., 2016a). In addition, nanotechnology helps in the development of new diagnostic tools and treatments that improve the quality of life of veterinary animals. Some studies employed nanomaterials in disease treatment such as African animal trypanosomiasis (Kroubi et al., 2010) as well as foot and mouth disease in cattle (Greenwood et al., 2008) and sheep (Mohanty et al., 2014). Recently, several studies evaluated the use of nanobiosensors in the detection of estrus, hormone levels, and metabolite profiles (Monerris et al., 2012; Sagadevan and Periasamy, 2014). Also, nanomaterial has the ability to preserve gonadal tissues, sperm, oocytes, and embryos (Saragusty and Arav, 2011). Meanwhile, quantum dots (QDs) improve the understanding of mammalian spermatozoon and oocyte movements as well as their interactions in a different physiological setting of fertility, as detected by Hill and Li (2017). Furthermore, the nanocomposites can make products and applications for obtaining efficient results in treatments and diagnosis (Gordon and Sagman, 2003). Also, the composites of drug molecules with nanomaterials elevated the efficacy of drug solubility and passed through the blood supply to the targeted affected tissues (Zhang et al., 2008). Moreover, several nanocomposites can be used in various applications such as nanoshells to destroy cancer cells, alumino-silicate nanoparticles to reduce bleeding, carbon nanoparticles as sensors and for drug delivery, gold nanoparticles (Au NPs) for diagnosis, silver nanoparticles (Ag NPs) as antimicrobial agents, and iron oxide nanoparticles to improve MRI imaging (Chakravarthi and Balaji, 2010; Hassan et al., 2015b). Additionally, other tools such as microfluidics, nanomaterial, and bioanalytical nanosensors have the potential to solve many challenges in the diagnosis and treatment of diseases (Meena et al., 2018). Therefore, this chapter was undertaken to spotlight the recent advances in nanotechnology and their application in the field of veterinary medicine. Also, this review includes a brief discussion of the use of nanomaterials and nanocomposites in human and animal science. Moreover, practical applications and ways to overcome the suspected toxicity of nanomaterials in veterinary medicine are fully discussed.

24.2 Nanomaterials and nanocomposite applications in veterinary medicine

There have been rapid advances in the fields of nanomaterials and nanocomposite applications in biomedical science related to human and animal health. A brief illustration of the beneficial fields of nanomaterials and nanocomposite application in animal science is shown in Fig. 24.1.

FIG. 24.1

Field of nanotechnology applications in veterinary medicine and animal science.

24.2.1 Nanomaterial applications in veterinary medicine

Nowadays, there are a variety of nanomaterials that have been used for human and animal science, including metal nanoparticles, carbon nanoparticles, nanoshells, QDs, nanoemulsions, chitosan nanoparticles (CS NPs), silica nanoparticles, nanosensors, and nanotechnology applications in food (Fig. 24.2).

Recently, nanomaterials have had several applications in biotechnology, biomedical science, engineering, and nanomedicine (Zhang et al., 2016). Some metals such as gold, zinc, silver, iron oxide, and copper are used to prepare nanoparticles (Mishra et al., 2009). Metal nanoparticles are employed in antimicrobial potentialities, biosensing, bioimaging, cancer therapy, and other beneficial preparations (Greenwood et al., 2008; Hassan et al., 2016a, b, 2017); they have resulted in efficient nanoproduct synthesis for human and animal health.

24.2.1.1 Antimicrobial agents

The worldwide health problem of microbial drug resistance has gained more attention with the discovery of new antimicrobial agents from metals such as silver, zinc, and copper to treat microbial infections (Moghimi, 2005; Wilczynski, 2000).

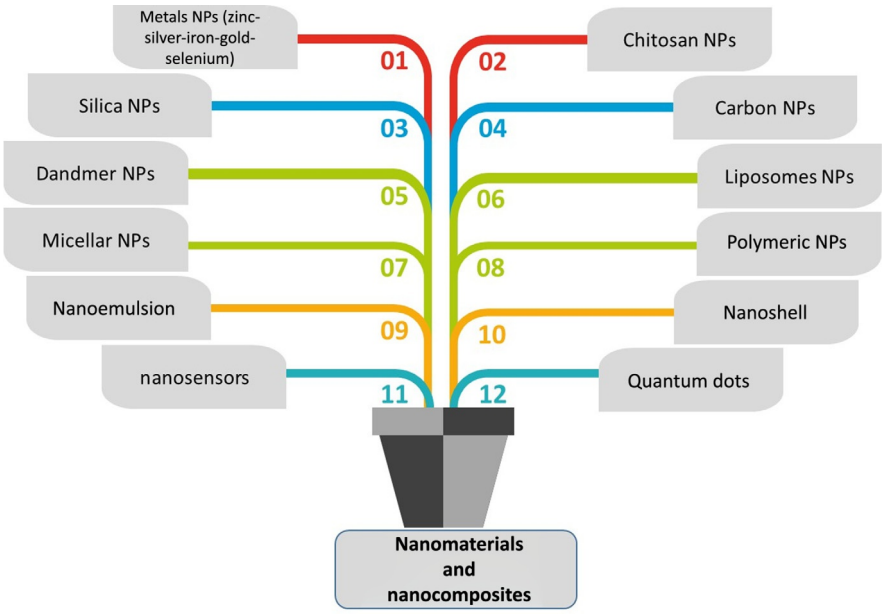

FIG. 24.2

Diagram of nanoparticle types used in veterinary medical applications and animal science.

The metal nanomaterials constitute effective antimicrobial agents against common pathogenic microorganisms (Gong et al., 2007; Hassan et al., 2013a, b; Nabawy, 2015). In addition, metal nanoparticles have greater useful advantages than large-sized metal particles (Stankic et al., 2016). Recently, Abd-Elsalam et al. (2016) reported that metal nanoparticles such as Ag, silver oxide (Ag_2O), titanium dioxide (TiO_2), silicon (Si), copper oxide (CuO), zinc oxide (ZnO), Au, calcium oxide (CaO), and magnesium oxide (MgO) have potential antifungal activity, whereas most metals provide novel antimicrobial potential (Taylor et al., 2011). Another study reported that the minimum inhibitory concentration (MIC) of zinc nanoparticles (Zn NPs) was (1.013–296 μg/mL) (Hosseini et al., 2011). However, Hassan et al. (2015a) showed the antimicrobial potential of Zn NPs against the dermatological infection of buffaloes through species such as *Trichophyton verucosum*, *Dermatophilus congolensis*, and *Staphyloccocus aureus*. Similarly, the authors detected the antimicrobial potential of Zn NPs against *Esherichia coli*, *S. aureas*, *Candida albicans*, and *Aspergillus flavus*, which caused mastitis in cattle. Regarding Ag NPs applications, they have several potential uses such as their antimicrobial, antiinflammatory, and anticancer properties (Ge et al., 2014; Hassan et al., 2016a, 2017; Zhang et al., 2016). Currently, Ag NPs showed antimicrobial effects against fungal causes of skin diseases in bovines (Hassan et al., 2013b); fungal and bacterial diarrhea and mastitis infection in buffaloes (Hassan et al., 2016a); and mastitis in goats (Gurunathan et al., 2009; Yuan et al., 2017). However, Refai et al. (2017) detected the antimicrobial effect of Ag NPs against *S. aureus* and *C. albicans*. Meanwhile, the

Ag NPs significantly reduced the viability of coliform bacteria in ilea contents of piglets (Fondevilaa et al., 2009). But in another study, no effects of enteric bacteria were observed in piglets administered Ag NPs (Sawosz et al., 2007). Furthermore, Hassan et al. (2013b) detected the antifungal potential of the Ag NPs against *C. albicans* and *Trichophyton mentagrophytes*. Ag NPs also showed the ability to inhibit the growth of fungal cells, particularly *C. albicans* and Dermatophytes (Lara et al., 2010). Kim et al. (2008) showed that the MIC of Ag NPs against pathogenic *Candida* spp. was 1 mg/mL of Ag NPs had higher potential than crud silver. The antifungal potential of nanosilver against *T. mentagrophytes* and the *Candida* species was detected by Kim et al. (2009). Moreover, the application of nanosilver in the biostabilization of footwear materials (1% solution) inhibited the growth of some mold (Falkiewicz-Dulik and Macura, 2008). Nanoparticles of iron oxide (Fe_2O_3 NPs) exhibited strong antimicrobial activity (Kaul et al., 2012; Sawai, 2003). Currently, Fe_2O_3 NPs are known to have antifungal potential against the growth of mycotoxigenic *A. flavus* while also altering their ability to produce aflatoxin (Ahmad et al., 2003; Lopes et al., 2002; Nabawy et al., 2014). Meanwhile, Hassan et al. (2013c) detected the antifungal effect of Fe_2O_3 NPs against *C. neoformance* that was recovered from respiratory diseases in cattle. Similarly, Nabawy et al. (2014) and Mouhamed et al. (2015) detected the antifungal potential of Fe_2O_3 NPs against the mycotoxigenic *Aspergillus* species that was isolated from feeds. In another study, Hassan et al. (2015b) yielded the efficient antimicrobial potential of Fe_2O_3 NPs against *Trichophyton verrucosum*, *T. mentagrophytes*, and the bacteria of *Dermatophilus* sp., which is isolated from bovine skin infections. Abd El-Tawab et al. (2018) discovered that Fe_2O_3 NPs have an more of an antifungal effect than Fe_3O_4 NPs. Nabawy et al. (2014) and Mouhamed et al. (2015) detected that aflatoxin B1 (AFB1) and ochratoxin production by respective fungal isolates was significantly diminished until complete inhibition by increasing the dose treatment with Fe_2O_3 NPs. Moreover, the antimicrobial action of metal nanoparticles was suggested as being due to disrupting and penetration of the cell membrane of microorganism, damage and rupture of the cell wall and leakage of cytoplasm contents (Gajbhiye et al., 2009; Hassan et al., 2014, 2015a, b). In another study, Khandelwal et al. (2014) determined that Ag NPs were able to prevent the penetration of a ruminant virus into animal cells by the destructive action of nanomaterials on viral cells. In another study, the antibacterial effects of Zn NPs against Gram-positive and Gram-negative bacteria occurred due to the penetration of nanoparticles into the cell membrane of bacteria and led to cell death (Arabi et al., 2012; Auffan et al., 2009; Rosi and Mirkin, 2005). Furthermore, the antibacterial activity of ZnO-NPs due to their interaction with bacterial cells caused microbial cell injury and could enter the cells (Jin et al., 2009; Stoimenov et al., 2002; Zhang et al., 2007). Currently, we evaluate the synthesis and characterization of some metal nanoparticles such as Zn NPs, Fe_2O_3 NPs, Ag NPs, and selenium NPs and their antimicrobial potential against the viability of microbial causes of cow mastitis, abortion, and diarrhea (Fig. 24.3A–C). The viability and growth of bacterial cells (*E. coli* and *S. aureas*) and fungal spores (*A. flavus* and *C. albicans*) significantly decreased as the used concentration on metal nanoparticles increased. When these isolates were observed by scanning electron

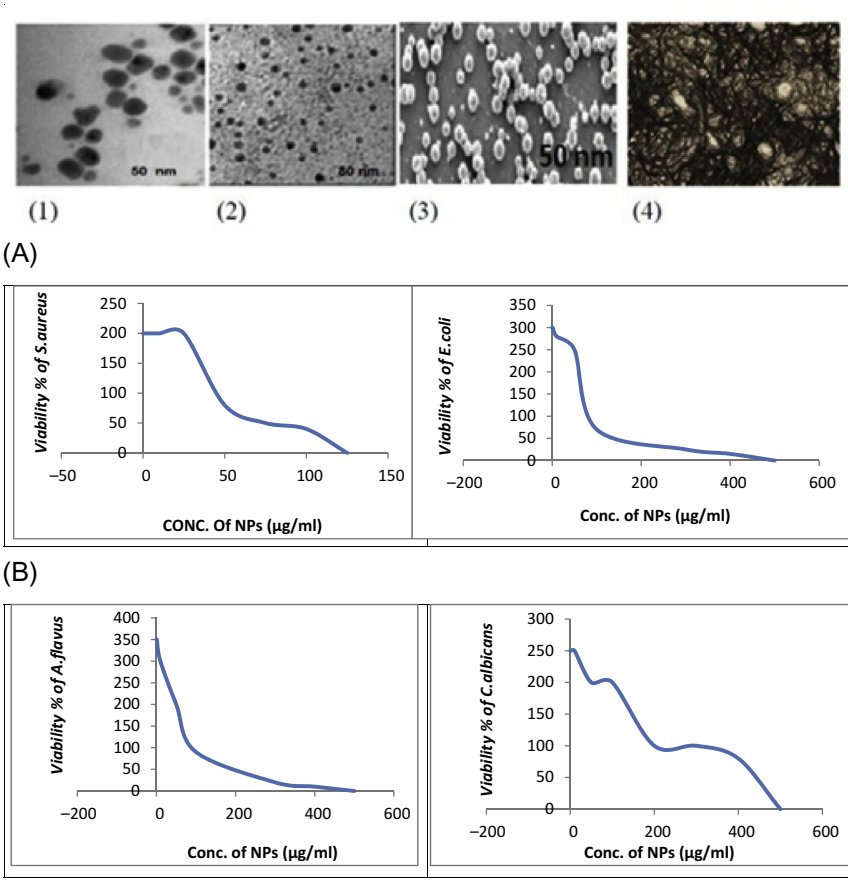

FIG. 24.3

(A) The SEM image of the particle size and distribution of some metal NPs: (1) Ag NPs, 50 nm; (2) Fe_2O_3 NPs, 80 nm; (3) Zn NPs, 50 nm; and (4) Se NPs, 60 nm. (B) Changes in viability % of bacterial cell at different conc. of NPs (*S. aureus* and *E. coli*). (C) Changes in viability % of fungal cell at different conc. of NPs (*A. flavus* and *C. albicans*).

(Continued)

microscopy (SEM), they showed complete destruction and death of the treated microbial cells (Fig. 24.3D).

Recently, Bai et al. (2018) detected that Au NPs decreased the cell viability of pathogenic bacteria in chicken. Meanwhile, the antibacterial potential of Au NPs against the *Bacillus* species and *E. coli* was detected by Zhou et al. (2012). Recently, Mohamed et al. (2017) detected the antibacterial activity of Au NPs against *Corynebacterium pseudotuberculosis*, which caused chronic caseous lymphadenitis and resulted in a major economic loss in goats and sheep. On the other hand, regarding

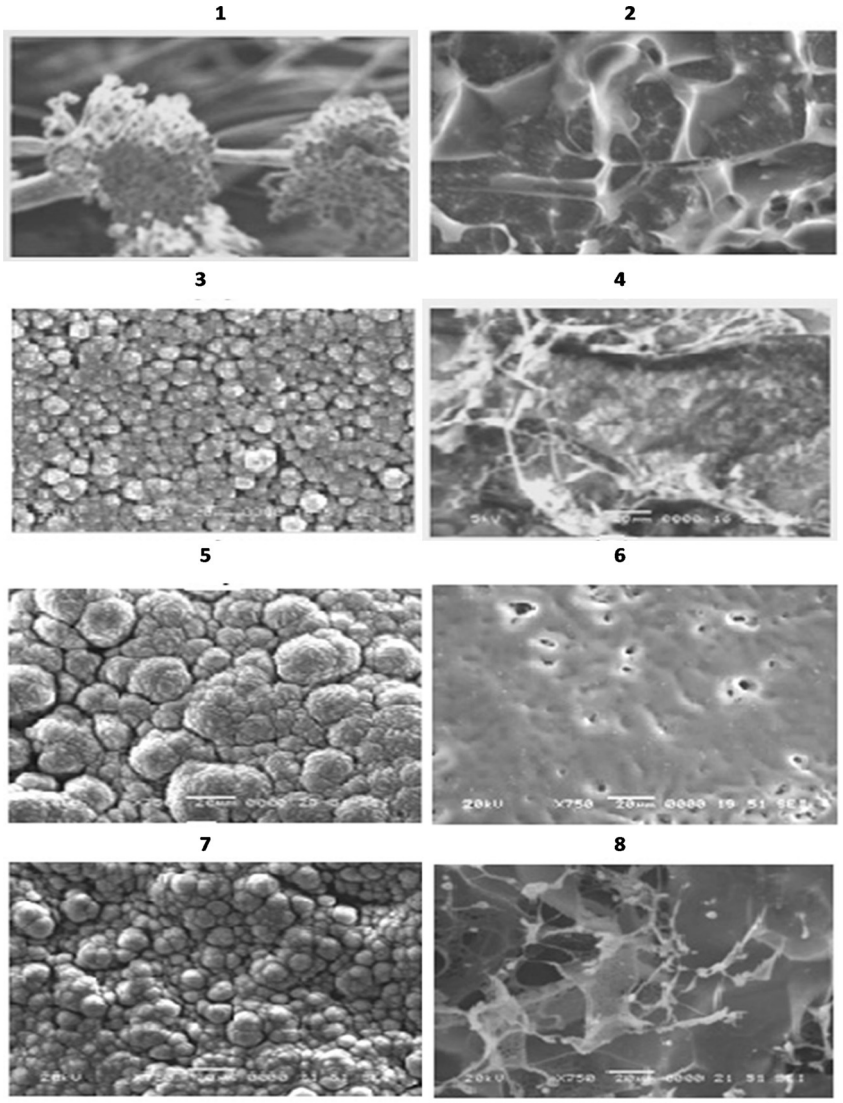

FIG. 24.3, CONT'D

(D) Scanning electron microscopy (SEM) of *Asperagillus* spp. conidia (1) before and (2) after treatment; *C. albicans* (3) before and (4) after treatment; *E. coli* O157:H7 (5) before and (6) after treatment, and of *S. aureus* (7) before and (8) after treatment with metal nanoparticles.

the single-walled carbon nanotubes (SWCNTs), it was detected that as the length decreased, the antibacterial activity increased (Yang et al., 2010). Meanwhile, suspensions such as phosphate-buffered saline decreased SWCNT toxicity and their interactions with bacterial cells, hence reducing the aggregation of cells (Kang et al., 2009). However, graphene oxides (GOs) exhibited stronger antimicrobial potential against food-borne bacteria (Kurantowicz et al., 2015). Boor (2006) detected the antimicrobial potential of CNTs against the activity of bacteria and fungi. In another study, the antimicrobial potential of SWCNT was investigated against bacteria, which caused the failure of bacterial film formation and caused cell death (Kang et al., 2007). SWCNTs are also toxic to bacterial cells that have the ability to interrupt bacterial membranes (Liu et al., 2009). Carbon nanotubes (CNTs) showed selective antibacterial agents (Fernandez-Lopez et al., 2001) and different forms of graphene materials against *Listeria monocytogenes* and *Salmonella* species (Ye et al., 2015). However, SWCNTs have potential antiviral activity against reovirus (Gurunathan et al., 2013). Similarly, Ye et al. (2015) detected the antiviral activity of GO against the pseudorabies virus DNA and the porcine epidemic diarrhea virus. Furthermore, other CNTs (fullerenes) and their derivatives showed antiviral activity against HIV (Friedman et al., 1993; Sijbesma et al., 1993) and the vesicular stomatitis virus (Kaesermann and Kempf, 1997).

The antifungal potential of chitosan and CS NPs against *Fusarium graminearum* colonies was evaluated, may be used as a novel nano-biopesticides (Kheiri et al., 2016) and a growth inhibitor for *Rhizopus* sp. and *Aspergillus niger* (Chookhongkha et al., 2012). CS NPs also have antimicrobial activity against *Staphylococcus saprophyticus* and *E. coli* (Soutter, 2013). In addition, nanosensors have antibacterial and antiviral potential, even if used in a very small amount, which improves the feedstock (Kuswandi et al., 2017; Vyas et al., 2015). Furthermore, nanoscience produces a novel nontoxic antimicrobial agent against various pathogens, including *Brucella*, *Mycobacterium bovis*, *S. aureus*, and *Rhodococcus equi* (Muktar et al., 2015) as well as fungi and bacteria that cause mastitis and aflatoxins in feeds (Hassan et al., 2016a, 2017) in cattle.

24.2.1.2 Mycotoxin degradation

Over the past decade, various mycotoxins were detected as the main contaminant for foods and feed products, infested with mycotoxigenic fungi which have the potential ability to produce one or more types of mycotoxins. Mycotoxins are carcinogenic and make other adverse effects on human and animal health. Hence, the degradation of mycotoxins can improve animal health and production. Recently, it was reported that ZnO NPs have antifungal potential against the growth of mycotoxigenic *A. flavus* while altering its ability for aflatoxin production (Ahmad et al., 2003; Hassan et al., 2013a; Lopes et al., 2002; Nabawy, 2015). Meanwhile, Hassan et al. (2013a) demonstrated the ability of zinc NPs to inhibit the growth of mycotoxigenic molds and respective mycotoxin production (aflatoxins, ochratoxins, fumonisin B1) at the concentrations of 8, 10, and 10 μg/mL of ZnO NPs, respectively. Aflatoxigenic *A. flavus* strains that require higher concentration of metals nanoparticles (250 μg/mL) than nonaflatoxigenic strains (150 μg/mL) to inhibit their growth in animal feeds

and aflatoxins production (Nabawy et al., 2014). Similarly, Mouhamed et al. (2015) reported that Zn NPs inhibit the growth of ochratoxigenic mold in feeds. Moreover, the inhibition of microbial growth by metal nanoparticles varies according to their particle size and dose levels of treatment (Shawky et al., 2014; Violeta et al., 2011). The first step in the degradation of mycotoxins by metal nanomaterials, Hassan et al. (2016a, b, 2017) successfully eliminated the carcinogenic effects of aflatoxins on vital organs such as the liver and kidney of rabbits by the addition of Zn NPs in the feed. Similarly, Abd El-Fatah et al. (2017) detected the ability of Zn NPs to eliminate the aflatoxicosis carcinogenic effects in rats. However, ZnO NPs can cause toxicity to vital internal organs in sheep (Allen et al., 1983). Similarly, the oral administration of Zn NPs in mice resulted in toxicity to their vital organs (Wang et al., 2008a).

Nowadays, researchers detected that the treatment of trichothecenes-producing *Fusarium poae* by Zn NPs and Ag NPs resulted in the inhibition of their growth viability as well as trichothecenes mycotoxin production while decreasing the density and quantity of biosynthetic genes as detected by RT-PCR. We also reported that the nanoemulsion of cinnamon and olive oils caused the complete inhibition of mycotoxigenic *Fusarium* growth and mycotoxin production at concentrations of 2%–3%. Gholami-Ahangaran and Zia-Jahromi (2013, 2014) reported the ability of Ag NPs to degrade aflatoxin in broiler chickens feed, Ag NPs are significantly elevated body weight gain and feed consumption. The significant application of magnetic nanoparticles (MNPs) in toxin degradation through dehydroxylation of the toxin (Mishima et al., 2007). Moreover, Gibson et al. (2011) modified nanodiamond substrates in carboxylation, hydrogenation, and hydroxylation for immobilization of the carcinogenic effects of mycotoxins, particularly AFB1 and ochratoxin A (OTA). Currently, the antimicrobial potential of CNTs against aflatoxigenic *A. flavus* and the prevention of aflatoxin production in feeds were investigated (Hassan et al., 2019). The obtained results showed that the viability of microbial cells was inhibited and complete prevention of aflatoxin production occurred at a concentration level of 125 μg/mL of CNTs.

24.2.1.3 Diagnosis and therapy of animal diseases

Veterinary applications of metal nanoparticles have been used in various fields related to animal disease diagnosis and treatment as well as biological sensing. Several metal nanomaterials such as Zn NPs have been significantly used in diagnostic and therapeutic activities in animal lymphomas, cutaneous cancers, transmissible venereal tumors, and equine sarcomas (Borzacchiello and Corteggio, 2009; Carr et al., 2001; Raguvaran et al., 2015; Scott and Miller, 2003). Recently, in dairy cattle, Gurunathan et al. (2018) showed the antibacterial potency of Ag NPs against causes of endometritis (*Prevotella melaninogenica* and *Arcanobacterum pyogenes*). Moreover, Asgary et al. (2016) used Ag NPs as adjuvants of the rabies virus in mice and dogs and observed that no toxicity occurred.

