International Journal of Pharmacology

ISSN 1811-7775

science alert

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Asian Network for Scientific Information

OPEN ACCESS International Journal of Pharmacology

ISSN 1811-7775
DOI: 10.3923/ijp.2017.340.350

Review Article
Nutritional and Pharmaceutical Applications of Nanotechnology: Trends and Advances

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Abstract

The concept of "Nanoparticle" is not applied to the individual molecules but it is usually used to indicate to the inorganic materials. These particles vary into different kinds due to their ability to carry different components and act to various conditions of the environment. The different sorts of nanoparticles are used in various sectors such as nutrition, pharmacy, medicine, drug delivery, therapeutics, vaccine formulations, diagnostics, chemical industry, biotechnology and biomedicine for safeguarding health of humans and animals as well as enhancing growth and production performances. The application of nanotechnology is very important in the 21st century to clean up the environment from contaminants by eco-friendly, sustainable, green and economically technologies. Nanotechnology became an essential element of pharmaceutical sciences and nanomaterials have found many applications in systems of drug delivery to enhance the therapeutic performance and efficacy of different drugs and medicines. Most of the current "Nano" systems of drug delivery are linage of conventional dosage forms like nanomicelles, nanoemulsions and nanosuspensions. Also, nanotechnology will have a major role in the future areas of animal nutrition research. Nano additives could be incorporated in capsules or micelles of protein or other natural feed or food component. The use of nutrient nanoparticles may improve the bioavailability of carried nutrients by the epithelial barriers of the gut and their susceptibility to gastrointestinal degradation by digestive enzymes. Offering the matter in a nano form may also improve the functionality of feed/food molecules to the benefit of final product quality.

Key words: Nanoparticles, nanomedicine, drug delivery, pharmacology, nutrition, human, animal, poultry, production

Received: January 25, 2017 **Accepted:** March 24, 2017 **Published:** April 15, 2017

Citation: Mohamed Ezzat Abd El-Hack, Mahmoud Alagawany, Mayada Ragab Farag, Muhammad Arif, Mohamed Emam, Kuldeep Dhama, Muhammad Sarwar and Maryam Sayab, 2017. Nutritional and pharmaceutical applications of nanotechnology: Trends and advances. Int. J. Pharmacol., 13: 340-350.

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Nanotechnology is an avant-garde technology aiming mainly to create materials with different structure and enhancing quality of foodstuff at a molecular level. The nanoparticles size ranges from 1-100 nm[1,2]. Transforming a material from its normal status to nanoparticles, physical and chemical status will be changed. These changes are used in the favor of production, transportation, traceability, processing and food security[3,4]. Nanomaterials are not a brand new but these have been used in many fields such as the nutrition, diagnostics, chemical industry, biotechnology, therapeutics, drug delivery, vaccines and biomedicine, both for safeguarding health of both humans and animals[5-10]. Sufficient knowledge is missing in using nanotechnology in poultry meat industry. If nanotechnology completed its way in overcharging, it is expected to facilitate the production of unlimited amount of meat[11,12].

In animal feeding and nutrition, the general concept of nanomaterials has transformed the concept from giving nutrients for satisfying the growth requirement to the uses of nano-nutrients for improving the productive performance over the expected performance from the ordinary nutrient. Feed additive is a substance that is added to the diet or in the drinking water with a proper concentration but with no direct utilization as a required nutrient. But because of their chemical actions they are added in the diet[13]. As it well-known that the antibiotic use as a growth promoters which had quickly dominated that field over there alternative as they are cheap and efficient in a uniform manner, antibiotics were used for a prolonged period in a sub therapeutic dose as growth promoters, while are used in the therapeutic dose in the treatment of certain diseases. Unfortunately, the prolonged use of antibiotics as growth promoters lead to the retention of antibiotics in animal tissue which is consumed by the human leading to increased risk of antibiotic resistance[14]. With the social pressure increasing in the food security sector the use of antibiotics as growth promoters had been banned starting from 2006 in the European Community (CE 1831/2003)[13].