Several studies applied Au NPs in the diagnosis and detection of some viral infections in chickens (Nurulfiza et al., 2011); the foot and mouth disease virus (Ding et al., 2011); and the bluetongue virus in cows (Yin et al., 2011) and pigs

(Wang et al., 2013). Au NPs were used in the detection and diagnosis of some bacterial diseases in chickens (Moongkarndi et al., 2011), *Mycoplasma suis* in pigs (Meng et al., 2014), and bacterial toxins (Zhu et al., 2014). Also, Au NPs were applied in serological diagnosis of cystic echinococcosis (Jahani et al., 2014) and *E. coli* O157:H7 in feed and water in mastitis of cow (Hassan et al., 2015c) and canine parasitic infestation (Jiang et al., 2015). Other studies have detected that carbon-based nanomaterials (CBNs) such as CNTs, graphene (G), carbon fibers, and carbon nanoparticles have huge potential in biomedicine, nanoelectronics, and mechanical engineering (De-Volder et al., 2013; Le Croy et al., 2016). They can be used in disease diagnosis, gene therapy, and physiological treatments (Li et al., 2017; Wang et al., 2017). Nowadays, the varieties of nanomaterials and nanosensors have a significant value in all aspects of animal science such as the diagnosis of tuberculosis in bovines and the resulting therapy (Kuswandi et al., 2017; Sekhon, 2012).

24.2.1.4 Cancer detection, therapy, and imaging

It is interesting to report here that Zn NPs can kill cancer cells without affecting on normal immune cells and hence can be used as anticancer agents and for cancer diagnostic devices in humans and veterinary animals (Wang et al., 2009). On the other hand, a carbon nanoparticle suspension injection (CNSI) can act as a drug carrier, where it has the ability to adsorb drugs such as epirubicin and doxorubicin drugs (Xie et al., 2016), which are used in lymphatic chemotherapy (Yang et al., 2012). Currently, CNSI has been applied for clinical treatments as part of an injection during oncological surgery (Xie et al., 2017a). CNSI could be applied for lymphatic mapping as well as in parathyroid gland and lymph node tumor imaging, such as in gastric cancer (Li et al., 2016; Zhu et al., 2016) and breast cancer (Wu et al., 2015). Gu et al. (2015) and Zhu et al. (2016) successfully investigated relevancy of CNSI in lymph node dissection in the diagnosis of thyroid carcinoma. Furthermore, the CNSI might include in photothermal therapy, gene delivery, and serve as an immune adjuvant (Liu et al., 2013; Xie et al., 2017a, b). Meanwhile, the QDs polyethylene glycol (PEG)-functionalized carbon nanoparticles were nontoxic to mice after intravenous exposure (Yang et al., 2009). Moreover, CBNs can be utilized in the imaging of organs such as lymph nodes as well as physiological treatments (Li et al., 2017; Wang et al., 2017).

Wang et al. (2008b) evaluated silica nanoparticles (SNPs) in the imaging of tumor cells, where the primary or secondary antibodies immobilized onto the SNPs and attached them to cancer cells. Similarly, He et al. (2009) detected that the in vitro adoption of SNPs in methylene blue dyes initiated fluorescent imaging of HeLa cells and can be injected directly into the tumors in mouse causing its necrosis after laser radiation treatment. SNPs can also be used for the photodynamic therapy of cancer by producing singlet oxygen through fluorescence energy (Kim et al., 2007) and MNP employed in medical imaging (Mishima et al., 2007). Recently in sheep, Fe_2O_3 NPs were used for the diagnosis of tendon disease by fluorescent imaging (Scharf et al., 2015).

24.2.1.5 Drugs and vaccine delivery

The advance tools in nanotechnology developed new delivery systems and methods at the nanoscale level to produce chemical and biological reactions related to targeted sites and cells (Tomanek and Enbody, 2000). In the early stage, the use of nanotechnology in the treatment of *Salmonella typhi* infection in mice conjugated with ampicillin resulted in a decrease in the amount of ampicillin used. Therefore, their residues in animal tissues were reduced, which reflected the safety of produced food (Fattal et al., 1989). Significant applications of MNPs include pathogen detection, protein purification, and drug delivery (Mishima et al., 2007). Narducci (2007) injected the Ag NP-loaded rabies vaccine into dogs, checked them daily for 14 days, the obtained data noted that no abnormal signs. Recently, CS NPs have been widely studied for the delivery of antibiotic drugs (Cover et al., 2012; Zaki and Hafez, 2012) and anticancer drugs such as 5-fluorouracil, paclitaxel doxorubicin, letrozole, and saponin (Rejinold et al., 2011; Saboktakin et al., 2011). Several reports examined the application of CBNs in animal disease diagnosis and drug delivery (Li et al., 2017; Wang et al., 2017), and carbon-based drug delivery systems for cancer treatment (Reina et al., 2017). Furthermore, the use of nanotechnology in drug delivery reduces the amount of antibiotics administered for the treatment of diseased animals and hence reduces their residue in animal tissues.

24.2.1.6 Animal production, reproduction, nutrition, and breeding

The novel tools of diagnosis and treatment of animal diseases by recent nanotechnology have potentiated progressive advances in animal production and reproduction. The feed supplements at the nanoscale of nanocopper and nanochromium are more bioavailable to animals and poultry, allowing more interaction to occur in the gut and better absorbance (Gonzales-Eguia et al., 2009; Huang et al., 2009; Sirirat et al., 2013; Wang and Xu, 2004; Zha et al., 2009).

Recently, several studies detected that the supplementation of ZnONPs into poultry feeds to improve their growth performance, immune status, reproduction activity, and preventing microbial infections (Partha et al., 2015) and piglets and poultry (Lina et al., 2009; Yang and Sun, 2006). However, the bulk of the zinc was added as a feed additive to pigs to treat diarrhea caused by enterotoxigenic *E. coli* (Broom et al., 2006; Case and Carlson, 2002). The dietary supplementation of zinc-methionine in feeds of mastitis cows caused an elevation in milk production (Salama et al., 2003). Meantime, the addition of Zn NPs in cows that suffered from subclinical mastitis caused a reduction in the level of the somatic cell and improved milk production (Rajendran et al., 2013). However, the mastitis disease caused huge economic losses by reducing the milk yield. The most recovered organisms are *S. aureus*, *E. coli*, *C. albicans*, *A. flavus* and *A. niger*, and they can be successfully treated by ZnO NPs (Bajpa et al., 2012; Hassan et al., 2014; Jalal et al., 2011). Currently, Bai et al. (2018) screened the antibacterial potential of Zn NPs against *Staphylococcus epidermidis*, *Streptococcus agalactiae*, *Klebsiella pneumoniae*, and *E. coli* recovered from mastitis. On the other hand, in poultry, the addition of ZnO-NPs to feeds of broiler chicks significantly improved the growth, production, and dress

performance (Lina et al., 2009; Mishra et al., 2014). Within another function, it has the ability to potentiate economic importance in piglets via increasing their growth performance and feeding utility (Yang and Sun, 2006). Ag NPs in broiler chickens caused antimicrobial and growth-promoting effects, but the level of plasma immunoglobulin (IgG) was decreased (Pineda et al., 2012). Furthermore, nanographene is monitored in the measurement of blood parameters and the milk of large and small ruminant animals (Bischoff et al., 2010; McComb et al., 2010; Rahimi, 2013). In addition, the oral administration of milk containing casein nanoparticles conjugated with vitamin D to humans or animals reached the stomach in which nanocasein hydrolyzed separated from vitamin D, resulting in the elevation of their bioavailability (Haham et al., 2012). Several reports evaluated employed various nanoparticles to improve meat and egg quality. Wang and Xu (2004) added chromium nanoparticles (200 μg/kg) in pig feed, which caused an increase in muscle mass and improved pork quality. Similar results were detected in birds when chromium nanoparticles added to feed (500 μg/kg) caused the decreased cholesterol content of muscles and raised the feed efficiency (Zha et al., 2009). Huang et al. (2009) gave a nanocalcium compound to mice that resulted in its bioavailability and increased the density of bone minerals, which is higher than the use of calcium compounds on a large scale.

The administration of CS NPs loaded with chromium pigs feed resulted in an improvement in pork quality and the low-fat content of meat by decreasing the synthesis of fatty acids (Wang et al., 2012, 2014).

Regarding animal reproduction, nanotechnology develops nanobiosensors for detection of the reproductive and fertility status of animals for use in fertility control applications, the cryopreservation of gametes and embryos, and the detection of fertility hormones (Saragusty and Arav, 2011). They added that nanobiosensor devices can help in the detection of diseases, pathogens, estrus, hormone levels, and metabolites as tools for reproductive management. Similarly, the level of estrogen hormones in the blood of animals could be measured by implantation of nanotubes under the skin and hence the detection of estrus. This is due to the nanotubes binding with estradiol antibodies by fluorescence-producing signals that help in the control system of breeding (O'Connell et al., 2002). The state of animal breeding such as fertilization and the viability of sperm and eggs can be measured by nanofluid. In addition, metal nanoparticles are used for the cryopreservation of gonadal tissues, sperm, oocytes, and embryos to cause ultrafast cooling rates and homogeneous rewarming of the biological materials (Tomanek and Enbody, 2000).

24.2.1.7 Food and feed safety

Applications of nanomaterials are currently used for the meat and food industry, including the use of nanomaterials as carriers of food ingredients/additives that are placed directly into food or as a part of food packaging. In addition, this can improve the dispersing ability of fat-soluble additives in food products, enhance taste, and reduce the use of fat, salt, sugar and preservatives, preventing hypertension and cardiovascular disease in humans and animals. Nowadays, several applications of metal nanomaterials in veterinary medicine used Zn NPs as a food preservative

and feed additive. However, they are toxic to microorganisms and used as antimicrobial agents (Hosseini et al., 2011) and their addition in cow feeds resulted in a significant increase in milk production (Rajendran et al., 2013). In addition, they can be used in catalysis, sensors, environmental remediation, and personal care products of humans and animals (Raguvaran et al., 2015).

The nanocarriers enable nutritive substances to be resistant to protease enzymes and other desaturating compounds. Also, it may be increasing its ability to transfer across the intestinal membrane into blood. In addition, nanocarriers controlled release and better dispersion of nutrients in aqueous systems to water-insoluble food ingredients (Lee, 2010). Nanomaterials can produce novel tools for the detection of food-borne pathogens such as nanomaterials loaded with anti-*S. aureus* antibodies; gold and iron oxide nanoparticles yielded the rapid detection of *S. aureus* in milk (Sung et al., 2013). Similarly, nanotechnology could be applied in the science of biomedicine, food systems, food system security, and disease treatment delivery (Scott, 2005). Nowadays, the varieties of nanomaterials and nanosensors are of significant value in all aspects of animal science, and are used as additives to animal products and food safety (Muktar et al., 2015). In the near future, nanotechnology will potentiate in the production of "interactive" poultry meat that changes color, flavor, or nutrients (Meena et al., 2018).

24.2.2 Nanocomposite applications in veterinary medicine

Until now, the conjugated and functionalized nanoparticles have resulted in the formation of hybrid nanomaterials (nanocomposites) that have significant benefits to animal health and production. They can be used in drug delivery, MRI imaging, the delivery of therapeutic agents such as anticancer drugs, and disease diagnosis, particularly tumor imaging.

24.2.2.1 Antimicrobial agents

Nowadays, several studies have employed nanomaterials to avoid the toxic doses of metal nanoparticles for animal health. Hassan et al. (2016a, 2017) reported that synergistic and combination therapy has the ability to overcome microbial resistance to traditional antibiotics, resulting in more efficient antimicrobial and antitoxin activity of metal nanoparticles for the treatment of human and animal diseases. However, Mody et al. (2010) detected the availability of metal nanomaterial conjugation with drugs and other biomedical components of health importance. Hassan et al. (2016a) detected that the combination between Ag NPs and traditional antibiotics resulted in the requirement of lower concentrations from both to obtain the strong antimicrobial effects against *C. albicans*, *A. flavus*, *Salmonella*, and *S. aureas*. In addition, the combined and synergistic therapy of low dose levels of antibiotics and Ag NPs enhanced their antibacterial and antifungal effects (Gurunathan et al., 2014, 2015). The conjugation of nanosilver together with Fluconazole (antifungal) and Florfenico (antibacterial) have more potential to inhibit the growth of microbial causes of disease

in buffaloes rather than their single forms (Hassan et al., 2016a). This combination resulted in a decrease in Ag NPs dosage to avoid toxicity in the animal. Similarly, Smekalova et al. (2016) screened the antibacterial activity in the combined therapy of Ag NPs with penicillin G against *Actinobacillus pleuropneumoniae*. These activities are attributed to the potential of Ag NPs in killing and their destructive effects on microbial cells (Kim et al., 2008). In addition, the functionalized SWCNTs had an antiviral effect against reovirus (Gurunathan et al., 2013), HIV (Friedman et al., 1993), and vesicular stomatitis virus (Kaesermann and Kempf, 1997). Therefore, it is suggested that SWCNTs and multiwalled carbon nanotubes (MWCNTs) could be functionalized and combined with bioactive molecules to be a benefit in diverse biological applications (Endo et al., 2008). The carbohydrate-functionalized CNTs have antibacterial and antifungal potential against *E. coli*, *C. albicans*, *A. flavus* (Elkin et al., 2005), and *Bacillus anthracis* (Wang et al., 2008c). Meanwhile, the functionalized CNTs can influence the viability of cells by injection CNTs with complex cells (Kam et al., 2005). Also, CNTs were employed as cancer biomarkers (Thakare et al., 2010) and viruses therapy agent (Patolsky et al., 2004). CNTs have the ability to detect particular DNA sequences in cells (Tu et al., 2009). Zhu et al. (2015) and Zhang and Gurunathan (2016) determined the significant antibacterial effects of various carbon nanoparticles and nanocomposites against bacteria causing mastitis in cows. The well-functionalized CNTs have more beneficial effects on biological cells than the nonfunctionalized CNTs (Khalid et al., 2016). Hence, the benefit activity of CNTs is associated with the property of conjugation with other biological components (Dumortier et al., 2006). Therefore, there is significant importance in functionalized SWNTs for clinical applications in human and animal health (Fig. 24.4).

Several studies illustrated that the antimicrobial potential of liposomal formulations against several pathogenic bacterial species (Swenson et al., 1998). The liposome-encapsulated gentamicin has antibacterial potential against causes of mastitis in bovines such as *S. aureus* (MacLeod and Prescott, 1988). However, liposome-encapsulating tobramycin has broad-spectrum antibacterial effects against different kinds of bacteria (Sachetelli et al., 2000). In a study by Singla et al. (2016), liposome-encapsulating phage showed strong antibacterial potential against multidrug-resistant bacterial infections. Moreover, the liposomal AmB is an effective and less toxic antifungal than conventional agents in the treatment of mycotic respiratory infection in animals (Lambros et al., 1997; Leenders and De Marie, 1996) as well as yeast infections in mice (Khan et al., 2005) and dogs (Krawiec et al., 1996). In a recent study, Al-Qushawi et al. (2016) investigated the antimicrobial potentials of tilmicosin in poultry in its binding with the micelle's nanomaterials. Similarly, the antiviral activity of liposomal-encapsulated ribavirin was used in animals, resulting in increasing the drug safety efficacy and preventing replication of the virus (Kende et al., 1985; Makabi-Panzu et al., 1994). Also, it can be used as a carrier against different types of microorganisms, such as the influenza virus (Boraschi and Italiani, 2015), HAV, HIV (Qiao et al., 2016), and infectious *Plasmodium vivax* (Powles et al., 2015). Moreover, the conjugation of the hem-agglutinin-derived synthetic peptide with liposome induces antiviral protection against the lethal influenza virus (Rhee et al., 2012).

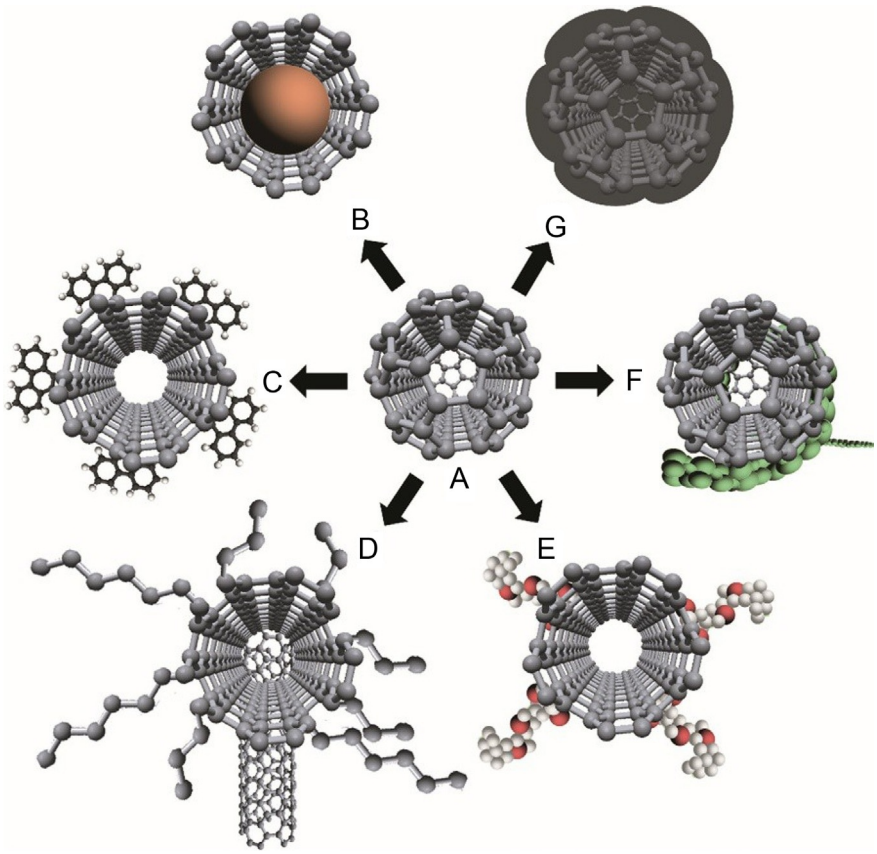

FIG. 24.4

Schematic of different methods of functionalizing SWNTs: (A) single-walled carbon nanotube, (B) endohedral functionalization with, for example, C60, (C) covalent sidewall functionalization, (D) defect-group functionalization, (E) noncovalent exohedral functionalization with surfactants, (F) noncovalent exohedral functionalization with polymers, and (G) metal plating of carbon nanotubes.

Copyright from reference Rakesh, P.S., Abdalla, A.M., Abdel Fattah, A., Ghosh, S., Puri, I.K., 2018. Chapter 2: Synthesis, characterization, and applications of carbon nanotubes functionalized with magnetic nanoparticles. In: Balasubramanian, G. (Ed.), Advances in Nanomaterials. Springer International Publishing AG 37. https:/doi.org/10.1007/978-3-319-64717-3_2 (web archive link).

Recently, the antimicrobial potential of polymeric nanoparticles composed of chitosan was evaluated against various causes of diseases such as *E. coli* O157: H7 (Doavi et al., 2016), *Pseudomonas aeruginosa* (Cui et al., 2015), the influenza virus (Oberoi et al., 2016), HBV (Lebre et al., 2016), filariasis (Malathi et al., 2015), and dengue (Hunsawong et al., 2015). Furthermore, the attached hybrid dendrimer-based nanomaterials with the biological molecules of the cell wall as proteins initiated the rapid destruction of bacterial cells (Xiao et al., 2016).

The antimicrobial potential of dendrimer-based nanocomposites caused inhibition of the growth of several pathogenic bacterial species via their ability to penetrate microbial cell membranes and cytoplasm contents with the final death of cells (Bai et al., 2018). Recently, Meena et al. (2018) reported that lipophilic substances and protection from degradation are the significant advantages of nanoemulsions. Essential oils obtained from *Mentha piperita* and encapsulated in chitosan nanogels with cinnamon acid showed antifungal potential against *A. flavus* (Beyki et al., 2014). Hassan et al. (2012a, b) used forskolin emulsions as antifungals against mycotoxigenic fungi (Hassan et al., 2012a, b). Hassan and Mansour (2003) and Hassan et al. (2008) determined that nanoemulsions of *Rhamnus cathartica* oil, molasses, and garlic extracts successfully eliminated the fungal contamination in tested feeds. Moreover, the nanoemulsions of natural oils are characterized by their physical activity and avoid chemical action. In addition, the contact of oil nanodrops with the membranes of bacteria, fungi, or enveloped viruses caused the leakage of cell contents and the death of organisms (Meena et al., 2018). The administration of conjugated penicillin or methicillin (β-lactam drug) to polymeric polyacrylate nanoparticles may increase the antibacterial activities of drugs. This due to the nanoparticles improves the destroying action of β-lactamase in the animal body and used against penicillin and methicillin-resistant *S. aureas* (Turos et al., 2007). Similarly, Ghosh et al. (2010) evaluated the antibacterial potential of tetracycline loaded into polymeric CS NPs against *E. coli* strains and the MIC was 700 μg/mL.

24.2.2.2 Mycotoxin degradation

The authors of this chapter evaluated the antifungal and antimycotoxin potentials of conjugated Ag NPs with olive oil against the mycotoxin-producing *Fusarium* sp. They caused the inhibition of fungus growth and the prevention of trichothecene and zearalenone production. In addition to antiflatoxins and antishiglla toxins, the antimicrobial potentials for nanoemulsions of cinnamon oil and Zn NPs were evaluated against isolated *A. flavus* and *E. coli* from feeds and diarrheic buffaloes. The results showed the complete inhibition of microbial growth and that toxin production requires lower levels of the combined form (100 μg/mL of Zn NPs and 1% of cinnamon oil) than the single use of Zn NPs (500 μg/mL) and cinnamon oil (3%) in treatment. In other studies, the role of MNPs in toxin decorporation was reported by Leroux (2007) while the reduction and removal of toxins from contaminated materials was detected by Wang et al. (2006). Similarly, mycotoxins such as aflatoxins and OTA were completely detoxified by the addition of Fe_2O_3 NPs to mycotoxicosis poultry feeds (Mouhamed et al., 2015; Nabawy et al., 2014). It is interesting to report that the synergistic and combination therapy of the lower doses of Zn NPs and ozone fumigation were able to cause the complete detoxification of AFB1 in poultry feed at lower nontoxic doses (40 ppm of ozone + 25 μg of Zn NPS/kg of yellow corn) (Hassan et al., 2017). The authors have evaluated olive oil and cinnamon oil emulsions against the mycotoxigenic *Fusarium* species and the production of trichothecene and zearalenone mycotoxins. These emulsions have antifungal and antimycotoxin potentials at concentrations of 2%–3%.

24.2.2.3 Diagnosis and therapy of animal diseases

In recent years, there have been progressive advances in the diagnosis and therapy of animal diseases, particularly using nanocomposites to improve diagnostic tools. The main types of MNPs are composed of iron oxide and have several applications in biomedicine through coating MNPs by biofunctional molecules to increase their sensitivity for many biological applications. Furthermore, biocompatibility, a large surface-to-volume ratio, and chemically reactive biomolecules provide a lot of chemically active sites for biomolecule conjugation, responsible for their functionalization and the encapsulation of other biological materials (Gupta and Gupta, 2005; Shokrollahi, 2013; Tartaj et al., 2003). The MNP structures and coating schemes with many other beneficial materials are of significant health importance to humans and animals; they are illustrated in Fig. 24.5.

In this direction, Gu et al. (2003) used vancomycin-conjugated FePt nanoparticles to detect vancomycin-resistant enterococci and other Gram-positive bacteria at low concentrations by increasing the ability of vancomycin to penetrate the microbial cells after conjugation. Moreover, Kaittanis et al. (2007) detected the high potential of immunomagnetic nanosensors (superparamagnetic iron oxide NPs) in the detection of *Mycobacterium avium* paratuberculosis. In another study, *E. coli* O157:H7 could be detected by dextran-coated iron oxide nanosensors or silica-coated iron oxide nanosensors (Kaittanis et al., 2008). Furthermore, MNPs will be useful for various biological applications in veterinary medicine and produce useful tools for disease diagnosis, MRI imaging, drug delivery, and cancer therapy (Michalet et al., 2005). The recent exposure of murine models to Fe_2O_3 NPs resulted in a significant decrease in inflammatory reactions such as footpad swelling and increased phagocytosis activity in the spleen (Shen et al., 2012). In addition, MNPs offer a simple and versatile platform for separating six histidines (6xHis)-tagged protein and increasing the protein binding capacity (Xu et al., 2004a, b). The production of heterodimers of two distinct nanospheres is a way to fabricate Fe_3O_4-Au heterodimers in a homogeneous organic solvent (Yu et al., 2005).

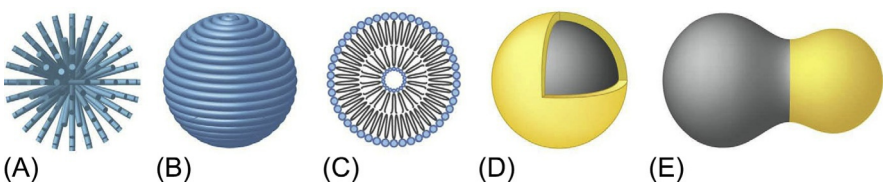

FIG. 24.5

Magnetic nanoparticle (MNP) structures and coating schemes. (A) End-grafted polymer-coated MNP; (B) MNP fully encapsulated in polymer coating; (C) liposome-encapsulated MNP; (D) core-shell MNP; and (E) heterodimer MNP.