Some elements as zinc and copper were included as growth promoters in the weaned piglets diets as they have used as growth promoters[15-17] but unfortunately they have been also banned because of their environmental hazard and retention in animal tissues. One of the positive side of using zinc (2500-3500 ppm as zinc oxide) or copper (150-250 ppm as copper sulphate) is modulating the microbial environment and the post weaning diarrhea[18-20], generally Cu and Zn promotes the productive performance[21,22]. The present review article highlights the trends and advances regarding the classification, mode of action and types in addition to pharmaceutical and nutritional application of nanoparticles in human, animal and poultry.

CLASSIFICATION OF NANOPARTICLES

Nanoparticles are classified as inorganic, organic, emulsions, dispersions and nano-clays depending on their chemical characteristics. Using organic nanoparticles improves the nutrient value through improving feed functionality. Another nomination to organic nanoparticles is nanocapsules, which aim to deliver vitamins or generally nutrient without affecting the taste or the appearance. The secret is the increase of the availability of the organic nanoparticle compared with the compared nutrient as the nanoparticles encapsulates the nutrients and facilitates their passage through the gastrointestinal tract into the blood stream. Organic nanoparticles include proteins, fat and sugar molecules. Nanoparticles are already known to be incorporated in feeds as micelles, liposomes and in processing as in biosensors, identification markers, shelf-life extenders and antimicrobials[23]. Figure 1 illustrates the synthesis of nanoparticles.

On the other side, inorganic nanoparticles are nano-scaled inorganic ingredients that already approved to be included in feed. Titanium dioxide, a feed colorant also can

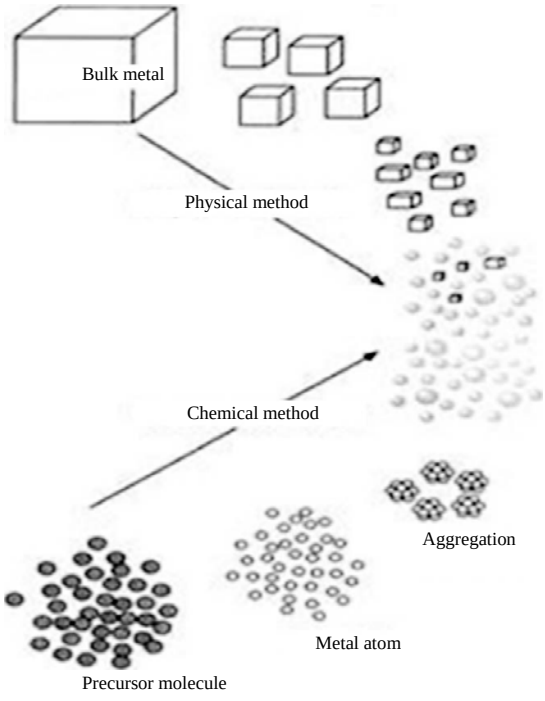

Fig. 1: Nanoparticles synthesis

be used as barrier from UV during packaging process. The most widely spread is the use of nano-silver as antimicrobial. Nano-silver has wide applications in fridge panels, storage boxes, packaging lines and other surfaces which come into contact with feed during manufacture, the general concept for using nano-silver particles is the ability of killing bacteria, so it minimize health risk. Also nano-clay platelets are used in feed packaging, minerals as silicon dioxide, calcium, magnesium and silver nanoparticles are used in water purifications and antimicrobial packaging and storage[24,25].

Digestion and absorption of nanoparticles: Nanoparticles can go to the gastrointestinal tract through food and water or through its administration in a therapeutic dose as ingestion or inhalation, which also can enter the GIT after its clearance from the respiratory tract[26]. The limiting step in the smart delivery into the GIT is the diffusion and accessibility through the GIT cells and mucous covering it. The smaller the particle the faster it can diffuse the mucus reaching to the intestinal lining passing through the GIT barrier reaching the blood stream.