In recent years, Au NPs have been characterized by their biocompatibility with human cells and the ability to conjugate with DNA, RNA, antibodies, and peptides (Shah et al., 2014), which has resulted in the initiation of novel nanodiagnostic tools (Syed and Bokhari, 2011). Some studies used Au NPs as biosensors in the synthesis of the immune-chromatographic strip for efficient diagnostic assays (Halfpenny and Wright, 2010; Syed and Bokhari, 2011) to detect antibodies against microbial antigens (Cui et al., 2008) and bacterial and viral diseases (Peng et al., 2008). Furthermore, the functionalized Ag NPs with some oils were used for treatment of dermatophytes diseases in animals (Bansod et al., 2015). The authors have determined that the conjugation of Ag NPs with olive oil resulted in significant and obvious antimicrobial effects against bacterial and fungal causes of mastitis in cows at concentrations of 300–500 μg/mL.

However, Parvongnukul and Lumb (1978) detected the useful application of functionalized graphite in the treatment of bone disorders in ovine. In addition, functionalized nanographene has several advantages that help in clinical applications in the therapy of animal diseases (Novoselov, 2004; Sanchez et al., 2012) and can also be used in various biomedical applications (Sun et al., 2008a, b). In another study, the polymers of nanomaterials can be prepared by adhesion of the natural biological compound as carbohydrates and protein molecules with a polymer that increases the efficacy of delivery of these compounds (Meena et al., 2018). In addition, several studies used natural polymeric nanoparticles in disease diagnosis such as inulin in anthrax (Feinen et al., 2014); *L. monocytogenes* (Rodriguez-Del et al., 2015), the influenza virus (Honda-Okubo et al., 2012), SARS-CoV (Honda-Okubo et al., 2015), HBV (Saade et al., 2013), and HIV (Petrovsky and Cooper, 2015).

Synthetic polymer nanoparticles were used in the treatment of several diseases (Cho et al., 2008). In addition, the synthetic polymeric nanoparticle drugs were used to detect several causes of animal diseases such as *S. aureus* (Colonna et al., 2013; Liu et al., 2017), tuberculosis (Lawlor et al., 2016; Parlane et al., 2012), *Brucella abortus*, *B. anthracis* (Zhao et al., 2014a, b), influenza (Oberoi et al., 2016), and *Plasmodium malariae* (Powles et al., 2015) infections. Also, QDs could be used to screen blood samples for certain proteins that may indicate certain diseases (Mohanty et al., 2014). QDs were applied in microbial detection such as pathogenic mycobacteria with CdSe QDs conjugated with streptavidin (Liandris et al., 2011). Hahn et al. (2005) used the brighter signal of streptavidin-conjugated CdSe/ZnS (core/shell) QDs for detection of the *E. coli* O157:H7 strain.

Modified CS NPs have the ability to decrease doses of used drugs in disease treatment, which can lower the costs associated with drug treatments (Aruna et al., 2013; Fang et al., 2007; Wang et al., 2011a) and also in antitumor treatments (Ghadi et al., 2014). Moreover, chitosan nanocomposites could be used for tumor therapy (Aruna et al., 2013; Cao and Zhou, 2005; Fang et al., 2007). Other studies by Lu et al. (1999) illustrated that the injection of a chitosan solution in articular cartilage increases the chondrocyte density and their genesis. The chitosan-based material can support chondrogenesis, activate produced new cartilage, and improve the long-term outcomes of cartilage repair in clinical settings (Suh and Matthew, 2000). In addition,

it can be used in gene therapy and have an adjuvant effect in vaccines in vivo (Peniche and Peniche, 2011; Shi et al., 2012).

Silica nanoparticles (SNPs) have been characterized by well-defined structures that enable them to be easily combined with other materials (Burns et al., 2006). In addition, their optical transparency allows excitation and emission light to pass through targeted cells (Shirahata, 2011). SNPs can also be conjugated with drug molecules and enter targeted cells in diseased animals, resulting from the effective accumulation of drugs inside cells and hence treatment (Taylor-Pashow et al., 2010; Wang et al., 2008b). Peled et al. (2012) diagnosed a respiratory mycobacterial infection in cattle using nanocomposite tools. Nanomaterials have the ability to conjugate with biological elements such as viral and phage cells and are used for bacterial detection (Billington et al., 2014).

Recently, Bai et al. (2018) reported that nanosensors can provide a diagnosis of subclinical bovine ketosis by using β-hydroxybutyrate (BHBA). In addition, nanosensor tools are used in the measurement of different physical and chemical blood parameters (Cui and Mumper, 2001; Hasuwa et al., 2010; Rolfe, 2012) and the detection of the constituents of animal excretions such as sweat, breath, and temperature (Neethirajan et al., 2017). Currently, various types of nanosensors can be utilized in the detection of cations, anions, organic compounds, and other toxic and microbial content in feed, food, and intelligent packaging (Lu and Bowles, 2013; Neethirajan et al., 2017). Generally, it is suggested that the action potentials of nanosensors are due to two detection principles: catalytic sensing (using enzymes, cells, tissues/organelles, and microorganisms) and affinity sensing (antibodies, nucleic acid, phages, bonding proteins, polymers, and synthetic proteins) as a diagnosis tools (Akkoyun et al., 2000). The first step in this direction, Wang et al. (2011b) used the nanocomposites of polyclonal antibodies and Au NPs for immunochromatographic strip detection of toxin contaminants in milk such as carcinogenic aflatoxin M1.

Nanoshells are composed of a dielectric core material such as silica conjugated with a metallic material layer can be injected into animals with targeted agents that search and attach to cancer cell receptors (Hirsch et al., 2003).

While QDs have many advantages over organic fluorescent dyes, they are brighter and easier to visualize than organic dyes. Hence, they can observe cell pathways and events inside the animal body as well as drug delivery to target tissues (Chakravarthi and Balaji, 2010). QDs also may be injected into the bloodstream of animals, and they may detect cells that are malfunctioning by illuminating the body with light and stimulating the QD to produce sufficient heat to kill the cancer cell (Freitas, 2005).

24.2.2.4 Cancer detection, therapy, and imaging

The nanocomposites and nanomaterials have the advantages to enter into the cancer cells and agglomerated to form large clusters inside tumor cells (Yigit et al., 2012). This helps in drug delivery, imaging, and cancer therapy (Fig. 24.6).

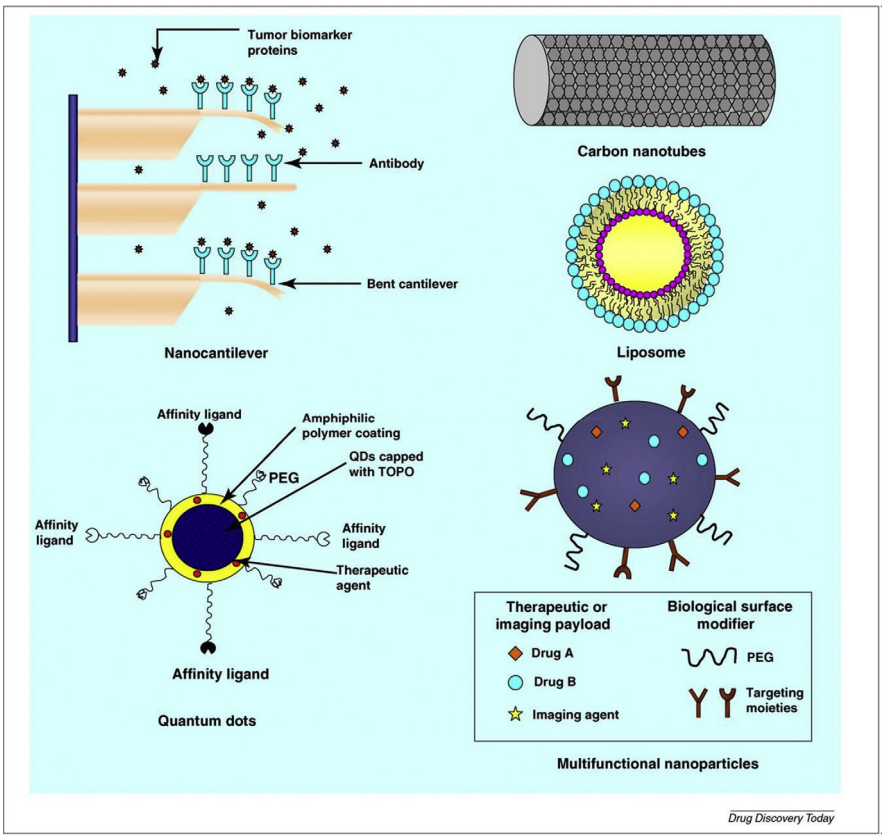

FIG. 24.6

Schematics of different nanotechnology-based tools used for cancer therapy and imaging. Liposomes are made up of lipid structures that can be made stealthy by PEGylation and encapsulating different therapeutic agents; these are used as a potential nanocarrier for cancer therapy. Nanocantilevers are array-like structures in which engineered tiny bars anchored at one end help in the detection of altered proteins present in certain types of cancers. Quantum dots are fluorescent nanocrystals that can be conjugated to a ligand by coating a polymeric layer onto it; therapeutic agents are encapsulated and used for cancer therapy. New synthetic methods have been developed to design multifunctional nanoparticles, in which we can encapsulate both therapeutic and imaging agents in a single nanocarrier system that will conjugate with more than one ligand on the surface. Thus, it will act as a novel multifunctional nanocarrier system with the capacity of targeted tumor imaging and the delivery of therapeutic agents.

The most recent drug delivery in targeted tissues was achieved by nanocarrier composites with biological molecules such as fluorescent nanostructured glucose- and sucrose-derived nanoparticles, which help successfully deliver therapeutic agents to lung carcinoma (Ajmal et al., 2015). Similarly, when injected, superparamagnetic nanoparticles made essentially from iron oxide target cancer cell receptors, enhance the location of cancer cells, and deliver the attached drug to kill the cancer cells. The encapsulation of QDs with SNPs and coating with PEGylated phospholipids and a paramagnetic lipid coating have been applied in animal science (Van-Schooneveld et al., 2008). Moreover, QDs also may be injected into the bloodstream of animals. Platinum-containing nanoparticles (FePt) without any surface coating may act as potential anticancer drugs (Gao et al., 2006; Yin et al., 2004). Magnetic NPs encapsulated with silica could be used as carriers for anticancer drugs and fluorescence molecules (Xu and Sun, 2013). In addition, the combination of FePt@Fe_2O_3 with yolk-shell nanoparticles has high cytotoxicity and strong MR contrast enhancement (Gao et al., 2007b; Peng and Sun, 2007). They added that it can encapsulate anticancer drugs. The functionalization of yolk-shell MNPs can target a specific tissue for delivering therapeutic agents and monitoring the transformation of the tumor by MRI. The MNPs can combine with QDs to exhibit magnetic and fluorescent properties (Gao et al., 2007a, 2008a; Gu et al., 2004) and sequentially grow metallic nanocomponents (Gu et al., 2005b). They added that exotic nanostructures such as yolk-shell nanoparticles are very stable because the biocompatible, compact Fe_3O_4 shells prevent the oxidative species from reaching the FePt (Gao et al., 2007b, 2008b). Ag NPs and FePt nanocomposites remediate tumors and radiation therapy in cats (Woods et al., 2012). Liposomes have the potential to provide several valuable tools in the diagnosis and therapy of tumors (Hofheinz et al., 2005; Johnston et al., 2007; Sadozai and Saeidi, 2013). They also have the ability to functionalize and conjugate with biologically valuable materials for use in animals as anticancer drugs (Alexis et al., 2010). It is interesting to report that the intravenous administration of conjugated Au NPs with Gum Arabic (GA) to swine helped in the detection of tumor tissues by Au NP constructs (Fent et al., 2009). Similarly, when conjugated, radioactive Au NPs with GA were injected intralesionally in canine animals suffering from prostate cancer. A successful entrance of Au NPs with drugs to the prostate tissues occurred, resulting in successful cancer therapy (Axiak-Bechtel et al., 2014). Au NPs can be used for cancer detection and imaging in dogs and mice (Chanda et al., 2014). The variations in the thickness of the nanoshells help with their use in diagnostic assays and tumor detection (Avaritt et al., 1997).

CNTs without any additive were toxic to mice lungs (Lam et al., 2004; Shvedova et al., 2005). The functionalization of CNTs was nontoxic to animals in conjunction with other beneficial materials (Schipper et al., 2008; Wu et al., 2008). Hence, the nonfunctionalized, long MWCNTs may be carcinogenic to mice (Ding et al., 2005). The drug is delivered for cancer therapy by liposomes characterized by the successful reach of drugs to the site of cancer cells that overcome the resistance of cancer for therapy (Malam et al., 2009). Zamboni et al. (2008) also detected the efficacy of docetaxel encapsulated in the liposome bilayer for treatments of cancers in the mice

prostate and pancreas as well as nonsmall-cell lung cancer. In a similar study, Torchilin (2005) and Sadozai and Saeidi (2013) detected the ability of liposome nanocomposites to treat canine cancers in the spleen. Meanwhile, Kleiter et al. (2010) showed that liposome-encapsulated muramyl tripeptide showed antitumor potential and prolonged disease-free survival in canines. Dendrimers are nanocomposites characterized by low cost, high potentiality in complexion or encapsulation with other beneficial biomaterials, and active destruction of the target cell membrane in cancer cells (Baker et al., 2001; Koda et al., 2008; Sekowski et al., 2008). In addition, these characteristics enable dendrimers to attach to drugs through a sphere on their surface and enter from the site of administration to targeted tissues via the blood vascular system, resulting in effective cancer therapy (Al-Jamal et al., 2009). The polymers also adhered to albumin molecules, which potentiated their delivery and could be used in cancer detection and therapy (Gradishar et al., 2005).

Recently, Meena et al. (2018) detected major benefits of CNTs for animal health and production. They can be used as sensors, antimicrobial agents, anticancer agents, and for drug delivery. Fernandez-Lopez et al. (2001) and Dilbaghi et al. (2013b) illustrated that dendrimers can be used in the diagnosis and therapy of tumors in animals as well as the detection of their nature by their ability to penetrate tumor cells and change the biochemical content of cytoplasm, leading to cell death.

Various studies have shown that mesoporous silica nanoparticles (MSNPs) have potential applications (Hom et al., 2009; Slowing et al., 2008, 2010; Vivero-Escoto et al., 2010c). MSNPs have a high surface area and volume, a stable mesostructure, a tunable pore diameter (2–10 nm), and a modifiable morphology (Vivero-Escoto et al., 2010a, b). Recently, MSNPs were effectively used to protect conjugated molecules and agents (Juan et al., 2011). They can be functionalized with nanostructures and employed for drug/gene delivery and sensing applications (Igor et al., 2007). The MSNPs were readily internalized by eukaryotic cells without detectable toxic effects (Radu et al., 2004). In addition, the surface functionalization of MSNPs was manipulated by the uptake efficiency of HeLa cancer cells (Slowing et al., 2006). In the meantime, the MSNPs were functionalized with folic acid to form folate receptors, which facilitated drug aggregation in target cells and hence gave a promising result in the regulation of human cancers in mice (Lu et al., 2010).

Today, there are different progressive advances in nanotechnology applications in the diagnosis and therapy of cancer that successfully target cancer cells without affecting normal, healthy cells (Fig. 24.7).

24.2.2.5 Bioimaging (X-ray, fluorescent, magnetic resonance imaging (MRI))

Today, the right diagnosis of human and animal diseases depends on visions of the activities of body cells and organs by imaging technology, which has progressively advanced. The essential nanomaterial is the MNPs that are used for various biological applications in veterinary medicine and produce useful tools for MRI imaging (Michalet et al., 2005). The MNPs can penetrate cell membranes and image the targeted tissues using magnetic resonance imaging (MRI) (Soenen et al., 2010)

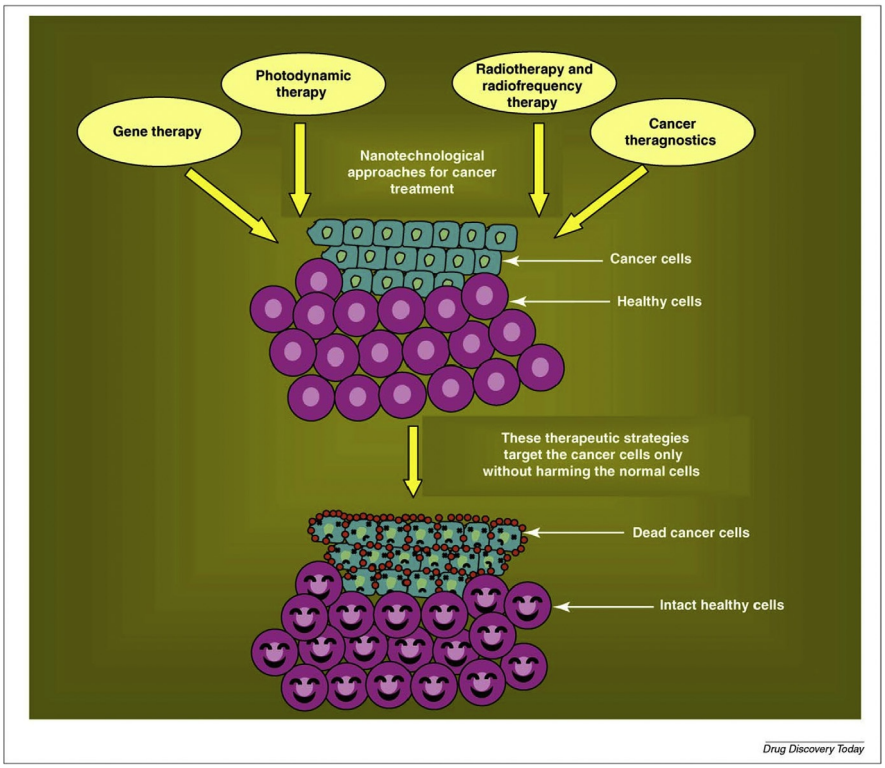

FIG. 24.7

Different approaches of nanotechnology such as gene therapy, photodynamic therapy, radio therapy, radiofrequency therapy, and cancer theragnostics are being applied for the treatment of cancer. These advanced technologies help target cancer cells only, without affecting normal cells. Ultimately, this leads to the death of the cancer cells while the normal healthy cells survive.

Data from Misra, R., Acharya, S. and Sahoo, S.K., 2010. Cancer nanotechnology: application of nanotechnology in cancer therapy. Drug Discov. Today 15 (19/20), 824–850, with permission from Elsevier.

and produce fluorescence through light signal activation (Ajmal et al., 2015; Croissant et al., 2014). Cheon and Lee (2008) reported that the conjugation of MNPs and dyes will lead to efficient MRI and optical imaging. Furthermore, Gu et al. (2005a) and Neuberger et al. (2005) revealed that porphyrin-modified Fe_3O_4 nanoparticles can act as a multifunctional nanomedicine that combines anticancer treatment and noninvasive MRI imaging. Similarly, Gao et al. (2006) detected that the conjugation of fluorescent vancomycin with fluorescein-amine stains or FePt@Van causes the quick, sensitive, and low-cost detection of bacteria by using fluorescence microscopy; it also offers the ability to enhance contrast in MRI. Kolecka et al. (2017) incubated canine stem cells with superparamagnetic iron oxide nanoparticles for 24 h.

The nano-sized materials entered the cells by endocytosis and acted as contrasts for the detection of the activity of canine stem cells. Long et al. (2015) also reported that the ultrasmall superparamagnetic nanoparticles could be used for MRI imaging for temporal lobe epilepsy and the detection of any abnormalities. In addition, the Fe_3O_4-Cd-Se heterodimer nanoparticles produced fluorescent MNPs that allow their intracellular movements to be controlled using magnetic force and a fluorescent microscope (Gao et al., 2008a). Another study detected the reduced coated graphene oxide used in the treatment and diagnosis of diseases in humans and animals. It may employ as an opt-acoustic transmitter for producing high-pressure and high-frequency ultrasound (Lee et al., 2015).

It is interesting to report that the hypernanocomposites of dendrimers can be used as alternative tools to the traditional dyes used as MRI contrasts as well as in genes and drug delivery for therapy (Kim and Zimmerman, 1998; Margerum et al., 1997; Samad et al., 2009). Nowadays, real-time sensitive imaging and sensing applications have been adopted with the development of QDs, which are crystalline materials with a facet and lattice structure that are analogous to bulk semiconductor materials. Several useful biomedical applications of QDs in biology have highlighted its potential in nanobiotechnology (Michalet et al., 2005). They can be used as sensors and detecting tools for biomarkers, pathogens, and immune-labeling of cells and tissues (Geszke-Moritz and Moritz, 2013; Kaittanis et al., 2010). Most QDs used for analytical applications are synthesized as core/shell structures (Geszke-Moritz and Moritz, 2013). They have greater stability and resistance to photo-bleaching. They exhibit both fluorescence and magnetism, such as Co@Cd-Se core-shell nanocomposites (Kim et al., 2005) and FePt-Zn S nanosponges (Gu et al., 2005b). Similarly, the MNPs can combine with QDs to exhibit magnetic and fluorescent properties for imaging target cells and organs (Gao et al., 2007a, b, 2008a, b). The modification of the QD surface gives rise to a variety of conjugation strategies with biomolecules such as vitamins, proteins, peptides, and antibodies, and initiates their entrance to targets in animal cells. Similarly, Maša (2016) illustrated that QDs produced a signal of fluorescence (fluorophores) to detect different biological events and helped in enhancing sensitivity in analyzing different biological processes. He added that different fluorophores transfer energy from biological events into specific lights that can be detected. The most effective target detection is achieved by coupling biomolecules (such as enzymes, antibodies, small molecules, and oligonucleotides) into fluorescents (Kaittanis et al., 2010). Furthermore, the combination of nano-sized particles and fluorescence has become a good alternative to detect biological events (Hötzer et al., 2012; Ruedas-Rama et al., 2012). Giri et al. (2005) added that QD barcodes were conjugated with single-stranded oligonucleotides that can hybridize to a target sequence and conjugate to a specific dye, resulting in a genetic biomarker that is measured by its optical emissions by a fluorescence signal. Moreover, QDs have a unique property such as highly bright and extremely photo-stable with longer excited-state lifetimes than classical fluorescent dyes and chemical degradation (Petryayeva et al., 2013).

Fluorescent bioconjugated silica NPs were also used in the encapsulation of fluorescent dye molecules, producing a highly amplified and reproducible signal (Zhao et al., 2004). Moreover, the rapid detection of *E. coli* O157:H7 was performed with a fluorescence microscope using SNPs encapsulated with dye (Tuitemwong et al., 2013). This produced effective detection rather than using dyes alone (He et al., 2009). The use of doped SNPs with fluorescent dyes, QDs, and metal NPs did not cause any changes in encapsulated agents (Tallury et al., 2010). Hence, SNPs have the advantage of robust materials while also being mechanically stable and transparent, enabling the stabilization and protection of encapsulated fluorophores. Moreover, Juan et al. (2011) quantified the biodistribution of SNPs doped in fluorescent dye and found that the main organs for accumulation were the liver and spleen, then passing to the stomach via fecal excretion. Currently, MRI is a recent imaging technology that is considered a noninvasive diagnostic tool with a high payload of molecules and molecular contrast agents (Na and Hyeon, 2009; Villaraza et al., 2010). In another study, MSNPs were used as an alternative to MRI contrast agents and the produced signal loss in the liver was detected (Taylor et al., 2008). The liver, kidney, and spleen are the main organs of carryover of nanomaterial after intravenous administration (Souris et al., 2010). Furthermore, MSNPs may applicable in biomedical imaging and develop new tools for clinical diagnosis and disease therapy (Lai et al., 2003; Lu et al., 2010; Radu et al., 2004). Another study reported that the biodistributions and detection of disease pathogenesis by biomarkers for therapeutic treatments (Cheon and Lee, 2008).

24.2.2.6 Drugs and vaccine delivery

The advances in nanotechnology enable us to develop delivery systems and tools at the nanoscale and to produce chemical and biological reactions related to targeted sites and cells (Tomanek and Enbody, 2000). Magnetic nanocomposites are useful for various biological applications in veterinary medicine and produce new tools for drug delivery and cancer therapy (Michalet et al., 2005). It is suggested that an efficient delivery system should have the capability to transport the desired guest molecules without any loss before reaching the targeted location (Radin et al., 2001). However, Rejman et al. (2004) showed that MSNPs can be efficiently employed as carriers for intracellular drug delivery as well as cell tracers and cytoplasmic biosensors. In addition, liposomes have been successfully used for targeted drugs, imaging agents, vaccines, and gene delivery (Bakker-Woudenberg et al., 2005; Hiszczyńska-Sawicka et al., 2012). Mesosilica nanoparticles (MSNPs) can be encapsulated in drugs to increase the delivery to target organs (Vallet-Regi et al., 2001) such as cadmium sulfide (Lai et al., 2003), gold (Liu et al., 2010; Torney et al., 2007), and iron oxide (Giri et al., 2005; Vivero-Escoto et al., 2009). Dendrimers (Radu et al., 2004) proteins (Zhao et al., 2009), and polymers have been developed (Liu et al., 2009; Radu et al., 2004). Several studies have detected the availability of fluorescent SNPs in gene therapy such as DNA probes and carriers (Lee et al., 2011b; Mintzer and Simanek, 2009; Wang et al., 2008b; Zhao et al., 2014a, b). They can also help in transferring genes in mice lungs using silica nanoparticles (Ravi et al., 2004).

Micelle nanoparticles are characterized by a hydrophobic core stabilized by a hydrophilic shell and used in transdermal therapeutics (Lee et al., 2011a). The micelle nanoparticles are highly water soluble due to their hydrophilic shell; hence, they have low toxicity and are used for the drug delivery of therapeutic agents (Koo et al., 2005). Scott-Moncrieff et al. (1994) determined that insulin mixed with micelles was efficiently absorbed in dogs, resulting in successful insulin delivery and therapy. Vail et al. (2012) currently uses the water-soluble micelle paclitaxel to efficiently treat tumors in dogs. The activity and safety of micelle paclitaxel are superior to lomustine by a high ability to enter the targeted cancer cells. Several studies illustrated that polymer compositions, structures, and properties potentiated its use in a biomedical application such as drug delivery (Moreno-Vega et al., 2012; Yang, 2000). The advantages of using polymer-drug conjugates include their ability to overcome drug resistance and to elicit immune-stimulatory effects (Ríhová et al., 2003; Sirova et al., 2007). Moreover, some studies detected that skin administration is the better route for the administration of polymer-based nanoparticles such as hydrogels containing dexamethasone for the treatment of psoriasis (Degim, 2006). Meanwhile, drug delivery can use polymers to coat MNPs and to encapsulate drugs to form nanocapsules or micelles (Gupta and Gupta, 2005), which may require complicated processes and result in modest efficiency. Klajnert and Bryszewska (2001) and Stecko et al. (2008) formed a dendrimer-based nanocomposite with vaccine preparation, increased the efficacy of vaccine delivery, and potentiated its immunogenicity. Furthermore, nanoemulsions of natural oils were successfully used in veterinary medicine as a drug delivery agent (Kang et al., 2004; Vandamme et al., 2011).

24.2.2.7 Animal production, reproduction, nutrition, and breeding

Today, there is progressive exploration and refinement in nanotechnology, which plays a significant role in animal production and reproduction. Some nanoparticles have been demonstrated to enhance fertility and protect spermatozoa through the functional groups they carry. Recently, QDs have been used to improve the detection of spermatozoon and oocyte movement and their interactions in a physiological setting. They potentiated the production of greater signal intensity than the old traditional method used in imaging gametes (Druart et al., 2009; Feugang et al., 2012; Long et al., 2005). Feugang et al. (2015) and Hasuwa et al. (2010) detected that the consumption of composed bioluminescence resonance energy transfer-conjugated quantum dot nanoparticles can be used in male pig gametes for the observation and imaging of fertilization events in deep gonadal tissues. The purification of semen is essential for successful artificial insemination in animals. Recently, coated MNPs with antibodies or lectins were used for the separation of damaged sperm from undamaged healthy sperm, while the conjugated antibodies with MNPs directed directed to ubiquitin characteristic material for defective sperm (Odhiambo et al., 2014; Petruska et al., 2014). In addition, the application of nanotechnology in sperm cryopreservation fixes the stability of sperm quality and prevents microbial pollution during storage (Bryla and Trzcinska, 2015). Antibiotic treatment may reduce the motility and activity of sperm; this problem will be solved by the use of nanoparticles

that replace extender antibiotics (Hargreaves et al., 1998). Also, mesoporous silica nanoparticles were loaded with DNA and transferred the sperm in vitro without changes in its quality (Barkalina et al., 2014). Pawar and Kaul (2012) detected that the incubation of buffalo sperm with low levels (10 μg/mL) of titanium led to successful fertilization. The administration of nanofunctionalized α-tocopherol dose for horses may increases the absorption and plasma concentration due to the oxidative status of racehorses become under intense training (Rey et al., 2013). The supplementation of Ag NPs singly or in combination with amino acids in chicken feed can improve their immune status (Bhanja et al., 2015). Similarly, Rey et al. (2014) demonstrated the potential of the administration of micellar nanoparticles conjugated with vitamin E to pigs in improving the health status of the animals.

Several studies have used nanobiosensors for animal reproduction and measurement of their fertility (Monerris et al., 2012; Sagadevan and Periasamy, 2014) and detection of the viability of reproductive organ functions and fetus (Saragusty and Arav, 2011). Furthermore, engineered nanoparticles with fluorescent probes visualize the events during ovulation and pregnancy in reproductive tissues (Feugang et al., 2015; Hasuwa et al., 2010). In addition, QDs have the ability to detect the mammalian spermatozoon and oocyte movement, which significantly helps in animal production (Hill and Li, 2017). Moreover, the small size of the biosensors and the high surface-to-volume ratio enable them to act as signal reporters in biosensors and reduce the time of target cells to be detectable by spectrophotometer, fluorescence microscope, and luminometer (Koedrith et al., 2015).

24.3 Mechanism of action of nanoparticles and nanocomposites

Greenwood et al. (2008) suggested that the formation of reactive oxygen species (ROS) and free radical production by nanomaterials causes the destruction of mitochondria, the denaturation of proteins, and the damage of DNA. Several studies have detected that ROS production can be found in C60 fullerenes, SWNTs, and QDs (Dilbaghi et al., 2013a). The mechanism of action of nanoparticles is briefly illustrated in Fig. 24.8.

The nanomaterial potentials such as anticancer, antimicrobial, and other activities against target cells resulted in the penetration and disruption of the cell membrane and cell death. Particularly, when the microbial cells that were treated by metal nanoparticles were examined by a scanning electron microscope, cell membrane damage and adhered nanoparticles to the respiratory sequence of cytoplasm were observed, followed by the death of target cells (Gajbhiye et al., 2009; Hassan et al., 2013b, 2014, 2015a, b; Nabawy, 2015). Another suggestion is the interaction between the constituents of target cells with the oxygen atom and metal ions of metal nanoparticles, which can cause damaged cell components and death (Brayner et al., 2006; Matei et al., 2010; Moraru et al., 2003; Violeta et al., 2011).

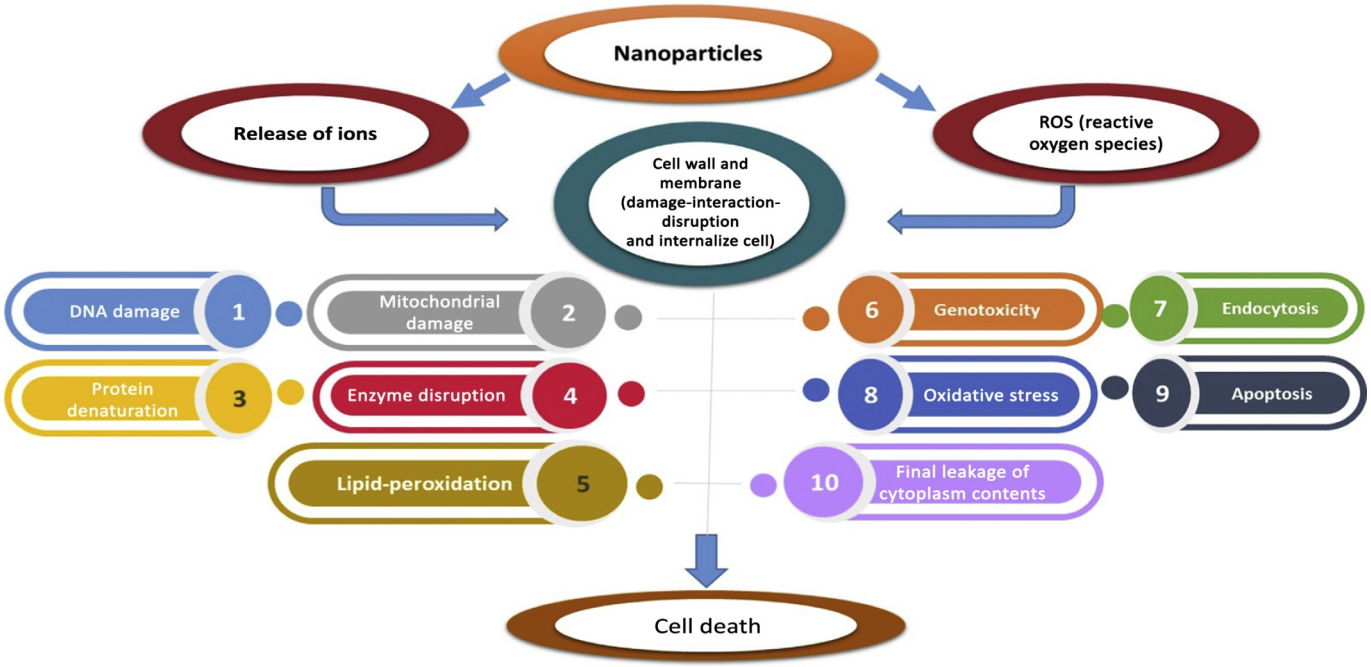

FIG. 24.8

The mechanism of action of nanoparticles and nanocomposites.

24.4 Toxicity risk of nanoparticles

In spite of the progressive and valuable tools of biosensor applications in animal science, their toxicity risk to animals and the environment is the essential reason for limiting their use in human and animal science (Donaldson et al., 2004; Oberdörster and Kuhlbusch, 2018). In addition to nanotechnology applications in several aspects of biomedicine, there are potential toxicity hazards to the environment and users as well (Baltic et al., 2013). Oxidative stress and inflammation are caused by affected tissue fibers or secondary mutations (Aschberger et al., 2011). In general, nanomaterial toxicity varies according to nano-sized particles, the health states of the humans and animals, the administered doses, and the time of exposure (Aschberger et al., 2011; Maynard, 2006; Rim et al., 2013). Also, the efficient evaluation of nanoparticle toxicity risk must include their particle size and shape, crystalline form, functionalization, and purity (Aschberger et al., 2011).

Some nanoparticles are toxic to sperm; this is adversely reflected as it decreases its viability in vitro due to overdoses and long exposure to zinc oxide and titanium oxide nanoparticles (Pawar and Kaul, 2012). The incubation of the sperm with the concentrations of 100–500 μg/mL of Zn NPs resulted in the death of sperm within a few minutes (Barkhordari et al., 2013). Pawar and Kaul (2012) detected that the incubation of buffalo sperm with 100 μg/mL of titanium oxide nanoparticles reduced its viability. Several studies have reported that metal nanoparticles may induce toxicity by their ability to easily access the skin, lungs, and brain, causing adverse effects in biological functions. The toxicity of Zn NP nanoparticles to animals and the environment must be briefly studied before they are used as a feed additive. Therefore, the measurement of effective nontoxic doses of metal nanoparticles in laboratory animal models must be undertaken to study the suitability of their field application (Abd El-Fatah et al., 2017; Asharani et al., 2008; Hassan et al., 2017; Shaw et al., 2008). Until now, there has been a lack of toxicological effects of nanoparticles on health (Savolainen et al., 2010). So, the toxicological aspects of nanomaterials require further continuous studies to be completely understood (Fig. 24.9).

Regarding the route of exposure to nanomaterials, ingestion is the main exposure route for humans and animals (Aschberger et al., 2011). Upon ingestion, the nanomaterials enter the gastrointestinal tract to the intestines and are eliminated rapidly through the liver and spleen (Oberdörster et al., 2004). The ingestion mainly results from the presence of nanoparticles in food due to direct contact of nanopackaging to food (Baltic et al., 2013; Bouwmeester et al., 2009). The nanoparticles are distributed in the liver and spleen in circulation (Baltic et al., 2013; Silvestre et al., 2011). Inhalation and the skin are other routes of nanoparticle toxicity, which are detected mainly in the laboratory and in industry workers in nanomaterial production factories (Aschberger et al., 2011).

Another study described that inhalation and skin exposure to magnesium oxide nanoparticles allows them to enter the nerve cells and central nervous system (Elder et al., 2009). Nurkiewicz et al. (2008) demonstrated that the inhalation of nano-sized

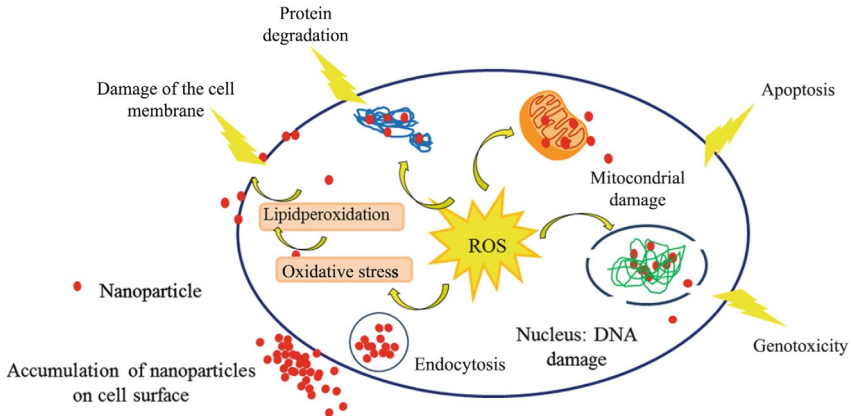

FIG. 24.9

Schematic mechanism of cytotoxic activity of nanoparticles (NPs).

Copyright from reference Romero, C.M, Alvarez, A., Martínez, M.A., Chaves, S., 2018. Fungal nanotechnology: a new approach toward efficient biotechnology application. In: Prasad, R., Kumar, V., Kumar, M., Wang, S. (Eds.), Fungal Nano bionics: Principles and Applications. Springer, Singapore.

titanium dioxide reached systemic circulation in rats. Tinkle et al. (2003) and Tsuji et al. (2006) detected the ability of nanomaterials to enter healthy human skin during constant flexing, causing many controversial effects (Monteiro-Riviere et al., 2007).

In other studies, the Zn NPs detected the availability of penetrated skin tissue (Baltic et al., 2013; Sharma et al., 2009) and have carcinogenic effects such as asbestos-caused fibrosis in the lungs (Muller et al., 2008). The inhalation of high doses of nano-TiO_2 also has the potential for lung carcinogenesis (Aschberger et al., 2011). Furthermore, the entrance of nanoparticles via the bloodstream may affect blood vessel function and cause blood clot formation and other adverse effects on the cardiovascular system, as in the case of inhalation of ambient ultrafine particles (Pekkanen et al., 2002). Similar microvascular dysfunction was observed in rats after inhalation exposure to low concentrations of nano-sized titanium dioxide (Nurkiewicz et al., 2008) and platelet aggregation and vascular thrombosis after inhalation exposure to SWCNTs and MWCNTs (Radomski et al., 2005). Some studies reported that nanomaterials can penetrate the blood and are distributed in body organ cell tissues, and sometimes transmitted to the fetus via the blood supply (Baltic et al., 2013; Silvestre et al., 2011).

In the near future, more progressive advancement in nanobiomedical science and availability to improve animal health is needed. They will have the potential to solve many problems related to animal disease diagnosis, animal production, reproduction, and good hygienic practices during rearing and maintaining of food animals. The possible applications of the technology are almost incredible in relation to livestock. Although much research is needed before nanotechnology applications are used in veterinary and animal sciences, in particular the toxicity risk.

24.5 Conclusions and future perspectives

Until now, nanotechnology has offered significant advances in the development of novel technology in human and veterinary medicine as a synthesis of new materials and tools that help increase animal health and production. Several applications of nanomaterials are used to produce strategies for disease diagnosis, drug delivery, animal nutrition, breeding and reproduction, additives to animal products, and finally food safety for human and animal health. In addition, they are used for tumor detection, production of tumor vaccines, tissue engineering, MRI images, sensor development, and the detection of pathogens, proteins, and biological molecules. These applications resulted in the development of novel nanodrugs such as metal nanoparticles (particularly, Zn NPs, Ag NPs, Au NPs, and MNPs), liposomes, polymeric nanoparticles, dendrimers, CS NPs, QDs, etc. The use of metallic nanoparticles in nanomedicine has the ability to improve imaging and therapeutic drug delivery for the treatment of cancer in humans and veterinary medicine. The nanomaterials and nanocomposites bind with biological fluids to help control drug release and hence are used in the synthesis of biological markers, imaging, drug delivery systems, and disease detection.

In addition, the potential of nanoparticles in disease treatment and diagnosis, antimicrobial, anticancer and other activities of metals nanoparticles against target cells resulted from disruption of cell membrane, damage, rupture of cell wall and leakage in inter cellular components and finally cell death. The toxicity of nanomaterials is mainly due to oxidative stress. The exact mechanism of the formation and generation of ROS requires more study to be completely understood. Oxidative stress resulting from the use of nanomaterials can cause inflammation, fibrosis, genotoxicity, and cancers.

In the future, there will be progressive advances in nanobiomedical science and use in improving animal health. It will have the potential to solve many problems related to animal health, animal production, reproduction, and good hygienic practices during rearing and maintaining of food animals. The possible applications of the technology are almost incredible in relation to livestock. However, special attention is required for the known toxicological aspects of nanomaterials prior to application in veterinary and animal sciences. Because there is no brief knowledge about toxicology studies available, hence much research is urgently needed before nanotechnology applications can be used, in particular their toxicity risk.

Acknowledgments

The authors of this chapter gratefully acknowledge Dr. M.K. Refai, professor of microbiology, Cairo University, for his continuous assistance and advice in initiating the achievement of this work.

References

Abd El-Fatah, S., Bakry, H.H., Abo Salem, M.E.S., Hassan, A.A., 2017. Comparative study between the use of bulk and nanoparticles of zinc oxide in amelioration the toxic effects of aflatoxins in rats. Benha Vet. Med. J. 33 (2), 329–342.

Abd El-Tawab, A.A., Ahmed, M.A., El- Diasty, E.M., El-Hofy, F.I., Ahmed, Y.M., 2018. A comparative study on antifungal activity of Fe_2O_3, and Fe_3O_4 nanoparticles. Int. J. Adv. Res. 6 (1), 189–194.

Abd-Elsalam, K.A., Hashim, A., Alghuthaymi, M.A., Bahkali, A.H., 2016. Nanobiotechnological strategies for molud and mycotoxin control. In: Grumezescu, A.M. (Ed.), Nanotechnology in Food Industry, Volume VI, Food Preservation. Elsevier, pp. 337–364.

Ahmad, A., Mukherjee, P., Senapati, S., Mandal, D., Khan, M.I., 2003. Extracellular biosynthesis of silver nanoparticles using the fungus *Fusarium oxysporum*. Colloids Surf. B Biointerfaces 8, 313–318.

Ajmal, M., Yunus, U., Matin, A., Haq, N.U., 2015. Synthesis, characterization and in vitro evaluation of methotrexate conjugated fluorescent carbon nanoparticles as drug delivery system for human lung cancer targeting. J. Photochem. Photobiol. B 153, 111–120.

Akkoyun, A., Kohen, V., Bilitewski, U., 2000. Detection of sulphamethazine with an optical biosensor and anti-idiotypic antibodies. Sens. Actuators B 70, 12–18.

Alexis, F., Pridgen, E.M., Langer, R., Farokhzad, O.C., 2010. Nanoparticle technologies for cancer therapy. Handb. Exp. Pharmacol. 197, 55–86.

Al-Jamal, W.T., Al-Jamal, K.T., Tian, B., Cakebread, A., Halket, J.M., Kostarelos, K., 2009. Tumor targeting of functionalized quantum dot-liposome hybrids by intravenous administration. Mol. Pharm. 6, 520–530.

Allen, J.G., Masters, H.G., Peet, R.L., Mullins, K.R., Lewis, R.D., Skirrow, S.Z., Fry, J., 1983. Zinc toxicity in ruminants. J. Comp. Pathol. 93, 363–377.

Al-Qushawi, A., Rassouli, A., Atyabi, F., Peighambari, S.M., Esfandyari-Manesh, M., Shams, G.R., Yazdani, A., 2016. Preparation and characterization of three tilmicosin-loaded lipid nanoparticles: physicochemical properties and in-vitro antibacterial activities. Iran. J. Pharm. Res. 15, 663–676.

Arabi, Y.M., Dara, S.I., Memish, Z., Al Abdulkareem, A., Tamim, H.M., Al-Shirawi, N., Parrillo, J.E., Dodek, P., Lapinsky, S., Feinstein, D., 2012. Antimicrobial therapeutic determinants of outcomes from septic shock. Hepatology 56 (6), 2305–2315.

Aruna, U., Rajalakshmi, R., Indira-Muzib, Y., 2013. Role of chitosan nanoparticles in cancer therpy. Int. J. Innov. Pharm. Res. 4, 318–324.

Aschberger, K., Micheletti, C., Sokull-Klüttgen, B., Christensen, F.M., 2011. Analysis of currently available data for characterising the risk of engineered nanomaterials to the environment and human health; lessons learned from four case studies. Environ. Int. 37 (6), 1143–1156.

Asgary, V., Shoari, A., Baghbani-Arani, F., Sadat Shandiz, S.A., Khosravy, M.S., Janani, A., Bigdeli, R., Bashar, R., Cohan, R.A., 2016. Green synthesis and evaluation of silver nanoparticles as adjuvant in rabies veterinary vaccine. Int. J. Nanomedicine 11, 3597–3605.

Asharani, P.V., Wu, Y.L., Gong, Z., Valiyaveettil, S., 2008. Toxicity of silver nanoparticles in zebrafish models. Nanotechnology 19, 255102–255110.

Auffan, M., Rose, J., Bottero, J.Y., Lowry, G.V., Jolivet, J.P., Wiesner, M.R., 2009. Towards a definition of inorganic nanoparticles from an environmental, health and safety perspective. Nat. Nanotechnol. 4, 634–641.

Avaritt, R.D., Sarkar, D., Halas, N.J., 1997. Plasmon resonance shifts of Au-coated Au 25 nanoshells: insight into multicomponent nanoparticle growth. Phys. Rev. Lett. 78, 4217–4220.

Axiak-Bechtel, S.M., Upendran, A., Lattimer, J.C., Kelsey, J., Cutler, C.S., Selting, K.A., Bryan, J.N., Henry, C.J., Boote, E., Tate, D.J., 2014. Gum Arabic-coated radioactive gold nanoparticles cause no short-term local or systemic toxicity in the clinically relevant canine model of prostate cancer. Int. J. Nanomedicine 9, 5001–5011.

Bai, D.P., Lin, X.Y., Huang, Y.F., Zhang, X.F., 2018. Theranostics aspects of various nanoparticles in veterinary medicine. Int. J. Mol. Sci. 19, 3299–3331.

Bajpa, I., Saha, N., Basu, B., 2012. Moderate intensity static magnetic field has bactericidal effect on *E. coli* and *S. epidermidis* on sintered hydroxyapatite. J. Biomed. Mater. Res. B Appl. Biomater. 100, 1206–1217.

Baker, J.R., Quintana, A., Piehler, L., Banazak-Holl, T.D., Raczka, E., 2001. The synthesis and testing of anti-cancer therapeutic nanodevices. Biomed. Microdevices 3, 61–69.

Bakker-Woudenberg, I.A., Schiffelers, R.M., Storm, G., Becker, M.J., Guo, L., 2005. Long-circulating sterically stabilized liposomes in the treatment of infections. Methods Enzymol. 391, 228–260.

Baltic, Z.M., Boskovic, M., Ivanovic, J., Dokmanovic, M., Janjic, J., Loncina, J., Baltic, T., 2013. Nanotechnology and its potential applications in meat industry. Tehn. Mesa. 54 (2), 168–175.

Bansod, S., Bawskar, M., Rai, M., 2015. In vitro effect of biogenic silver nanoparticles on sterilisation of tobacco leaf explants and for higher yield of protoplasts. IET Nanobiotechnol. 9, 239–245.

Barkalina, N., Jones, C., Kashir, J., Coote, S., Huang, X., Morrison, R., 2014. Effects of mesoporous silica nanoparticles upon the function of mammalian sperm in vitro. Nanomedicine 10, 859–870.

Barkhordari, A., Hekmatimoghaddan, S., Jebali, A., Khalili, M.A., Talebi, A., Noorani, M., 2013. Effect of zinc oxide nanoparticles on viability of human spermatozoa. Iran. J. Reprod. Med. 11, 767–771.

Beyki, M., Zhaveh, S., Tahere, S., Rahmani-Cherati, T., Abollahi, A., Mansour, B., Bayat, M., Tabatabaei, M., Mohsenifarc, A., 2014. Encapsulation of *Mentha piperita* essential oils in chitosan–cinnamic acid nanogel with enhanced antimicrobial growth against *Aspergillus flvus*. Ind. Crop Prod. 54, 310–319.

Bhanja, S.K., Hotowy, A., Mehra, M., Sawosz, E., Pineda, L., Vadalasetty, K.P., Kurantowicz, N., Chwalibog, A., 2015. In ovo administration of silver nanoparticles and/or amino acids influence metabolism and immune gene expression in chicken embryos. Int. J. Mol. Sci. 16, 9484–9503.

Billington, C., Hudson, J.A., D'Sa, E., 2014. Prevention of bacterial foodborne disease using nano biotechnology. Nanotechnol. Sci. Appl. 7, 73–83.

Bischoff, K., Gaskill, C., Erb, H.N., Ebel, J.G., Hillebrandt, J., 2010. Comparison of two methods for blood lead analysis in cattle: graphite-furnace atomic absorption spectrometry and LeadCare(R) II system. J. Vet. Diagn. Investig. 22 (5), 729–733.

Boor, K.J., 2006. Bacterial stress responses: What does not kill them can make them stronger. PLoS Biol. 4 (1), e23–e29.

Boraschi, D., Italiani, P., 2015. From antigen delivery system to adjuvanticy: the board application of nanoparticles in vaccinology. Vaccine 3, 930–939.

Borzacchiello, G., Corteggio, A., 2009. Equine sarcoid: state of the art. Ippologia 20, 7–14.

Bouwmeester, H., Dekkers, S., Noordam, M.Y., Hagens, W.I., Bulder, A.S., de Heer, C., Voorde, S.E.C.G., Wijnhoven, S.W.P., Marvin, H.J.P., Sips, A.J.A.M., 2009. Review of health safety aspects of nanotechnologies in food production. Regul. Toxicol. Pharmacol. 53, 52–62.

Brayner, R., Ferrari-Iliou, R., Brivois, N., Djediat, S., Benedetti, M.F., Fievet, F., 2006. Toxicological impact studies based on *Escherichia coli* bacteria in ultrafine ZnO nanoparticles colloidal medium. Nano Lett. 6, 866–870.

Broom, L.J., Miller, H.M., Kerr, K.G., Knapp, J.S., 2006. Effects of zinc oxide and Enterococcus faecium SF68 dietary supplementation on the performance, intestinal microbiota and immune status of weaned piglets. Res. Vet. Sci. 80, 45–54.

Bryla, M., Trzcinska, M., 2015. Quality and fertilizing capacity of boar spermatozoa during liquid storage in extender supplemented with different antibiotics. Anim. Reprod. Sci. 163, 157–163.

Burns, A., Ow, H., Wiesner, U., 2006. Fluorescent core-shell silica nanoparticles: towards "Lab on Particle" architectures for nanobiotechnology. Chem. Soc. Rev. 35, 1028–1042.

Cao, J., Zhou, N.J., 2005. Progress in antitumor studies of chitosan. Chin. J. Biochem. Pharm. 26 (2), 127.

Carr, E.A., Théon, A.P., Madewell, B.R., Griffey, S.M., Hitchcock, M.E., 2001. Bovine papillomavirus DNA in neoplastic and nonneoplastic tissues obtained from horses with and without sarcoids in the western United States. Am. J. Vet. Res. 62, 741–744.

Case, C.L., Carlson, M.S., 2002. Effect of feeding organic and inorganic sources of additional zinc on growth performance and zinc balance in nursery pigs. J. Anim. Sci. 80, 1917–1924.

Chakravarthi, V.P., Balaji, S.N., 2010. Applications of nanotechnology in veterinary medicine. Vet. World 3 (10), 477–480.

Chanda, N., Upendran, A., Boote, E.J., Zambre, A., Axiak, S., Selting, K., Katti, K.V., Leevy, W.M., Afrasiabi, Z., Vimal, J., 2014. Gold nanoparticle based X-ray contrast agent for tumor imaging in mice and dog: a potential nano-platform for computer tomography theranostics. J. Biomed. Nanotechnol. 10, 383–392.

Chen, H., Weiss, J., Shahidi, F., 2006. Nanotechnology in nutraceuticals and functional foods. Food Technol. 60 (3), 30–36.

Cheon, J., Lee, J., 2008. Synergistically integrated nanoparticles as multimodal probes for nanobiotechnology. Acc. Chem. Res. 41, 1630–1640.

Cho, K., Wang, X., Nie, S., Chen, Z.G., Shin, D.M., 2008. Therapeutic nanoparticles for drug delivery in cancer. Clin. Cancer Res. 14, 1310–1316.

Chookhongkha, N., Sopondilok, T., Photchanachai, S., 2012. Effect of chitosan and chitosan nanoparticles on fungal growth and chilli seed quality. Proc. Int. Conf. Postharvest Pest Dis. Manag. Export. Hortic. Crops 973, 231–237.

Colonna, C., Dorati, R., Conti, B., Caliceti, P., Genta, I., 2013. Sub-unit vaccine against *S. aureus*-mediated infections: set-up of nano-sized polymeric adjuvant. Int. J. Pharm. 452, 390–401.

Cover, N.F., Yuen, S.L., Parsons, A.K., Kumar, A., 2012. Synergetic effects of doxycycline-loaded chitosan nanoparticles for improving drug delivery and efficacy. Int. J. Nanomedicine 7, 2411–2419.

Croissant, J., Chaix, A., Mongin, O., Wang, M., Clement, S., Raehm, L., 2014. Two-photon-triggered drug delivery via fluorescent nanovalves. Small 10, 1752–1755.

Cui, Z., Mumper, R.J., 2001. Chitosan-based nanoparticles for topical genetic immunization. J. Control. Release 75, 409–419.

Cui, S., Zhou, S., Chen, C., Qi, T., Zhang, C., Oh, J., 2008. A simple and rapid immunochromatographic strip test for detecting antibody to porcine reproductive and respiratory syndrome virus. J. Virol. Methods 152, 38–42.

Cui, Z., Han, D., Sun, X., Zhang, M., Feng, X., Sun, C., Gu, J., Tong, C., Lei, L., Han, W., 2015. D-Mannose-modified chitosan microspheres enhance OprF-OprI-mediated protection of mice against *Pseudomonas aeruginosa* infection via induction of mucosal immunity. Appl. Microbiol. Biotechnol. 99, 667–680.

Da Silva, C.G., Rueda, F., Löwik, C.W., Ossendorp, F., Cruz, L.J., 2016. Combinatorial prospects of nano-targeted chemoimmunotherapy. Biomaterials 83, 308–320.

Davis, M.E., Chen, Z.G., Shin, D.M., 2008. Nanoparticle therapeutics: an emerging treatment modality for cancer. Nat. Rev. Drug Discov. 7, 771–782.

Degim, I.T., 2006. New tools and approaches for predicting skin permeability. Drug Discov. Today 11, 517–523.

De-Volder, M.F., Tawfick, S.H., Baughman, R.H., Hart, A.G., 2013. Carbon nanotubes: present and future commercial applications. Science 339 (6119), 535–539.

Dilbaghi, N., Kaur, H., Ahuja, M., Kumar, S., 2013a. Evaluation of tropicamide-loaded tamarind seed xyloglucan nano-aggregates for ophthalmic delivery. Carbohydr. Polym. 94, 286–291.

Dilbaghi, N., Kaur, H., Kumar, R., Arora, P., Kuma, S., 2013b. Nanoscale device for veterinary technology: trends and future prospective. Adv. Mater. Lett. 4 (3), 175–184.

Ding, L.H., Stilwell, J., Zhang, T.T., Elboudwarej, O., Jiang, H.G., Selegue, J.P., Cooke, P.A., Gray, J.A., Chen, F.Q.F., 2005. Molecular characterization of the cytotoxic mechanism of multiwall carbon nanotubes and nano-onions on human skin fibroblast. Nano Lett. 5 (12), 2448–2464.

Ding, Y.Z., Liu, Y.S., Zhou, J.H., Chen, H.T., Zhang, J., Ma, L.N., Wei, G., 2011. A highly sensitive detection for foot-and-mouth disease virus by gold nanopariticle improved immuno-PCR. Virol. J. 8 (148), 1–5.

Doavi, T., Mousavi, S.L., Kamali, M., Amani, J., Fasihi-Ramandi, M., 2016. Chitosan-based intranasal vaccine against *Escherichia coli* O157:H7. Iran. Biomed. J. 20, 97–108.

Donaldson, K., Donaldson, K., Stone, V., Tran, C.L., Kreyling, W., Borm, P.J., 2004. Nanotoxicology. Occup. Environ. Med. 61, 727–728.

Druart, X., Cognie, J., Baril, G., Clement, F., Dacheux, J.L., Gatti, J.L., 2009. In vivo imaging of in situ motility of fresh and liquid stored ram spermatozoa in the ewe gential tract. Reproduccion 138, 45–53.

Dumortier, H., Lacotte, S., Pastorin, G., Marega, R., Wu, W., Bonifazi, D., Briand, J.P., Prato, M., Muller, S., Bianco, A., 2006. Functionalized carbon nanotubes are non-cytotoxic and preserve the functionality of primary immune cells. Nano Lett. 6 (7), 1522–1528.

Duncan, R., Gaspar, R., 2011. Nanomedicine(s) under the microscope. Mol. Pharm. 8, 2101–2141.

Elder, A., Lynch, I., Grieger, K., Chan-Remillard, S., Gatti, A., Gnewuch, H., 2009. Human health risks of engineered nanomaterials: critical knowledge gaps in nanomaterials risk assessment. In: Linkov, I., Steevens, J. (Eds.), Nanomaterials: Risks and Benefits. Springer, Dordrecht, pp. 3–29.

Elkin, T., Jiang, X., Taylor, S., Lin, W., Gu, L., Yang, H., Brown, J., Collins, S., Sun, S., 2005. Immune-carbon nanotubes and recognition of pathogens. Chem. Biochem. 6 (4), 640–643.

Endo, M., Strano, M.S., Ajayan, P.M., 2008. Potential applications of carbon nanotubes. Appl. Phys. 111, 13–61.

Falkiewicz-Dulik, M., Macura, A.B., 2008. Nanosilver as substance biostabilising footwear materials in the foot mycosis prophylaxis. Mikolog. Lekar. 15, 145–150.

Fang, G.J., Hong, Y., Jiang, Y.Y., 2007. Comparison of antitumor effects of chitosan nanoparticles from different sources in vitro. J. Clin. Rehabil. Tissue Eng. Res. 11, 9696–9709.

Farokhzad, O.C., Langer, R., 2009. Impact of nanotechnology on drug delivery. ACS Nano 3, 16–20.

Fattal, E., Youssef, M., Couvreur, P., Andremont, A., 1989. Treatment of experimental salmonellosis in mice with ampiciline-bound nanoparticles. Antimicrob. Agents Chemother. 33, 1540–1543.

Feinen, B., Petrovsky, N., Verma, A., Merkel, T.J., 2014. Advax-adjuvanted recombinant protective antigen provides protection against inhalational anthrax that is further enhanced by addition of murabutide adjuvant. Clin. Vaccine Immunol. 21, 580–586.

Fent, G.M., Casteel, S.W., Kim, D.Y., Kannan, R., Katti, K., Chanda, N., Katti, K., 2009. Bio distribution of maltose and gum Arabic hybrid gold nanoparticles after intravenous injection in juvenile swine. Nanomedicine 5, 128–135.

Fernandez-Lopez, S., Kim, H.S., Choi, E.C., Delgado, M., Granja, J.R., Khasanov, A., Kraehenbuehl, K., Long, G., Weinberger, D.A., Wilcoxen, K.M., 2001. Antibacterial agents based on the cyclic D, L-alpha-peptide architecture. Nature 412, 452–455.

Feugang, J.M., Youngblood, R.C., Greene, J.M., Fahad, A.S., Monroe, W.A., Willard, S.T., 2012. Application of quantum dot nanoparticles for potential non-invasive bio-imaging of mammalian spermatozoa. J. Nanobiotechnol. 10, 45–52.

Feugang, J.M., Youngblood, R.C., Greene, J.M., Willard, S.T., Ryan, P.L., 2015. Self-illuminating quantum dots for non-invasive bioluminescence imaging of mammalian gametes. J. Nanobiotechnol. 13 (38), 1–16.

Fondevilaa, M., Herrera, R., Casallasa, M.C., Abeciaa, L., Duchab, J.J., 2009. Silver nanoparticles as a potential antimicrobial additive for weaned pigs. Anim. Feed Sci. Technol. 150, 259–269.

Freitas, R.A., 2005. Microbivores: artifcial mechanical phagocytes using digest and discharge protocol. J. Evol. Technol. 14, 1–52.

Friedman, S.H., De Camp, D.L., Sijbesma, R.P., 1993. Inhibition of the HIV-1 protease by fullerene derivatives: model building studies and experimental verification. J. Am. Chem. Soc. 115, 6506–6509.

Gajbhiye, M., Kesharwani, J., Ingle, A., Gade, A., Rai, M., 2009. Fungus-mediated synthesis of silver nanoparticles and their activity against pathogenic fungi in combination with fluconazole. Nanomed. Nanotechnol. Biol. Med. 5, 382–386.

Gajjar, P., Pettee, B., Britt, D.W., Huang, W., Johnson, W.P., Anderson, J., 2009. Antimicrobial activities of commercial nanoparticles against an environmental soil microbe, *Pseudomonas putida* KT2440. J. Biol. Eng. 3, 9–22.

Gao, J.H., Li, L., Ho, P.L., Mak, G.C., Gu, H.W., Xu, B., 2006. Combining fluorescent probes and biofunctional magnetic nanoparticles for rapid detection of bacteria in human blood. Adv. Mater. 18, 3145–3148.

Gao, J.H., Zhang, B., Gao, Y., Pan, Y., Zhang, X.X., Xu, B., 2007a. Fluorescent magnetic nanocrystals by sequential addition of reagents in a one-pot reaction: a simple preparation for multifunctional nanostructures. J. Am. Chem. Soc. 129, 11928–11935.

Gao, J.H., Liang, G.L., Zhang, B., Kuang, Y., Zhang, X.X., Xu, B., 2007b. FePt@CoS_2 yolk-shell nanocrystals as a potent agent to kill HeLa cells. J. Am. Chem. Soc. 129, 1428–1433.

Gao, J.H., Liang, G.L., Cheung, J.S., Pan, Y., Kuang, Y., Zhao, F., Zhang, B., Zhang, X.X., Wu, E.X., Xu, B., 2008a. Multifunctional yolk-shell nanoparticles: a potential MRI contrast and anticancer agent. J. Am. Chem. Soc. 130, 11828–11833.

Gao, J.H., Zhang, W., Huang, P.B., Zhang, B., Zhang, X.X., Xu, B., 2008b. Intracellular spatial control of fluorescent magnetic nanoparticles. J. Am. Chem. Soc. 130, 3710–3711.

Ge, L., Li, Q., Wang, M., Ouyang, J., Li, X., Xing, M.M., 2014. Nanosilver particles in medical applications: synthesis, performance, and toxicity. Int. J. Nanomed. 9, 2399–2407.

Geszke-Moritz, M., Moritz, M., 2013. Quantum dots as versatile probes in medical sciences: synthesis, modification and properties. Korean J. Couns. Psychother. 33, 1008–1021.

Ghadi, A., Mahjoub, S., Tabandeh, F., Talebnia, F., 2014. Synthesis and optimization of chitosan nanoparticles: potential applications in nanomedicine and biomedical engineering. Caspian. J. Intern. Med. 5 (3), 156–161.

Gholami-Ahangaran, M., Zia-Jahromi, N., 2013. Nanosilver effects on growth parameters in experimental aflatoxicosis in broiler chickens. Toxicol. Ind. Health 29, 121–125.

Gholami-Ahangaran, M., Zia-Jahromi, N., 2014. Effect of nanosilver on blood parameters in chickens having aflatoxicosis. Toxicol. Ind. Health 30, 192–196.

Ghosh, D., Pramanik, A., Sikdar, N., Ghosh, S.K., Pramanik, P., 2010. Amelioration studies on optimization of low molecular weight chitosan nanoparticle preparation, characterization with potassium per sulfate and silver nitrate combined action with aid of drug delivery to tetracycline resistant bacteria. Int. J. Pharm. Sci. Drug Res. 2, 247–253.

Gibson, N.M., Luo, T.J., Brenner, D.W., Shenderova, O., 2011. Immobilization of mycotoxins on modified nanodiamond substrates. Biointerphases 6, 210–217.

Giri, S., Trewyn, B.G., Stellmaker, M.P., Lin, V.S.Y., 2005. Stimuli-responsive controlled-release delivery system based on mesoporous silica nanorods capped with magnetic nanoparticles. Angew. Chem. Int. Ed. 44, 5038–5044.

Gong, P., Li, H., He, X., Wang, K., Hu, J., Zhang, S., Yang, X., 2007. Preparation and antibacterial activity of Fe_3O_4@Ag nanoparticles. Nanotechnology 18 (28), 1000–1010.

Gonzales-Eguia, A., Fu, C., Lu, F., Lien, T., 2009. Effects of nanocopper on copper availability and nutrients digestibility, growth performance and serum traits of piglets. Livest. Sci. 126, 122–129.

Gordon, N., Sagman, U., 2003. Nanomedicine Taxonomy: Briefing Paper. Canadian Nanobusiness Alliance. February 2003.

Gradishar, W.J., Tjulandin, S., Davidson, N., Shaw, H., Desai, N., Bhar, P., Hawkins, M., O'Shaughnessy, J., 2005. Phase III trial of nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil-based paclitaxel in women with breast cancer. J. Clin. Oncol. 23, 7794–7803.

Greenwood, D.L.V., Dynonc, K., Kalkanidis, M., Sue, X., Plebanskid, M., Scheerlinck, J.Y., 2008. Vaccination against foot-and-mouth disease virus using peptides conjugated to nano-beads. Vaccine 26 (22), 2706–2713.

Gu, H.W., Ho, P.L., Tsang, K.W.T., Yu, C.W., Xu, B., 2003. Using biofunctional magnetic nanoparticles to capture Gram-negative bacteria at an ultra-low concentration. J. Am. Chem. Soc. 125 (51), 15702–15703.

Gu, H.W., Zheng, R.K., Zhang, X.X., Xu, B., 2004. Facile one-pot synthesis of bifunctional heterodimers of nanoparticles: a conjugate of quantum dot and magnetic nanoparticles. J. Am. Chem. Soc. 126, 5664–5665.

Gu, H.W., Xu, K.M., Yang, Z.M., Chang, C.K., Xu, B., 2005a. Synthesis and cellular uptake of porphyrin decorated iron oxide nanoparticles—a potential candidate for bimodal anticancer therapy. Chem. Commun. 9, 4270–4272.

Gu, H.W., Zheng, R.K., Liu, H., Zhang, X.X., Xu, B., 2005b. Direct synthesis of a bimodal nanosponge based on FePt and ZnS. Small 1, 402–406.

Gu, J., Wang, X., Nie, W., Wang, W., Shang, J., 2015. Potential role for carbon nanoparticles identification and preservation in situ of parathyroid glands during total thyroidectomy and central compartment node dissection. Int. J. Clin. Exp. Med. 8, 9640–9648.

Gupta, A.K., Gupta, M., 2005. Synthesis and surface engineering of iron oxide nanoparticles for biomedical applications. Biomaterials 26, 3995–4021.

Gurunathan, S., Kalishwaralal, K., Vaidyanathan, R., Venkataraman, D., Pandian, S.R., Muniyandi, J., Hariharan, N., Eom, S.H., 2009. Biosynthesis, purification and characterization of silver nanoparticles using *Escherichia coli*. Colloids Surf. B Biointerfaces 74, 328–335.

Gurunathan, S., Han, J.W., Kim, J.H., 2013. Green chemistry approach for the synthesis of biocompatible graphene. Int. J. Nanomedicine 8, 2719–2732.

Gurunathan, S., Han, J.W., Kwon, D.N., Kim, J.H., 2014. Enhanced antibacterial and antibiofilm activities of silver nanoparticles against Gram-negative and Gram-positive bacteria. Nanoscale Res. Lett. 9, 373.

Gurunathan, S., Han, J.W., Park, J.H., Kim, E., Choi, Y.J., Kwon, D.N., Kim, J.H., 2015. Reduced graphene oxide-silver nanoparticle nanocomposite: a potential anticancer nanotherapy. Int. J. Nanomedicine 10, 6257–6276.

Gurunathan, S., Choi, Y.J., Kim, J.H., 2018. Antibacterial efficacy of silver nanoparticles on endometritis caused by *Prevotella melaninogenica* and *Arcanobacterum pyogenes* in dairy cattle. Int. J. Mol. Sci. 19, 1210.

Haham, M., Ish-Shalom, S., Nodelman, M., Duek, I., Segal, E., Kustanovich, M., 2012. Stability and bioavailability of vitamin D nanoencapsulated in casein micelles. Food Funct. 3, 737–744.

Hahn, M.A., Tabb, J.S., Krauss, T.D., 2005. Detection of single bacterial pathogens with semiconductor quantum dots. Anal. Chem. 77, 4861–4869.

Halfpenny, K.C., Wright, D.W., 2010. Nanoparticle detection of respiratory infection. Wiley Interdiscip. Rev. Nanomed. Nanobiotechnol. 2, 277–290.

Hargreaves, C.A., Rogers, S., Hills, F., Rahman, F., Howell, R.J.S., Homa, S.T., 1998. Effects of co-trimoxazole, erythromycin, amoxycillin, tetracycline and chloroquine on sperm function in vitro. Hum. Reprod. 13, 1878–1886.

Hassan, A.A., Mansour, M.K., 2003. New trials of use of molasses and garlic extracts for competing mycotoxicosis. Kafr El-Sheikh Vet. Med. J. 1 (1), 653–680 (1st Sci. Congress, Fac. Vet. Med., Tanta University).

Hassan, A.A., El Shorbagy, M.M., El-Barawy, A.M., Hassan, M.A., 2008. Study the availability of using buckthorn (*Rhamnus cathartica*) plant extract in laboratory control of some bacterial and fungal diseases. 5th Sci. Cong. Minufiya Vet. J. 5 (1), 27–39.

Hassan, A.A., El-Mokhttar, N.M., Mansour, M.K., Hassan, R.A., Abdel Hadi, M., Lotfi, H.M., 2012a. Efficacy of use of forskolin plant extract in control of toxic effects of aflatoxicosis in food. J. Am. Sci. 8 (11), 225–236.

Hassan, A.A., Hassan, M.A., Sayed El Ahl, R.M.H., Darwish, A.S., 2012b. Prevalence of yeast infections in small ruminants with particular references to their treatment by some natural herbal extracts. Bull. Environ. Pharm. Life Sci. 1 (3), 12–22.

Hassan, A.A., El-Shafae, H., Mahmoud, H.H., 2013a. Effect of zinc oxide nanoparticles on the growth of mycotoxigenic mould. J. Stud. Chem. Process Technol. 1 (4), 66–74.

Hassan, A.A., Mansour, M.K., Mahmoud, H.H., 2013b. Biosynthesis of silver nanoparticles (Ag-NPs) (a model of metals) by *Candida albicans* and its antifungal activity on some fungal pathogens (*Trichophyton mentagrophytes* and *Candida albicans*). New York Sci. J. 6 (3), 27–34.

Hassan, A.A., Rashid, M.A., Oraby, N.H., El-Araby, K.S., Minshawy, M., 2013c. Using of molecular biology techniques for detection of *C. neoformance* in respiratory disorders in cow with references to its control by nanoparticles of iron oxide. Egypt. J. Appl. Sci. 28 (12), 433–448.

Hassan, A.A., Oraby, N.H., Mohamed, A.E., Mahmoud, H.H., 2014. The possibility of using zinc oxide nanoparticles in controlling some fungal and bacterial strains isolated from buffaloes. Egypt. J. Appl. Sci. 29, 58–83.

Hassan, A.A., Mahmoud, H.K., Taha, H., Sayed El-Ahl, R.H., Mahmoud, H.H., 2015a. Herbal biosynthesis of zinc nanoparticles and evaluation of their antifungal and antibacterial effect for buffaloes skin affections. Int. J. Curr. Res. 7 (12), 24338–24349.

Hassan, A.A., Oraby, N.H., El-Dahshan, E.M., Ali, M.A., 2015b. Antimicrobial potential of iron oxide nanoparticles in control of some causes of microbial skin affection in cattle. Eur. J. Acad. Essays 2 (6), 20–31.

Hassan, A.R., De la Escosura-Muñiz, A., Merkoçi, A., 2015c. Highly sensitive and rapid determination of *Escherichia coli* O157:H7 in minced beef and water using electrocatalytic gold nanoparticle tags. Biosens. Bioelectron. 67, 511–515.

Hassan, A.A., Mansour, M.K., Oraby, N.H., Mohamed, A.M., 2016a. The efficiency of using silver nanoparticles singly and in combination with traditional antimicrobial agents in control of some fungal and bacterial affection of buffaloes. Int. J. Curr. Res. 8 (04), 29758–29770.

Hassan, A.A., Mansour, K.M., Ibrahim, I.E., Sayed El-Ahl, R.H., Al-Kalamawey, N.M., El Kattan, Y.A., Ali, M.A., 2016b. Efficacy of zinc oxide nanoparticles and curcumin in amelioration the toxic effects in aflatoxicated rabbits. Int. J. Curr. Microbiol. Appl. Sci. 5 (12), 795–818.

Hassan, A.A., El-Mokhtar, N.M., El-Hamaky, A.M., 2017. Evaluation of the efficacy of Ozone fumigation and zinc oxide nanoparticles in control of aflatoxins contamination in cattle feeds. Anim. Health Res. J. 5 (4A), 165–180.

Hassan, A.A., Sayed El-Ahl, R.H., El Hamaky, A.M.A., Oraby, N.H., 2019. Chapter 23: Toxic and benefit effects of carbon nanomaterials on human and animal health. In: Carbon Nanomaterials for Agri-Food and Environmental Applications. Elsevier (in press).

Hasuwa, H., Muro, Y., Ikawa, M., Kato, N., Tsujimoto, Y., Okabe, M., 2010. Transgenic mouse sperm that have green acrosome and red mitochondria allow visualization of sperm and their acrosome reaction in vivo. Exp. Anim. 59, 105–107.

He, Y., Kang, Z.H., Li, Q.S., Tsang, C.H., Fan, C.H., Lee, S.T., 2009. Ultra stable, highly fluorescent, and water-dispersed silicon-based nanospheres as cellular probes. Angew. Chem. Int. Ed. Engl. 48, 128–132.

Hill, E.K., Li, J., 2017. Current and future prospects for nanotechnology in animal production. J. Anim. Sci. Biotechnol. 8 (1), 26–40.

Hirsch, L.R., Stafford, R.J., Bankson, J.A., 2003. Nanoshell-mediated near-infrared thermal therapy of tumors under magnetic resonance guidance. Proc. Natl. Acad. Sci. U. S. A. 100 (23), 13549–13554.

Hiszczyńska-Sawicka, E., Li, H., Boyu, X.J., Akhtar, M., Holec-Gasior, L., Kur, J., Bickerstaffe, R., Stankiewicz, M., 2012. Induction of immune responses in sheep by vaccination with liposome-entrapped DNA complexes encoding *Toxoplasma gondii* MIC3 gene. Pol. J. Vet. Sci. 15, 3–9.

Hofheinz, R.D., Gnad-Vogt, S.U., Beyer, U., Hochhaus, A., 2005. Liposomal encapsulated anti-cancer drugs. Anticancer Drugs 16 (7), 691–707.

Hom, C., Lu, J., Tamanoi, F., 2009. Silica nanoparticles as a delivery system for nucleic acid based reagents. J. Mater. Chem. 19, 6308–6316.

Honda-Okubo, Y., Saade, F., Petrovsky, N., 2012. Advax™, a polysaccharide adjuvant derived from delta inulin, provides improved influenza vaccine protection through broad-based enhancement of adaptive immune responses. Vaccine 30, 5373–5381.

Honda-Okubo, Y., Barnard, D., Ong, C.H., Peng, B.H., Tseng, C.T., Petrovsky, N., 2015. Severe acute respiratory syndrome-associated coronavirus vaccines formulated with delta inulin adjuvants provide enhanced protection while ameliorating lung eosinophilic immunopathology. J. Virol. 89, 2995–3007.

Hosseini, S.S., Roudbar, M.S., Joshaghani, H.R., Eskandari, M., 2011. Antifungal effect of sodium dodecil sulfate and nano particle ZnO on growth inhibition of standard strain of *Candida albicans*. J. Gorgan Univ. Med. Sci. 12 (4), 200–205.

Hötzer, B., Medintz, I.L., Hildebrandt, N., 2012. Fluorescence in nanobiotechnology: sophisticated fluorophores for novel applications. Small 8, 2297–2326.

Hu, S., Zhang, Y., 2010. Endostar-loaded PEG-PLGA nanoparticles: in vitro and in vivo evaluation. Int. J. Nanomedicine 5, 1039–1048.

Huang, S., Chen, J.C., Hsu, C.W., Chang, W.H., 2009. Effects of nano calcium carbonate and nano calcium citrate on toxicity in ICR mice and on bone mineral density in an ovariectomized mice model. Nanotechnology 20, 375102–375110.

Hunsawong, T., Sunintaboon, P., Warit, S., Thaisomboonsuk, B., Jarman, R.G., Yoon, I.K., Ubol, S., Fernandez, S., 2015. Immunogenic properties of a BCG adjuvant chitosan nanoparticle-based dengue vaccine in human dendritic cells. PLoS Negl. Trop. Dis. 9 (9), 1–18.

Igor, I., Slowing, B., Trewyn, G., Giri, S., Victor, S., Lin, Y., 2007. Mesoporous silica nanoparticles for drug delivery and bios. Appl. Adv. Funct. Mater. 17, 1225–1236.

Jahani, Z., Meshgi, B., Rajabi-Bzl, M., Jalousian, F., Hasheminasab, S., 2014. Improved serodiagnosis of hydrated cyst disease using gold nanoparticle labeled antigen B in naturally infected sheep. Iran. J. Parasitol. 9, 218–925.

Jalal, A., Rashid, N., Ahmed, N., Iftikhar, S., Akhtar, M., 2011. *Escherichia coli* signal peptidase recognizes and cleaves the signal sequence of xylanase from a newly isolated *Bacillus subtilis* strain R5. Biochemistry 76, 347–349.

Jiang, W., Liu, Y., Chen, Y., Yang, Q., Chun, P., Yao, K., Han, X., Wang, S., Yu, S., Liu, Y., 2015. A novel dynamic flow immunochromatographic test (DFICT) using gold nanoparticles for the serological detection of *Toxoplasma gondii* infection in dogs and cats. Biosens. Bioelectron. 72, 133–139.

Jin, T., Sun, D., Su, J.Y., Zhang, H., Sue, H.J., 2009. Antimicrobial efficacy of zinc oxide quantum dots against *Listeria monocytogenes*, *Salmonella enteritidis*, and *Escherichia coli* O157:H7. J. Food Sci. 74, 46–52.

Johnston, M.J., Semple, S.C., Klimuk, S.K., Ansell, S., Maurer, N., Cullis, P.R., 2007. Characterization of the drug retention and pharmacokinetic properties of liposomal nanoparticles containing dihydrosphinomyelin. Biochim. Biophys. Acta 1768, 1121–1127.

Juan, L., Vivero, E., Huang, Y.T., 2011. Inorganic-organic hybrid nanomaterials for therapeutic and diagnostic imaging applications. Int. J. Mol. Sci. 12, 3888–3927.

Kaesermann, F., Kempf, C., 1997. Photodynamic inactivation of enveloped viruses by buckminsterfullerene. Antiviral Res. 34, 65–70.

Kaittanis, C., Naser, S.A., Perez, J.M., 2007. One-step, nanoparticle- mediated bacterial detection with magnetic relaxation. Nano Lett. 7, 380–383.

Kaittanis, C., Nath, S.A., Perez, J.M., 2008. Rapid nanoparticle-mediated monitoring of bacterial metabolic activity and assessment of antimicrobial susceptibility in blood with magnetic relaxation. PLoS ONE 3 (9). e3253.

Kaittanis, C., Santra, S., Perez, J.M., 2010. Emerging nanotechnology-based strategies for the identification of microbial pathogenesis. Adv. Drug Deliv. Rev. 62, 408–423.

Kam, N.W.S., O'Connell, M., Wisdom, J.A., Dai, H., 2005. Carbon nanotubes as multifunctional biological transporters and near-infrared agents for selective cancer cell destruction. Proc. Natl. Acad. Sci. U. S. A. 102 (33), 11600–11605.

Kang, B.K., Chon, S.K., Kim, S.H., Jeong, S.Y., Kim, M.S., Cho, S.H., 2004. Controlled release of paclitaxel from microemulsion containing PLGA and evaluation of anti-tumor activity in vitro and in vivo. Int. J. Pharm. 286, 147–156.

Kang, S., Pinault, M., Pfefferle, L.D., Elimelech, M., 2007. Single-walled carbon nanotubes exhibit strong antimicrobial activity. Langmuir 23 (17), 8670–8673.

Kang, S., Mauter, M.S., Elimelech, M., 2009. Microbial cytotoxicity of carbon based nanomaterials: implications for river water and wastewater effluent. Environ. Sci. Technol. 43 (7), 2648–2653.

Kaul, R.K., Kumar, P., Burman, U., Joshi, P., Agrawal, A., Raliya, R., Tarafdar, G.C., 2012. Magnesium and iron nanoparticles production using microorganisms and various salts. Mater. Sci.-Pol. 30 (3), 254–258.

Kende, M., Alving, C.R., Rill, W.L., Swartz, G.M., Canonico, P.G., 1985. Enhanced efficacy of liposome-encapsulated ribavirin against Rift Valley fever virus infection in mice. Antimicrob. Agents Chemother. 27, 903–937.

Khalid, P., Hussain, S.A., Suman, A.V., Arun, A.B., 2016. Toxicology of carbon nanotubes—a review. Int. J. Appl. Eng. Res. 11 (1), 148–157.

Khan, M.A., Nasti, T.H., Owais, M., 2005. Incorporation of amphotericin B in tuftsin-bearing liposomes showed enhanced efficacy against systemic cryptococcosis in leucopenic mice. J. Antimicrob. Chemother. 56, 726–731.

Khandelwal, N., Kaur, G., Chaubey, K.K., Singh, P., Sharma, S., Tiwari, A., Singh, S.V., Kumar, N., 2014. Silver nanoparticles impair Peste des petits ruminant's virus replication. Virus Res. 190, 1–7.

Kheiri, A., Moosawi, S.A., Malihipour, A., Saremi, H., Nikkhah, M., 2016. Application of chitosan and chitosan nanoparticles for the control of *Fusarium* head blight of wheat *Fusarium graminearum* in vitro and greenhouse. Int. J. Biol. Macromol. 93 (A), 1261–1272.

Kim, Y., Zimmerman, S.C., 1998. Applications of dendrimers in bio-organic chemistry. Curr. Opin. Chem. Biol. 2, 733–742.

Kim, H., Achermann, M., Balet, L.P., Hollingsworth, J.A., Klimov, V.I., 2005. Synthesis and characterization of Co/CdSe core/shell nanocomposites: bifunctional magnetic-optical nanocrystals. J. Am. Chem. Soc. 127, 544–546.

Kim, S., Ohulchanskyy, T.Y., Pudavar, H.E., Pandey, R.K., Prasad, P.N., 2007. Organically modified silica nanoparticles co-encapsulating photosensitizing drug and aggregation-enhanced two-photon absorbing fluorescent dye aggregates for two photon photodynamic therapy. J. Am. Chem. Soc. 129, 2669–2675.

Kim, K.J., Sung, W.S., Moon, S.K., Choi, J.S., Kim, J.G., Lee, D.G., 2008. Antifungal effect of silver nanoparticles on dermatophytes. J. Microbiol. Biotechnol. 18, 1482–1484.

Kim, C.K., Ghosh, P., Rotello, V.M., 2009. Multimodal drug delivery using gold nanoparticles. Nanoscale 1, 61–67.

Klajnert, B., Bryszewska, M., 2001. Dendrimers: properties and applications. Acta Biochim. Pol. 48, 199–208.

Kleiter, M., Tichy, A., Willmann, M., Pagitz, M., Wolfesberger, B., 2010. Concomitant liposomal doxorubicin and daily palliative radiotherapy in advanced feline soft tissue sarcomas. Vet. Radiol. Ultrasound 51, 349–355.

Koda, S., Inoue, Y., Iwata, H., 2008. Gene transfection into adherent cells using electroporation on a dendrimer-modified gold electrode. Langmuir 24, 13525–13531.

Koedrith, P., Thasiphu, T., Weon, J.I., Boonprasert, R., Tuitemwong, K., Tuitemwong, P., 2015. Recent trends in rapid environmental monitoring of pathogens and toxicants: potential of nanoparticle-based biosensor and applications. Sci. World J. 510982, 1–12.

Kolecka, M.A., Arnhold, S., Schmidt, M., Reich, C., Kramer, M., Failing, K., Von Pückler, K., 2017. Behavior of adipose-derived canine mesenchymal stem cells after superparamagnetic iron oxide nanoparticles labeling for magnetic resonance imaging. BMC Vet. Res. 13 (1), 62.

Koo, O.M., Rubinstein, I., Onyuksel, H., 2005. Role of nanotechnology in targeted drug delivery and imaging: a concise review. Nanomedicine 1, 193–212.

Krawiec, D.R., McKiernan, B.C., Twardock, A.R., Swenson, C.E., Itkin, R.J., Johnson, L.R., Kurowsky, L.K., Marks, C.A., 1996. Use of an amphotericin B lipid complex for treatment of blastomycosis in dogs. J. Am. Vet. Med. Assoc. 209, 2073–2075.

Kroubi, M., Daulouede, S., Karembe, H., Jallouli, Y., Howsam, M., Mossalayi, D., Vincendeau, P., Betbeder, D., 2010. Development of a nanoparticulate formulation of diminazene to treat African trypanosomiasis. Nanotechnology 21 (50), 1–8.

Kurantowicz, N., Strojny, B., Sawosz, E., Jaworski, S., Kutwin, M., Grodzik, M., 2015. Biodistribution of a high dose of diamond, graphite, and graphene oxide nanoparticles after multiple intraperitoneal injections in rats. Nanoscale Res. Lett. 10, 398–405.

Kuswandi, B., Futra, D., Heng, L.Y., 2017. Chapter 15—Nanosensors for the detection of food contaminants. In: Nanotechnology Applications in Food, pp. 307–333. https://doi.org/10.1016/B978-0-12-811942-6.00015-7.

Lai, C.Y., Trewyn, B.G., Jeftinija, D.M., Jeftinija, K., Xu, S., Jeftinija, S., Lin, V.S.Y., 2003. A mesoporous silica nanosphere-based carrier system with chemically removable CdS nanoparticle caps for stimuli-responsive controlled release of neurotransmitters and drug molecules. J. Am. Chem. Soc. 125, 4451–4459.

Lam, C.W., James, J.T., McCluskey, R., Hunter, R.L., 2004. Pulmonary toxicity of single wall carbon nanotubes in mice 7 and 90 days after intratracheal instillation. Toxicol. Lett. 77 (1), 126–134.

Lambros, M.P., Bourne, D.W., Abbas, S.A., Johnson, D.L., 1997. Disposition of aerosolized liposomal amphotericin B. J. Pharm. Sci. 86, 1066–1069.

Lara, H.H., Ayala-Núnez, N.V., Turrent, L.C.I., Padilla, C.R., 2010. Bacteriicidal effect of silver nanoparticles against multidrug-resistant. World J. Microbiol. Biotechnol. 26, 615–621.

Lawlor, C., O'Connor, G., O'Leary, S., Gallagher, P.J., Cryan, S.A., Keane, J., O'Sullivan, M.P., 2016. Treatment of mycobacterium tuberculosis-infected macrophages with poly (lactic-co-glycolic acid) microparticles drives NFκB and autophagy dependent bacillary killing. PLoS ONE 11. e0149167.

Le Croy, G.E., Yang, S.T., Yang, F., Liu, Y., Fernando, K.S., Bunker, C.E., Sun, Y.P., 2016. Functionalized carbon nanoparticles: syntheses and applications in optical bioimaging and energy conversion. Coord. Chem. Rev. 320, 66–81.

Lebre, F., Borchard, G., Faneca, H., Lima, M.C., Borges, O., 2016. Intranasal administration of novel chitosan nanoparticle/DNA complexes induces antibody response to hepatitis B surface antigen in mice. Mol. Pharm. 13, 472–482.
Lee, K.T., 2010. Quality and safety aspects of meat products as affected by various physical manipulations of packaging materials. Meat. Sci. 86, 138–150.
Lee, A.L., Wang, Y., Pervaiz, S., Fan, W., Yang, Y.Y., 2011a. Synergistic anticancer effects achieved by co-delivery of TRAIL and paclitaxel using cationic polymeric micelles. Macromol. Biosci. 11, 296–307.
Lee, K.G., Kim, J.C., Wi, R., Min, J.S., Ahn, J.K., Kim, D.H., 2011b. Synthesis of stable silica-dye hybrid nanomaterial as DNA carrier. J. Nanosci. Nanotechnol. 11, 686–690.
Lee, C., Kim, J., Zhang, Y., Jeon, M., Liu, C., Song, L., Lovell, J.F., Kim, C., 2015. Dual-color photoacoustic lymph node imaging using nanoformulated naphthalocyanines. Biomaterials 73, 142–148.
Leenders, A.C., De Marie, S., 1996. The use of lipid formulations of amphotericin B for systemic fungal infections. Leukemia 10, 1570–1575.
Leroux, J.C., 2007. Injectable nanocarriers for biodetoxification. Nat. Nanotechnol. 2, 679–684.
Li, X.D., Gao, J.Y., Yang, Y., 2013. Nanomaterials in the application of tumor vaccines: advantages and disadvantages. OncoTargets Ther. 6, 629–634.
Li, Z., Ao, S., Bu, Z., Wu, A., Wu, X., Shan, F., Ji, X., Zhang, Y., Xing, Z., Ji, J., 2016. Clinical study of harvesting lymph nodes with carbon nanoparticles in advanced gastric cancer: a prospective randomized trial. World J. Surg. Oncol. 14 (1), 88–100.
Li, Y., Zheng, X., Zhang, X., Liu, S., Pei, Q., Zheng, M., Xie, Z., 2017. Porphyrin-based carbon dots for photodynamic therapy of hepatoma. Adv. Healthc. Mater. 6. 1600924-333333.
Liandris, E., Gazouli, M., Andreadou, M., Sechi, L.A., Rosu, V., Ikonomopoulos, J., 2011. Detection of mycobacteria based on functionalized quantum dots coupled with immunomagnetic separation. PLoS ONE 6, e20026.
Lina, T., Jianyang, J., Fenghua, Z., Huiying, R., Wenli, L., 2009. Effect of nano-zinc oxide on the production and dressing performance of broiler. Chin. Agric. Sci. Bull. 2 (3), 831–840.
Liu, S., Wei, L., Hao, L., Fang, N., Chang, M.W., Xu, R., Yang, Y., Chen, Y., 2009. Sharper and faster nano darts kill more bacteria: a study of antibacterial activity of individually dispersed pristine single-walled carbon nanotube. ACS Nano 3 (12), 3891–3902.
Liu, R., Zhang, Y., Zhao, X., Agarwal, A., Mueller, L.J., Feng, P., 2010. pH-responsive nanogated ensemble based on gold-capped mesoporous silica through an acid-labile acetal linker. J. Am. Chem. Soc. 132, 1500–1501.
Liu, Y., Zhao, B., Sun, B., Chen, C., 2013. Understanding the toxicity of carbon nanotubes. Acc. Chem. Res. 46, 702–713.
Liu, Z., Zhu, Y., Liu, X., Yeung, K.W., Wu, S., 2017. Construction of poly (vinyl alcohol)/poly (lactide-glycolide acid)/vancomycin nanoparticles on titanium for enhancing the surface self-antibacterial activity and cytocompatibility. Colloids Surf. B Biointerfaces 151, 165–177.
Long, J.Z., Lackan, C.S., Hadjantonakis, A.K., 2005. Genetic and spectrally distinct in vivo imaging: embryonic stem cells and mice with widespread expression of a monomeric red fluorescent protein. BMC Biotechnol. 5, 1–11.
Long, Q., Li, J., Luo, Q., Hei, Y., Wang, K., Tian, Y., Yang, J., Lei, H., Qiu, B., Liu, W., 2015. MRI tracking of bone marrow mesenchymal stem cells labeled with ultra-small superparamagnetic iron oxide nanoparticles in a rat model of temporal lobe epilepsy. Neurosci. Lett. 606, 30–35.

Lopes, D., Romana, D., Brown, K.H., Guinard, J.X., 2002. Sensory trial to assess the acceptability of zinc fortificants added to iron-fortified wheat products. J. Food Sci. 67, 461–465.
Lu, J., Bowles, M., 2013. How will nanotechnology affect agricultural supply chains. Int. Food Agribus. Man. 16, 21–42.
Lu, J.X., Prudhommeaux, F., Meuier, A., Sedel, L., Guillemin, G., 1999. Effects of chitosan on rat knee cartilages. Biomaterials 20, 1937–1944.
Lu, J., Liong, M., Li, Z., Zink, J.I., Tamanoi, F., 2010. Biocompatibility, biodistribution, and drug-delivery efficiency of mesoporous silica nanoparticles for cancer therapy in animals. Small 6, 1794–1805.
MacLeod, D.L., Prescott, J.F., 1988. The use of liposomally-entrapped gentamicin in the treatment of bovine *Staphylococcus aureus* mastitis. Can. J. Vet. Res. 52, 445–450.
Makabi-Panzu, B., Lessard, C., Perron, S., Désormeaux, A., Tremblay, M., Poulin, L., Beauchamp, D., Bergeron, M.G., 1994. Comparison of cellular accumulation, tissue distribution, and anti-HIV activity of free and liposomal 2t, 3t-dideoxycytidine. AIDS Res. Hum. Retroviruses 10, 1463–1470.
Malam, Y., Loizidou, M., Seifalian, A.M., 2009. Liposomes and nanoparticles: nanosized vehicles for drug delivery in cancer. Trends Pharmacol. Sci. 30, 592–599.
Malathi, B., Mona, S., Thiyagarajan, D., Kaliraj, P., 2015. Immunopotentiating nano-chitosan as potent vaccine carter for efficacious prophylaxis of filarial antigens. Int. J. Biol. Macromol. 73, 131–713.
Margerum, L.D., Campion, B.K., Koo, M., Shargill, N., Lai, J.J., Marumoto, A., Sontum, P.C., 1997. Gadolinium(III) DO3A macrocycles and polyethylene glycol coupled to dendrimers effect of molecular weight on physical and biological properties of macromolecular magnetic resonance imaging contrast agents. J. Alloys Compd. 249, 185–190.
Maša, P.R., 2016. Nanotechnology in food safety and quality assessment: potentiality of nanoparticles in diagnosis of foodborne pathogens. Agricultura 13 (1–2), 21–32.
Matei, E., Enculescu, I., Vasilache, V., Teodorescu, C.M., 2010. Cobalt doped ZnO prepared by electrochemistry: chemistry, morphology, and magnetism. Phys. Status Solidi 207 (11), 2517–2522.
Maynard, A.D., 2006. Nanotechnology: assessing the risks. Nano Today 1 (2), 2–33.
McComb, T., Bischoff, K., Thompson, B., Smith, M.C., Mohammed, H.O., Ebel, J., Hillebrandt, J., 2010. An investigation of blood selenium concentrations of goats in New York State. J. Vet. Diagn. Invest. 22, 696–701.
Meena, N.S., Sahni, Y.P., Thakur, D., Singh, R.P., 2018. Applications of nanotechnology in veterinary therapeutics. J. Entomol. Zool. Stud. 6 (2), 167–175.
Meng, K., Sun, W., Zhao, P., Zhang, L., Cai, D., Cheng, Z., Guo, H., Liu, J., Yang, D., Wang, S., 2014. Development of colloidal gold-based immunochromatographic assay for rapid detection of *Mycoplasma suis* in porcine plasma. Biosens. Bioelectron. 55, 396–399.
Michalet, X., Pinaud, F.F., Bentolila, L.A., Tsay, J.M., Doose, S., Li, J.J., Sundaresan, G., Wu, A.M., Gambhir, S.S., Weiss, S., 2005. Quantum dots for live cells, in vivo imaging, and diagnostics. Science 307, 538–544.
Mintzer, M.A., Simanek, E.E., 2009. Nonviral vectors for gene delivery. Chem. Rev. 109, 259–302.
Mishima, F.T.S., Izumi, Y., Nishijima, S., 2007. Development of magnetic field control for magnetically targeted drug delivery system using a superconducting magnet. IEEE Trans. Appl. Supercond. 17, 2303–2306.

Mishra, B., Patel, B.B., Tiwari, S., 2009. Colloidal nanocarriers: a review on formulation technology, types and applications toward targeted drug delivery. Nanomedicine 6, 9–24.
Mishra, A., Swain, R.K., Mishra, S.K., Panda, N., Sethy, K., 2014. Growth performance and serum biochemical parameters as affected by nano zinc supplementation in layer chicks. Indian J. Anim. Nutr. 31, 384–388.
Mody, V.V., Siwale, R., Singh, A., Mody, H.R., 2010. Introduction to metallic nanoparticles. J. Pharm. Bioallied Sci. 2, 282–289.
Moghimi, S., 2005. Nanomedicine: prospective diagnostic and therapeutic potential. Asia Pac. Biotech News 9, 1072–1077.
Mohamed, T., Matou-Nasri, S., Farooq, A., Whitehead, D., Azzawi, M., 2017. Polyvinylpyrrolidone-coated gold nanoparticles inhibit endothelial cell viability, proliferation, and ERK1/2 phosphorylation and reduce the magnitude of endothelial-independent dilator responses in isolated aortic vessels. Int. J. Nanomedicine 12, 8813–8830.
Mohanty, N.N., Palai, T.K., Prusty, B.R., Mohapatra, J.K., 2014. An overview of nanomedicine in veterinary science. Vet. Res. Int. 2, 90–95.
Monerris, M.J., Arévalo, F.J., Fernández, H., Zon, M.A., Molina, P.G., 2012. Integrated electrochemical immunosensor with gold nanoparticles for the determination of progesterone. Sens. Actuators B 166, 586–592.
Monteiro-Riviere, N.A., Inman, A.O., Ryman-Rasmussen, J.P., 2007. Dermal effects of nanomaterials. In: Monteiro-Riviere, N.A., Tran, C.L. (Eds.), Nanotoxicology—Characterization, Dosing and Health Effects. Informa Healthcare, New York, USA.
Moongkarndi, P., Rodpai, E., Kanarat, S., 2011. Evaluation of an immunochromatographic assay for rapid detection of *Salmonella enterica* serovars typhimurium and enteritidis. J. Vet. Diagn. Invest. 23, 797–801.
Moraru, C.I., Panchapakesan, C.P., Huang, Q., Takhistove, P., Liu, S., Kokini, J.L., 2003. Nanotechnology: a new frontier in food science. Food Technol. 57 (12), 24–29.
Moreno-Vega, A.I., Gómez-Quintero, T., Nuñez-Anita, R.E., Acosta-Torres, L.S., Castaño, V., 2012. Polymeric and ceramic nanoparticles in biomedical applications. J. Nanotechnol. 2012, 1–10.
Mouhamed, A.E., Hassan, A.A., Hassan, M.A., El Hariri, M., Refai, M.K., 2015. Effect of metal nanoparticles on the growth of ochratoxigenic moulds and ochratoxin A production isolated from food and feed. Int. J. Res. Stud. Biosci. 3 (9), 1–14.
Muktar, Y., Bikila, T., Keffale, M., 2015. Application of nanotechnology for animal health and production improvement: a review. World Appl. Sci. J. 33 (10), 1588–1596.
Muller, J., Decordier, I., Hoet, P.H., Lombaert, N., Thomassen, L., Huaux, F., Lison, D., Kirsch-Volders, M., 2008. Clastogenic and aneugenic effects of multi-wall carbon nanotubes in epithelial cells. Carcinogenesis 29, 427–433.
Na, H.B., Hyeon, T., 2009. Nanostructured T1 MRI contrast agents. J. Mater. Chem. 19, 6267–6273.
Nabawy, G.A., 2015. Effect of Metal Element Nanoparticles in the Growth of Aflatoxogenic *A. flavus* and Aflatoxin Production in Feed. Master thesis in Veterinary Science (Microbiology), Faculty of Veterinary Medicine, Cairo University.
Nabawy, G.A., Hassan, A.A., Sayed El-Ahl, R.H., Refai, M.K., 2014. Effect of metal nanoparticles in comparison with commercial antifungal feed additives on the growth of *A. flavus* and aflatoxin B1 production. J. Global Biosci. 3 (6), 954–971.
Narducci, D., 2007. An introduction to nanotechnologies: what's in it for us? Vet. Res. Commun. 1, 131–137.

National Nanotechnology Initiative, 2006. Available from: http://www.nano.gov/html/facts/whatIsNano.html. (Accessed 15 May 2006).

Neethirajan, S., Tuteja, S.K., Huang, S.T., Kelton, D., 2017. Recent advancement in biosensors technology for animal and livestock health management. Biosens. Bioelectron. 98, 398–407.

Neuberger, T., Schopf, B., Hofmann, H., Hofmann, M., Von-Rechenberg, B., 2005. Superparamagnetic nanoparticles for biomedical applications: possibilities and limitations of a new drug delivery system. J. Magn. Magn. Mater. 293, 483–496.

Novoselov, K.S., 2004. Development and Applications of Mesoscopic Hall Microprobes. Ph.D. thesis, Radboud University Nijmegen, Nijmegen, Netherlands.

Nurkiewicz, T.R., Porter, D.W., Hubbs, A.F., Cumpston, J.L., Chen, B.T., Frazer, D.G., Castranova, V., 2008. Nanoparticle inhalation augments particle-dependent systemic microvascular dysfunction. Part. Fibre Toxicol. 5, 1. https://doi.org/10.1186/1743-8977-5-1.

Nurulfiza, I., Hair-Bejo, M., Omar, A.R., Aini, I., 2011. Immunochromatographic gold-based test strip for rapid detection of infectious bursal disease virus antibodies. J. Vet. Diagn. Invest. 23, 320–324.

O'Connell, M.J., Bachilo, S.M., Huffaman, C.B., Moore, V.C., Strano, M.S., Haroz, E.H., Rialon, K.L., Boul, P.J., Noon, W.H., Kittrell, C., Ma, J., Hauge, R.H., Weisman, R.B., Smalley, R.E., 2002. Band gap fluorescence from individual singlewalled carbon nanotubes. Science 297 (5581), 593–596. planning workshop, 18–19 November, Forum (Wash.).

Oberdörster, G., Kuhlbusch, T.A.J., 2018. In vivo effects: methodologies and biokinetics of inhaled nanomaterials. NanoImpact 10, 38–60.

Oberdörster, G., Sharp, Z., Atudorei, V., Elder, A., Gelein, R., Kreyling, W., Cox, C., 2004. Translocation of inhaled ultrafine particles to the brain. Inhal. Toxicol. 16 (6–7), 437–445.

Oberoi, H.S., Yorgensen, Y.M., Morasse, A., Evans, J.T., Burkhart, D.J., 2016. PEG modified liposomes containing CRX-601 adjuvant in combination with methylglycol chitosan enhance the murine sublingual immune response to influenza vaccination. J. Control. Release 223, 64–74.

Odhiambo, J.F., DeJarnette, J.M., Geary, T.W., Kennedy, C.E., Suarez, S.S., Sutovsky, M., 2014. Increased conception rates in beef cattle inseminated with nanopurified bull semen. Biol. Reprod. 91, 1–10.2.

Parlane, N.A., Compton, B.J., Hayman, C.M., Painter, G.F., Basaraba, R.J., Heiser, A., Buddle, B.M., 2012. Phosphatidylinositol di-mannoside and derivates modulate the immune response to and efficacy of a tuberculosis protein vaccine against *Mycobacterium bovis* infection. Vaccine 30, 580–588.

Partha, S., Swain, D., Rajendran, S.B.N., Rao, Dominic, G., 2015. Preparation and effects of nano mineral particle feeding in livestock: a review. Vet. World 8, 888–891. 8/July-2015/12.pdf.

Parvongnukul, K., Lumb, W.V., 1978. Evaluation of polytetrafluoroethylene-graphite-coated total hip prostheses in goats. Am. J. Vet. Res. 39, 221–228.

Patel, D.V., Singh, S.P., Shukla, H.R., Devanand, C.P., Kasiraj, R., 2010. Superovulatory response to FSH and embryo recovery rate in *Pandharpuri buffaloes* (*Bubalus bubalis*). Buffalo Bull. 29 (4), 244–249.

Patolsky, F., Zheng, G., Hayden, O., Lakadamyali, M., Zhuang, X., Lieber, C.M., 2004. Electrical detection of single viruses. Proc. Natl. Acad. Sci. U. S. A. 101, 14017–14022.

Pawar, K., Kaul, G., 2012. Toxicity of titanium oxide nanoparticles causes functionality and DNA damage in buffalo (*Bubalus bubalis*) sperm in vitro. Toxicol. Ind. Health. https://doi.org/10.1177/0748233712462475.

Peer, D., Karp, J.M., Hong, S., Farokhzad, O.C., Margalit, R., Langer, R., 2007. Nanocarriers as an emerging platform for cancer therapy. Nat. Nanotechnol. 2, 751–760.

Pekkanen, J., Peters, A., Hoek, G., Tiittanen, P., Brunekreef, B., de Hartog, J., Heinrich, J., Ibald-Mulli, A., Kreyling, W.G., Lanki, T., Timonen, K.L., Vanninen, E., 2002. Particulate air pollution and risk of ST-segment depression during repeated submaximal exercise tests among subjects with coronary heart disease: the Exposure and Risk Assessment for Fine and Ultrafine Particles in Ambient Air (ULTRA) study. Circulation 106 (8), 933–938.

Peled, N., Ionescu, R., Nol, P., Barash, O., McCollum, M., VerCauteren, K., Koslow, M., Stahl, R., Rhyan, J., Haick, H., 2012. Detection of volatile organic compounds in cattle naturally infected with *Mycobacterium bovis*. Sens. Actuators B 40 (171–172), 588–594.

Peng, S., Sun, S.H., 2007. Synthesis and characterization of monodisperse hollow Fe_3O_4 nanoparticles. Angew. Chem. Int. Ed. 46, 4155–4158.

Peng, F., Wang, Z., Zhang, S., Wu, R., Hu, S., Li, Z., Wang, X., Bi, D., 2008. Development of an immunochromatographic strip for rapid detection of H9 subtype avian influenza viruses. Clin. Vaccine Immunol. 15, 569–574.

Peniche, H., Peniche, C., 2011. Chitosan nanoparticles: a contribution to nanomedicine. Polym. Int. 60, 883–909.

Petrovsky, N., Cooper, P.D., 2015. Advax™, a novel microcrystalline polysaccharide particle engineered from delta inulin, provides robust adjuvant potency together with tolerability and safety. Vaccine 33, 5920–5926.

Petruska, P., Capcarova, M., Sutovsky, P., 2014. Antioxidant supplementation and purification of semen for improved artificial insemination in livestock species. Turk. J. Vet. Anim. Sci. 38, 643–652.

Petryayeva, E., Algar, W.R., Medintz, I.L., 2013. Quantum dots in bioanalysis: a review of applications across various platforms for fluorescence spectroscopy and imaging. Appl. Spectrosc. 67, 215–252.

Pineda, L., Chwalibog, A., Sawosz, E., Lauridsen, C., Engberg, R., Elnif, J., Hotowy, A., Sawosz, F., Gao, Y., Ali, A., 2012. Effect of silver nanoparticles on growth performance, metabolism and microbial profile of broiler chickens. Arch. Anim. Nutr. 66, 416–429.

Powles, L., Xiang, S.D., Selomulya, C., Plebanski, M., 2015. The use of synthetic carriers in malaria vaccine design. Vaccine 3, 894–929.

Qiao, C., Liu, J., Yang, J., Li, Y., Weng, J., Shao, Y., Zhang, X., 2016. Enhanced non-inflammasome mediated immune responses by mannosylated zwitterionic-based cationic liposomes for HIV DNA vaccines. Biomaterials 85, 1–17.

Radin, S., Ducheyne, P., Kamplain, T., Tan, B.H., 2001. Silica sol-gel for the controlled release of antibiotics. I. Synthesis, characterization, and in vitro release. J. Biomed. Mater. Res. 57, 313–320.

Radomski, A., Jurasz, P., Alonso-Escolano, D., Drews, M., Morandi, M., Malinski, T., Radomski, M.W., 2005. Nanoparticle-induced platelet aggregation and vascular thrombosis. Br. J. Pharmacol. 146 (6), 882–893.

Radu, D.R., Lai, C.Y., Jeftinija, K., Rowe, E.W., Jeftinija, S., Lin, V.S.Y., 2004. A polyamidoamine dendrimer-capped mesoporous silica nanosphere-based gene transfection reagent. J. Am. Chem. Soc. 126, 13216–13217.

Raguvaran, R., Anju, M., Balvinder, K.M., 2015. Zinc oxide nanoparticles: opportunities and challenges in veterinary sciences. Immunol. Res. 11 (2), 2–8.

Rahimi, E., 2013. Lead and cadmium concentrations in goat, cow, sheep, and buffalo milks from different regions of Iran. Food Chem. 136, 389–391.

Rajendran, D., Kumar, G., Ramakrishnan, S., Thomas, K.S., 2013. Enhancing the milk production and immunity in Holstein Friesian crossbred cow by supplementing novel nano zinc oxide. Res. J. Biotechnol. 8, 11–17.

Ravi, M., Kumar, M.N.V., Sameti, M., Mohapatra, S.S., Kong, X., Lockey, R.F., Bakowsky, U., Lindenblatt, G., Schmidt, H., Lehr, C.M., 2004. Cationic silica nanoparticles as gene carriers: synthesis, characterization and transfection efficiency in vitro and in vivo. J. Nanosci. Nanotechnol. 4, 876–881.

Refai, H., Badawy, M., Hassan, A., Sakr, H., Baraka, Y., 2017. Antimicrobial effect of biologically prepared silver nanoparticles (AgNPs) on two different obturator's soft linings in maxillectomy patients. Eur. Acad. Res. 4 (1), 15–25.

Reina, G., González-Dominguez, J.M., Criado, A., Vázquez, E., Bianco, A., Prato, M., 2017. Promises, facts and challenges for graphene in biomedical applications. Chem. Soc. Rev. 46, 4400–4416.

Rejinold, N.S., Muthunarayanan, M., Muthuchelian, K., Chennazhi, K.P., Shanti, V., Nair, R., Jayakumar, R., 2011. Saponin-loaded chitosan nanoparticles and their cytotoxicity to cancer cell lines in vitro. Carbohydr. Polym. 84, 407–416.

Rejman, J., Oberle, V., Zuhorn, I.S., Hoekstra, D., 2004. Size-dependent internalization of particles via the pathways of clathrin- and caveolae-mediated endocytosis. Biochem. J. 377, 159–169.

Rey, A.I., Segura, J., Arandilla, E., López-Bote, C.J., 2013. Short- and long-term effect of oral administration of micellized natural vitamin E (D-α-tocopherol) on oxidative status in racehorses under intense training. J. Anim. Sci. 91, 1277–1284.

Rey, A., Amazan, D., Cordero, G., Olivares, A., López-Bote, C.J., 2014. Lower oral doses of micellized α-tocopherol compared to α-tocopheryl acetate in feed modify fatty acid profiles and improve oxidative status in pigs. Int. J. Vitam. Nutr. Res. 84, 229–243.

Rhee, J.W., Kim, D., Park, B.K., Kwon, S., Cho, S., Lee, I., Park, M.S., Seo, J.N., Kim, Y.S., Choi, H.S., 2012. Immunization with a hemagglutinin-derived synthetic peptide formulated with a CpG-DNA-liposome complex induced protection against lethal influenza virus infection in mice. PLoS One. 7. e48750.

Ríhová, B., Strohalm, J., Prausová, J., Kubácková, K., Jelínková, M., Rozprimová, L., Sírová, M., Plocová, D., Etrych, T., Subr, V., 2003. Cytostatic and immunomobilizing activities of polymer-bound drugs: experimental and first clinical data. J. Control. Release 91, 1–16.

Rim, K.T., Song, S.W., Kim, H.Y., 2013. Oxidative DNA damage from nanoparticle exposure and its application to workers' health: a literature review. Saf. Health Work 4 (4), 177–186.

Rodriguez-Del, R.E., Marradi, M., Calderon-Gonzalez, R., Frande-Cabanes, E., Penadés, S., Petrovsky, N., Alvarez-Dominguez, C., 2015. A gold glyco-nanoparticle carrying a Listeriolysin O peptide and formulated with Advax™ delta inulin adjuvant induces robust T-cell protection against listeria infection. Vaccine 33, 1465–1473.

Rolfe, P., 2012. Micro- and nanosensors for medical and biological measurement. Sens. Mater. 24, 275–302.

Rosi, N.L., Mirkin, C.A., 2005. Nanostructures in biodiagnostics. Chem. Rev. 105, 1547–1562.

Ruedas-Rama, M.J., Walters, J.D., Orte, A., Hall, E.A.H., 2012. Fluorescent nanoparticles for intracellular sensing: a review. Anal. Chim. Acta 751, 1–23.

Saade, F., Honda-Okubo, Y., Trec, S., Petrovsky, N., 2013. A novel hepatitis B vaccine containing Advax™, a polysaccharide adjuvant derived from delta inulin, induces robust humoral and cellular immunity with minimal reactogenicity in preclinical testing. Vaccine 31, 1999–2007.

Saboktakin, M.R., Tabatabaie, R.M., Maharramov, A., Ramazanov, M.A., 2011. Synthesis and characterization of biodegradable thiolated chitosan nanoparticles as targeted drug delivery system. J. Nanomed. Nanotechnol. 4 (1), 1–5.

Sachetelli, S., Khalil, H., Chen, T., Beaulac, C., Sénéchal, S., Lagacé, J., 2000. Demonstration of a ion mechanism between a fluid bactericidal liposomal formulation and bacterial cells. Biochim. Biophys. Acta 1463, 254–266.

Sadozai, H., Saeidi, D., 2013. Recent developments in liposome-based veterinary therapeutics. ISRN Vet. Sci. 2013, 1–8. Article ID 167521.

Sagadevan, S., Periasamy, M., 2014. Recent trends in nanobiosensors and their applications—a review. Rev. Adv. Mater. Sci. 36, 62–69.

Saini, R., Saini, S., Sharma, S., 2010. Nanotechnology: the future medicine. J. Cutan. Aesthet. Surg. 3, 32–33.

Salama, A.A., Caja, G., Albanell, E., Such, X., Casals, R., Plaixats, J., 2003. Effects of dietary supplements of zinc-methionine on milk production, udder health and zinc metabolism in dairy goats. J. Dairy Res. 70, 9–17.

Samad, A., Alam, M.I., Saxena, K., 2009. Dendrimers: a class of polymers in the nanotechnology for the delivery of active pharmaceuticals. Curr. Pharm. Des. 15, 2958–2969.

Sanchez, V.C., Jachak, A., Hurt, R.H., Kane, A.B., 2012. Biological interactions of graphene-family nanomaterial: an interdisciplinary review. Chem. Res. Toxicol. 25, 15–34.

Saragusty, J., Arav, A., 2011. Current progress in oocyte and embryo cryopreservation by slow freezing and vitrification. Reproduction 141, 1–19.

Savolainen, K., Alenius, H., Norppa, H., Pylkkänen, L., Tuomi, T., Kasper, G., 2010. Risk assessment of engineered nanomaterials and nanotechnologies—a review. Toxicology 269 (2–3), 92–104.

Sawai, J., 2003. Quantitative evaluation of antibacterial activities of metallic oxide powders (ZnO, MgO and CaO) by conduct metric assay. J. Microbiol. Methods 54, 177–182.

Sawosz, E., Binek, M., Grodzik, M., Zielińska, M., Sysa, P., Szmidt, M., Niemiec, T., Chwalibog, A., 2007. Influence of hydrocolloidal silver nanoparticles on gastrointestinal microflora and morphology of enterocytes of quails. Arch. Anim. Nutr. 61, 444–451.

Scharf, A., Holmes, S., Thoresen, M., Mumaw, J., Stumpf, A., Peroni, J., 2015. Superparamagnetic iron oxide nanoparticles as a means to track mesenchymal stem cells in a large animal model of tendon injury. Contrast Media Mol. Imaging 10, 388–397.

Schipper, M.L., Nakayama, R.N., Davis, G.R., Kam, N.W., Chu, P., Liu, Z., Sun, X., Dai, H., Gambhir, S.S., 2008. A pilot toxicology study of single-walled carbon nanotubes in a small sample of mice. Nat. Nanotechnol. 3 (4), 216–221.

Scott, N.R., 2005. Nanotechnology and animal health. Rev. Sci. Tech.—Off. Int. Epizoot. 24, 425–432.

Scott, D.W., Miller, W.H., 2003. Treatment with individualized homeopathic remedies unsuccessful. Can. Vet. J. 44, 273.

Scott-Moncrieff, J.C., Shao, Z., Mitra, A.K., 1994. Enhancement of intestinal insulin absorption by bile salt-fatty acid mixed micelles in dogs. J. Pharm. Sci. 83, 1465–1469.

Sekhon, B.S., 2012. Drug-drug co-crystals. DARU J. Pharm. Sci. 20 (1), 20–45.

Sekowski, S., Miłowska, K., Gabryelak, T., 2008. Dendrimers in biomedical sciences and nanotechnology. Postepy Hig. Med. Dosw. 62, 725–733.

Shah, M., Badwaik, V., Kherde, Y., Waghwani, H.K., Modi, T., Aguilar, Z.P., Rodgers, H., Hamilton, W., Marutharaj, T., Webb, C., Lawrenz, M.B., Dakshinamurthy, R., 2014. Gold nanoparticles: various methods of synthesis and antibacterial applications. Front. Biosci. 19, 1320–1344.

Sharma, V., Shukla, R.K., Saxena, N., Parmar, D., Das, M., Dhawan, A., 2009. DNA damaging potential of zinc oxide nanoparticles in human epidermal cells. Toxicol. Lett. 185 (3), 211–218.

Shaw, S.Y., Westly, E.C., Pittet, M.J., Subramanian, A., Schreiber, S.L., Weissleder, R., 2008. Perturbational profiling of nanomaterial biologic activity. Proc. Natl. Acad. Sci. U. S. A. 105, 7387–7392.

Shawky, N., Hassan, A.A., Sayed El Ahl, R.M., Mahmoud, H.H., 2014. Evaluation of the antimicrobial effect of zinc oxide nanoparticles on *Listeria monocytogenes* and *Candida albicans* isolated from infected Egyptian buffalo suffering from abortion. In: 2nd Scientific Conference of Scientific Association of Animal Health Research Institute. vol. 2–4, pp. 110–119.

Shen, C.C., Liang, H.J., Wang, C.C., Liao, M.H., Jan, T.R., 2012. Iron oxide nanoparticles suppressed T helper 1 cell-mediated immunity in a murine model of delayed-type hypersensitivity. Int. J. Nanomedicine 7, 2729–2737.

Shi, S.F., Jia, J.F., Guo, X.K., Zhao, Y.P., Chen, D.S., Guo, Y.Y., Cheng, T., Zhang, X.L., 2012. Biocompatibility of chitosan-coated iron oxide nanoparticles with osteoblast cells. Int. J. Nanomed. 7, 5593–5602.

Shirahata, N., 2011. Silica nanocrystals: a controlled organic-inorganic interface and its implications of color-tuning and chemical design toward sophisticated architectures. Phys. Chem. Chem. Phys. 13, 7284–7294.

Shokrollahi, H., 2013. Structure, synthetic methods, magnetic properties and biomedical applications of ferrofluids. Mater. Sci. Eng. C Mater. Biol. Appl. 33, 2476–2487.

Shvedova, A.A., Kisin, E.R., Mercer, R.T., Murray, A.R., Johnson, V.G., Potapovich, A.L., Tyurina, L.W., Gorelik, O., Arepalli, S., Schwegler, D.B., Baron, P., 2005. Unusual inflammatory and fibrogenic pulmonary responses to single-walled carbon nanotubes in mice. Am. J. Physiol. Lung Cell. Mol. Physiol. 289 (5), L698–L708.

Sijbesma, R., Srdanov, G., Wudl, F., 1993. Synthesis of a fullerene derivative for the inhibition of HIV enzymes. J. Am. Chem. Soc. 115, 6510–6512.

Silvestre, C., Duraccio, D., Cimmino, S., 2011. Food packaging based on polymer nanomaterials. Prog. Polym. Sci. 36, 1766–1782.

Singla, S., Harjai, K., Katare, O.P., Chhibber, S., 2016. Encapsulation of bacteriophage in liposome accentuates its entry in to macrophage and shields it from neutralizing antibodies. PLoS ONE 11. e0153777.

Sirirat, N., Lu, J.J., Hung, A.T.Y., Lien, T.F., 2013. Effect of different levels of nanoparticles chromium picolinate supplementation on performance, egg quality, mineral retention, and tissues minerals accumulation in layer chickens. J. Agric. Sci. 5, 150–159.

Sirova, M., Strohalm, J., Subr, V., Plocova, D., Rossmann, P., Mrkvan, T., Ulbrich, K., Rihova, B., 2007. Treatment with HPMA copolymer-based doxorubicin conjugate containing human immunoglobulin induces long-lasting systemic anti-tumour immunity in mice. Cancer Immunol. Immunother. 56, 35–47.

Slowing, I., Trewyn, B.G., Lin, V.S.Y., 2006. Effect of surface functionalization of MCM-41-type mesoporous silica nanoparticles on the endocytosis by human cancer cells. J. Am. Chem. Soc. 128 (46), 14792–14793.

Slowing, I.I., Vivero-Escoto, J.L., Wu, C.W., Lin, V.S.Y., 2008. Mesoporous silica nanoparticles as controlled release drug delivery and gene transfection carriers. Adv. Drug Deliv. Rev. 60, 1278–1288.
Slowing, I.I., Vivero-Escoto, J.L., Trewyn, B.G., Lin, V.S.Y., 2010. Mesoporous silica nanoparticles: structural design and applications. J. Mater. Chem. 20, 7924–7937.
Smekalova, M., Aragon, V., Panacek, A., Prucek, R., Zboril, R., Kvitek, L., 2016. Enhanced antibacterial effect of antibiotics in combination with silver nanoparticles against animal pathogens. Vet. J. 209, 174–179.
Soenen, S.J.H., Himmelreich, U., Nuytten, N., Pisanic, T.R., Ferrari, A., De Cuyper, M., 2010. Intracellular nanoparticle coating stability determines nanoparticle diagnostics efficacy and cell functionality. Small 6, 2136–2145.
Souris, J.S., Lee, C.H., Cheng, S.H., Chen, C.T., Yang, C.S., Ho, J.A., Mou, C.Y., Lo, L.W., 2010. Surface charge-mediated rapid hepatobiliary excretion of mesoporous silica nanoparticles. Biomaterials 31, 5564–5574.
Soutter, W.L., 2013. Chitosan Nanoparticles Properties and Applications., pp. 1–5. https://www.azonano.com/article.aspx?ArticleID=3232.
Stankic, S., Suman, S., Haque, F., Vidic, J., 2016. Pure and multi metal oxide nanoparticles: synthesis, antibacterial and cytotoxic properties. J. Nanobiotechnol. 14, 73. https://doi.org/10.1186/s12951-016-0225-6.
Stecko, S., Jurczak, M., Urbańczyk-Lipkowska, Z., Solecka, J., Chmielewski, M., 2008. Synthesis of pyrrolizidine alkaloids via 1,3-dipolar cycloaddition involving cyclic nitrones and unsaturated lactones. Carbohydr. Res. 343, 2215–2220.
Stoimenov, P.K., Klinger, R.L., Marchin, G.L., Klabunde, K.J., 2002. Metal oxide nanoparticles as bactericidal agents. Langmuir 18, 6679–6686.
Suh, J.K.F., Matthew, H.W.T., 2000. Application of chitosan-based polysaccharide biomaterials in cartilage tissue engineering: a review. Biomaterials 21, 2589–2598.
Sun, C., Lee, J.S., Zhang, M., 2008a. Magnetic nanoparticles in MR imaging and drug delivery. Adv. Drug Deliv. Rev. 60 (11), 1252–1265.
Sun, X., Liu, Z., Welsher, K., Robinson, J.T., Goodwin, A., Zaric, S., Dai, H., 2008b. Nanographene oxide for cellular imaging and drug delivery. Nano Res. 1, 203–212.
Sung, Y.J., Suk, H.J., Sung, H.Y., Li, T., Poo, H., Kim, M.G., 2013. Novel antibody/gold nanoparticle/magnetic nanoparticle nanocomposites for immunomagnetic separation and rapid colorimetric detection of *Staphylococcus aureus* in milk. Biosens. Bioelectron. 43, 432–439.
Swenson, C.E., Perkins, W.R., Roberts, P., Ahmad, I., Stevens, R., Stevens, D.A., Janoff, A.S., 1998. In vitro and in vivo antifungal activity of amphotericin B lipid complex: are phospholipases important? Antimicrob. Agents Chemother. 42, 767–771.
Syed, M.A., Bokhari, S.H.A., 2011. Gold nanoparticle based microbial detection and identification. J. Biomed. Nanotechnol. 7, 229–237.
Tallury, P., Malhotra, A., Byrne, L.M., 2010. Nanobioimaging and sensing of infectious diseases. Adv. Drug Deliv. Rev. 62, 424–437.
Tartaj, P., Morales, M., Veintemillas, V.S., Gonzlez-Carreo, T., Serna, C.J., 2003. The preparation of magnetic nanoparticles for applications in biomedicine. J. Phys. D Appl. Phys. 36, 182–197.
Taylor, L., Rodwell, B., 2001. Outbreak of foetal infection with bovine pestivirus in a central Queensland beef herd. Aust. Vet. J. 79, 682–685.
Taylor, K.M.L., Kim, J.S., Rieter, W.J., An, H., Lin, W., Lin, W., 2008. Mesoporous silica nanospheres as highly efficient MRI contrast agents. J. Am. Chem. Soc. 130, 2154–2155.

Taylor, E., Thomas, J., Webster, R., 2011. Reducing infections through nanotechnology and nanoparticles. Int. J. Nanomed. 6, 1463–1473.

Taylor-Pashow, K.M.L., Rocca, J., Huxford, R.C., Lin, W., 2010. Hybrid nanomaterials for biomedical applications. Chem. Commun. 46, 5832–5849.

Thakare, V.S., Das, M., Jain, A.K., Patil, S., Jain, S., 2010. Carbon nanotubes in cancer theragnosis. Nanomedicine 5 (8), 1277–1301.

Thornton, P.K., 2010. Livestock production: recent trends, future prospects. Philos. Trans. R. Soc. Lond. B Biol. Sci. 365, 2853–2867.

Tinkle, S.S., Antonini, J.M., Rich, B.A., Roberts, J.R., Salmen, R., DePree, K., Adkins, E.J., 2003. Skin as a route of exposure and sensitisation in chronic beryllium disease. Environ. Health Perspect. 111 (9), 1202–1208.

Tomànek, D., Enbody, R.J. (Eds.), 2000. Science and Application of Nanotubes. Kluwer Academic/Plenum Publishers, New York.

Torchilin, V.P., 2005. Lipid-core micelles for targeted drug delivery. Curr. Drug Deliv. 2, 319–327.

Torney, F., Trewyn, B.G., Lin, V.S.Y., Wang, K., 2007. Mesoporous silica nanoparticles deliver DNA and chemicals into plants. Nat. Nanotechnol. 2, 295–300.

Tsuji, J.S., Maynard, A.D., Howard, P.C., 2006. Research strategies for safety evaluation of nanomaterials, Part IV: risk assessment of nanoparticles. Toxicol. Sci. 89 (1), 42–50.

Tu, X., Manohar, S., Jagota, A., Zheng, M., 2009. DNA sequence motifs for structure specific recognition and separation of carbon nanotubes. Nature 460 (7252), 250–253.

Tuitemwong, P., Songvorawit, N., Tuitemwong, K., 2013. Facile and sensitive epifluorescent silica nanoparticles for the rapid screening of EHEC. J. Nanomater. 2013, 1–8.

Turos, E., Reddy, G.S.K., Greenhalgh, K., Ramaraju, P., Abeylath, S.C., Jang, S., 2007. Penicillin-bound polyacrylate nanoparticles: restoring the activity of β-lactam antibiotics against MRSA. Bioorg. Med. Chem. Lett. 17, 3468–3472.

Vail, D.M., Von Euler, H., Rusk, A.W., Barber, L., Clifford, C., Elmslie, R., Fulton, L., Hirschberger, J., Klein, M., London, C., 2012. A randomized trial investigating the efficacy and safety of water-soluble micellar paclitaxel (Paccal Vet) for treatment of nonresectable grade 2 or 3 mast cell tumors in dogs. J. Vet. Intern. Med. 26, 598–607.

Vallet-Regi, M., Ramila, A., del Real, R.P., Perez-Pariente, J., 2001. A new property of MCM-41: drug delivery system. Chem. Mater. 13, 308–311.

Vandamme, K., Vesna, M., Eric, C., Paul, R.J., Chris, V., 2011. Adjuvant effect of Gantrez®AN nanoparticles during oral vaccination of piglets against F4+enterotoxigenic *Escherichia coli*. Vet. Immunol. Immunopathol. 139, 148–155.

Van-Schooneveld, M.M., Vucic, E., Koole, R., Zhou, Y., Stocks, J., Cormode, D.P., Tang, C.Y., Gordon, R.E., Nicolay, K., Meijerink, A., 2008. Improved biocompatibility and pharmacokinetics of silica nanoparticles by means of a lipid coating: a multimodality investigation. Nano Lett. 8, 2517–2525.

Villaraza, A.J.L., Bumb, A., Brechbiel, M.W., 2010. Macromolecules, dendrimers, and nanomaterials in magnetic resonance imaging: the interplay between size, function, and pharmacokinetics. Chem. Rev. 110, 2921–2959.

Violeta, V., Catalin, P., Constantin, F., Monica, A., Marius, B., 2011. Nanoparticles applications for improving the food safety and food processing. In: 7th International Conference on Materials Science and Engineering—BRAMAT. Brasov. 24–26 February 2011, pp. 77–81.

Vivero-Escoto, J.L., Slowing, I.I., Wu, C.W., Lin, V.S.Y., 2009. Photoinduced intracellular controlled release drug delivery in human cells by gold-capped mesoporous silica nanosphere. J. Am. Chem. Soc. 131, 3462–3463.

Vivero-Escoto, J.L., Slowing, I.I., Lin, V.S.Y., 2010a. Tuning the cellular uptake and cytotoxicity properties of oligonucleotide intercalator-functionalized mesoporous silica nanoparticles with human cervical cancer cells HeLa. Biomaterials 31, 1325–1333.

Vivero-Escoto, J.L., Slowing, I.I., Trewyn, B.G., Lin, V.S.Y., 2010b. Mesoporous silica nanoparticles for intracellular controlled drug delivery. Small 6, 1952–1967.

Vivero-Escoto, J.L., Trewyn, B.G., Lin, V.S.Y., 2010c. Mesoporous silica nanoparticles: synthesis and applications. Annu. Rev. Nano Res. 3, 191–231.

Vyas, S.S., Jadhav, S.V., Majee, S.B., Shastri, J.S., Patravale, V.B., 2015. Development of immunochromatographic strip test using fluorescent, micellar silica nanosensors for rapid detection of *B. abortus* antibodies in milk samples. Biosens. Bioelectron. 70, 254–260.

Wang, M.Q., Xu, Z.R., 2004. Effect of chromium nanoparticle on growth performance, carcass characteristics, pork quality and tissue chromium in finishing pigs. J. Anim. Sci. 17, 1118–1122.

Wang, L., Yang, Z.M., Gao, J.H., Xu, K.M., Gu, H.W., Zhang, B., Zhang, X.X., Xu, B., 2006. A biocompatible method of decorporation: bisphosphonate-modified magnetite nanoparticles to remove uranyl ions from blood. J. Am. Chem. Soc. 128, 13358–13359.

Wang, B., Feng, W., Wang, M., Wang, T.C., Gu, Y.Q., Zhu, M.T., Ouyang, H., Shi, J.W., Zhang, F., Zhao, Y.L., 2008a. Acute toxicological impact of nano- and submicro-scaled zinc oxide powder on healthy adult mice. J. Nanopart. Res. 10, 263–276.

Wang, L., Zhao, W., Tan, W., 2008b. Bioconjugated silica nanoparticles: development and applications. Nano Res. 1, 99–115.

Wang, H., Gu, L., Lin, Y., Lu, F., Meziani, M.J., Luo, P.G., Wang, G., Cao, L., Sun, Y.P., 2008c. Unique aggregation of anthrax (*Bacillus anthracis*) spores by sugar coated single walled carbon nanotubes. J. Am. Chem. Soc. 128 (41), 13364–13365.

Wang, H., Wingett, D., Engelhard, M.H., Feris, K., Reddy, K.M., Turner, P., Layne, J., Hanley, C., Bell, J., Tenne, D., 2009. Fluorescent dye encapsulated ZnO particles with cell-specific toxicity for potential use in biomedical applications. J. Mater. Sci. Mater. Med. 20, 11–22.

Wang, J.J., Zeng, Z.W., Xiao, R.Z., Xie, T., Zhou, G.L., Zhan, X.R., Wang, S.L., 2011a. Recent advances of chitosan nanoparticles as drug carriers. Int. J. Nanomedicine 6, 765–774.

Wang, J.J., Liu, B.H., Hsu, Y.T., Yu, F.Y., 2011b. Sensitive competitive direct enzyme-linked immunosorbent assay and gold nanoparticle immunochromatographic strip for detecting aflatoxin M1 in milk. Food Control 22, 964–969.

Wang, M.Q., Wang, C., Li, H., Du, Y.J., Tao, W.J., Ye, S.S., 2012. Effects of chromium-loaded chitosan nanoparticles on growth, blood metabolites, immune traits and tissue chromium in finishing pigs. Biol. Trace Elem. Res. 149, 197–203.

Wang, X., Dang, E., Gao, J., Guo, S., Li, Z., 2013. Development of a gold nanoparticle-based oligonucleotide microarray for simultaneous detection of seven swine viruses. J. Virol. Methods 191, 9–15.

Wang, M.Q., Wang, C., Du, Y.J., Li, H., Tao, W.J., Ye, S.S., 2014. Effects of chromium-loaded chitosan nanoparticles on growth, carcass characteristics, pork quality, and lipid metabolism in finishing pigs. Livest. Sci. 161, 123–129.

Wang, P., Liu, J., GAO, H., Hu, Y., Hou, X., Le Croy, G.E., Bunker, C.E., Liu, Y., Sun, Y.P., 2017. Host–guest carbon dots as high-performance fluorescence probes. J. Mater. Chem. 5, 6328–6335.

Wilczynski, M., 2000. Anti-microbial porcelain enamels. Ceram. Eng. Sci. Proc. 21, 81–83.

Woods, S., De Castro Marques, A.I., Renwick, M.G., Argyle, S.A., Yool, D.A., 2012. Nanocrystalline silver dressing and subatmospheric pressure therapy following neoadjuvant radiation therapy and surgical excision of a feline injection site sarcoma. J. Feline Med. Surg. 14, 214–218.

Wu, P., Chen, X., Hu, N., Tam, U.C., Blixt, O., Zettl, A., Bertozzi, C.R., 2008. Biocompatible carbon nanotubes generated by functionalization with glycodendrimers. Angew. Chem. 120 (27), 5100–5103.

Wu, X., Lin, Q., Chen, G., Lu, J., Zeng, Y., Chen, X., Yan, Y., 2015. Sentinel lymph node detection using carbon nanoparticles in patients with early breast cancer. PLoS ONE 10, 14–22. e01357.

Xiao, Q., Yadavalli, S.S., Zhang, S., Sherman, S.E., Fiorin, E., da Silva, L., Wilson, D.A., Hammer, D.A., André, S., Gabius, H.J., 2016. Bioactive cell-like hybrids coassembled from (glyco) dendrimersomes with bacterial membranes. Proc. Natl. Acad. Sci. U. S. A. 113, 1134–1141.

Xie, P., Tang, X., Li, L., Qian, Z., Ran, M., Zhang, X., Xin, X., Luo, H., 2016. Drug-loaded carbon nanoparticle suspension injection, drug selection, releasing behavior, in vitro cytotoxicity and in vivo lymph node targeting. J. Nanosci. Nanotechnol. 16, 6910–6918.

Xie, P., Yang, S.T., He, T., Yang, S., Tang, X.H., 2017a. Bioaccumulation and toxicity of carbon nanoparticles suspension injection in intravenously exposed mice. Int. J. Mol. Sci. 18 (12), 2562–2570.

Xie, P., Xin, Q., Yang, S.T., He, T., Huang, Y., Zeng, G., Ran, M., Tang, X.H., 2017b. Skeleton labeled 13C-carbon nanoparticles for the imaging and quantification in tumor drainage lymph nodes. Int. J. Nanomed. 12, 4891–4899.

Xu, C., Sun, S., 2013. New forms of superparamagnetic nanoparticles for biomedical applications. Adv. Drug Deliv. Rev. 65, 732–743.

Xu, C.J., Xu, K.M., Gu, H.W., Zheng, R.K., Liu, H., Zhang, X.X., Guo, Z.H., Xu, B., 2004a. Dopamine as a robust anchor to immobilize functional molecules on the iron oxide shell of magnetic nanoparticles. J. Am. Chem. Soc. 126, 9938–9939.

Xu, C.J., Xu, K.M., Gu, H.W., Zhong, X.F., Guo, Z.H., Zheng, R.K., Zhang, X.X., Xu, B., 2004b. Nitrilotriacetic acid-modified magnetic nanoparticles as a general agent to bind histidine-tagged proteins. J. Am. Chem. Soc. 126, 3392–3393.

Yang, L.A.P., 2000. Physiochemical aspects of drug delivery and release from polymer-based colloids. Curr. Opin. Colloid Interface Sci. 51, 132–143.

Yang, Z.P., Sun, L.P., 2006. Effects of nanometre ZnO on growth performance of early weaned piglets. J. Shanxi Agric. Sci. 3, 24.

Yang, S.T., Wang, X., Wang, H., Lu, F., Luo, P.G., Cao, L., Meziani, M.J., Liu, J.H., Liu, Y., Chen, M., 2009. Carbon dots as nontoxic and high performance fluorescence imaging agents. J. Phys. Chem. 113, 18110–18114.

Yang, C., Mamouni, J., Tang, Y., Yang, L., 2010. Antimicrobial activity of single walled carbon nanotubes length effect. Langmuir 26 (20), 16013–16019.

Yang, H., Sun, C., Fan, Z., Tian, X., Yan, L., Du, L., Keelan, J.A., 2012. Effects of gestational age and surface modification on materno-fetal transfer of nanoparticles in murine pregnancy. Sci. Rep. 2, 847–855.

Ye, S., Shao, K., Li, Z., Guo, N., Zuo, Y., Li, Q., Lu, Z., Chen, L., He, Q., Han, H., 2015. Antiviral activity of graphene oxide: how sharp edged structure and charge matter. ACS Appl. Mater. Interfaces 7, 21571–21579.

Yigit, M.V., Moore, A., Medarova, Z., 2012. Magnetic nanoparticles for cancer diagnosis and therapy. Pharm. Res. 29, 1180–1188.

Yin, Y.D., Rioux, R.M., Erdonmez, C.K., Hughes, S., Somorjai, G.A., Alivisatos, P., 2004. Formation of hollow nanocrystals through the nanoscale Kirkendall effect. Science 304, 711–714.

Yin, H.Q., Jia, M.X., Shi, L.J., Yang, S., Zhang, L.Y., Zhang, Q.M., Wang, S.Q., Li, G., Zhang, J.G., 2011. Nanoparticle-based bio-barcode assay for the detection of bluetongue virus. J. Virol. Methods 178, 225–228.

Yu, H., Chen, M., Rice, P.M., Wang, S.X., White, R.L., Sun, S.H., 2005. Dumbbell-like bifunctional Au-Fe_3O_4 nanoparticles. Nano Lett. 5, 379–382.

Yuan, Y.G., Peng, Q.L., Gurunathan, S., 2017. Effects of silver nanoparticles on multiple drug-resistant strains of *Staphylococcus aureus* and *Pseudomonas aeruginosa* from mastitis-infected goats: an alternative approach for antimicrobial therapy. Int. J. Mol. Sci. 18, 569.

Zaki, N.M., Hafez, M.M., 2012. Enhanced antibacterial effect of ceftriaxone sodium-loaded chitosan nanoparticles against intracellular *Salmonella typhimurium*. AAPS PharmSciTech 13, 411–421.

Zamboni, W.C., Strychor, S., Joseph, E., Parise, R.A., Egorin, M.J., Eiseman, J.L., 2008. Tumor, tissue, and plasma pharmacokinetic studies and antitumor response studies of docetaxel in combination with 9-nitrocamptothecin in mice bearing SKOV-3 human ovarian xenografts. Cancer Chemother. Pharmacol. 62, 417–426.

Zha, L.Y., Zeng, J.W., Chu, X.W., Mao, L.M., Luo, H.J., 2009. Efficacy of trivalent chromium on growth performance, carcass characteristics and tissue chromium in heat-stressed broiler chicks. J. Sci. Food Agric. 89, 1782–1786.

Zhang, X.F., Gurunathan, S., 2016. Biofabrication of a novel biomolecule-assisted reduced graphene oxide: an excellent biocompatible nanomaterial. Int. J. Nanomedicine 11, 6635–6649.

Zhang, L., Jiang, Y., Ding, Y., Povey, M., York, D., 2007. Investigation into the antibacterial behavior of suspensions of ZnO nanoparticles (ZnO nanofluids). J. Nanopart. Res. 9, 479–489.

Zhang, L., Liu, W., Lin, L., Chen, D., Stenzel, M.H., 2008. Degradable disulfide core-cross-linked micelles as a drug delivery system prepared from vinyl functionalized nucleosides via the RAFT process. Biomacromolecules 9, 3321–3331.

Zhang, X.F., Liu, Z.G., Shen, W., Gurunathan, S., 2016. Silver nanoparticles: synthesis, characterization, properties, applications, and therapeutic approaches. Int. J. Mol. Sci. 17, 1534.

Zhao, X., Hilliard, L.R., Wang, K., Tan, W., 2004. Bioconjugated silica nanoparticles for bioanalysis. In: Encyclopedia of Nanoscience and Nanotechnology. vol. 1–10, American Scientific Publishers, Stevenson Ranch, CA, pp. 255–268. ISBN: 1-5883-001-2.

Zhao, Y.N., Trewyn, B.G., Slowing, I.I., Lin, V.S.Y., 2009. Mesoporous silica nanoparticle-based double drug delivery system for glucose-responsive controlled release of insulin and cyclic AMP. J. Am. Chem. Soc. 131, 8393.

Zhao, X., Lin, C.W., Wang, J., Oh, D.H., 2014a. Advances in rapid detection methods for foodborne pathogens. J. Microbiol. Biotechnol. 24, 297–312.

Zhao, Q., Wang, C., Liu, Y., Wang, J., Gao, Y., Zhang, X., Jiang, T., Wang, S., 2014b. PEGylated mesoporous silica as a redox-responsive drug delivery system for loading thiol-containing drugs. Int. J. Pharm. 477, 613–622.

Zhou, Y., Kong, Y., Kundu, S., Cirillo, J.D., Liang, H., 2012. Antibacterial activities of gold and silver nanoparticles against *Escherichia coli* and bacillus Calmette-Guérin. J. Nanobiotechnol. 10, 19.

Zhu, K., Dietrich, R., Didier, A., Doyscher, D., Märtlbauer, E., 2014. Recent developments in antibody-based assays for the detection of bacterial toxins. Toxins 6, 1325–1348.

Zhu, B., Liu, G.L., Ling, F., Wang, G.X., 2015. Carbon nanotube-based nanocarrier loaded with ribavirin against grass carp reovirus. Antiviral Res. 118, 29–38.

Zhu, Y., Chen, X., Zhang, H., Chen, L., Zhou, S., Wu, K., Wang, Z., Kong, L., Zhuang, H., 2016. Carbon nanoparticle-guided central lymph node dissection in clinically node-negative patients with papillary thyroid carcinoma. Head Neck 38, 840–845.

Further reading

Allison, A.G., Gregoriadis, G., 1974. Liposomes as immunological adjuvants. Nature 252, 252–260.

Misra, R., Acharya, S., Sahoo, S.K., 2010. Cancer nanotechnology: application of nanotechnology in cancer therapy. Drug Discov. Today 15 (19/20), 824–850.

Rakesh, P.S., Abdalla, A.M., Abdel Fattah, A., Ghosh, S., Puri, I.K., 2018. Chapter 2: Synthesis, characterization, and applications of carbon nanotubes functionalized with magnetic nanoparticles. In: Balasubramanian, G. (Ed.), Advances in Nanomaterials. Springer International Publishing AG, p. 37. https://doi.org/10.1007/978-3-319-64717-3_2. https://www.springer.com/cda/content/document/cda_downloaddocument/9783319647159-c1.pdf?SGWID=0-0-45-1623598-p181071311.

Romero, C.M., Alvarez, A., Martínez, M.A., Chaves, S., 2018. Fungal nanotechnology: a new approach toward efficient biotechnology application. In: Prasad, R., Kumar, V., Kumar, M., Wang, S. (Eds.), Fungal Nanobionics: Principles and Applications. Springer, Singapore.

Zhao, X., Tapec-Dytioco, R., Tan, W., 2003. Ultrasensitive DNA detection using highly fluorescent bioconjugated nanoparticles. J. Am. Chem. Soc. 125, 11474–11475.