Ingestion or swallow pathway: The absorption of nanoparticle is currently not fully understood but it will take one of the known pathways either by passive diffusion or active transport[17] by one way or another the nanoparticle will end up inside the intestinal tract, those with size less than 200 nm will go to the blood stream and those less than 100 nm are also absorbed to the organs[27]. As a general role the smaller the particle, the deeper it can go to organs. In organic nanoparticles as polystyrene and carbon-based nanoparticles such as fullerenes can be understood that they have some restrictions during usage, after ingestion of polystyrene nanoparticles of 100 nm or less it will be translocate by the lymph system to the liver and spleen, while other small particle can directly enter the blood stream and then trapped inside the liver and the spleen. Organic nanoparticles as casein micelles they behave similar to other nanoparticles and they are readily absorbed and highly bio-available but they are biodegradable, others as insulin encapsulated in vitamin B_{12}-dextran nanoparticles has been found recently that they are up taken from the GIT without degradation[28].

Taylor *et al.*[29] at Clemson University accept afresh developed Biofunctionalized Nanoparticles (BN). The BN begin to take the international acceptance as treatment for enteric infection, confined as antibody ablution agents above-mentioned to alteration and processing. Adherence to abdominal bank epithelial tissues is facilitated by adhesions or apparent molecules, on a bacterial corpuscle which admit the receptor sites on the epithelium. The goal of BN development is to actualize affection for these bacterial adhesions. In addition, it had been shown that the attendance of D-mannose inhibits the adherence of bacilli to the intestinal wall[30]. The BN are accepted to be adhesion-specific to the enter pathogen to jejune[31] and some preliminary research had shown apparent results that proves the BN accepted specific for the mannose receptor sites on the campylobacter cells. Apparent and that corpuscle accession or adapter amid the bacilli and BN may occur. Nanoparticles broadcast added calmly than solid particles and behave added like gas molecules in the air and like ample molecules in solutions, getting beneath accountable to sedimentation than bigger particles. This may accept implications as well for the movement of nanoparticles in tissue. Whether nanoparticles access and alteration aural the physique to altered organs can accept an acceptation accent for the impacts of nanoparticles on human.

MODE OF ACTION OF NANOPARTICLES

Chen *et al.*[32] enumerated the mechanism of action of the nanoparticles as follows: (1) Increasing the surface area to interact with biological support, (2) Prolonging compound residence time in gut, (3) Declining the impact of intestinal clearance mechanisms, (4) Penetrating into tissues within fine capillaries, (5) Crossing the epithelial lining fenestration like the liver, (6) Enabling the cells efficient uptake and (7) The perfect delivery of active compounds to the target places in the body.

KINDS OF NANOPARTICLES

Nanosuspension and nanocrystals: Crystalline shape is formed with aggregated nanocrystals, pure drug can be formed by a thin layer of surfactants and improper absorption of some drugs can be solved by nanocrystals (Fig. 2). The benefits over the traditional nanoparticle is the extend of loading, only low amount of steric and electrostatic surface for stabilization and high drug level can be accompanied with slow dissolution, so avoiding potential toxicity. Nanocrystals are utilized in many dosages and many forms[30]. Nanoparticles targets the mucosa of the GIT after been administrated orally as it targets the Mononuclear Phagocytic System (MPS) to treat the fungal mycobacterial infections and leishmaniasis, so it serves as one of the best delivery system for drugs as amphotericin B, tacrolimus, etc. Also nanocrystals allow the

safe passage effective passage through the capillaries. The FDA had approved the potential of effectiveness of nanoparticles as in Rapamune®, it has sirolimus which is an immunosuppressant drug to prevent rejection for organ transplantation. Also Emend®, which contains aprepitant and MK869 as treatment of emesis during cancer chemotherapy[24].

Liposomes: Liposomes are bi-layered circular vesicles as an aqueous volume in enclosed by the bi-layer membranes[28]. The bi-layer defines the liposomes structure in terms of size, surface and the number of bi-layers, this determines the amphiphilic characters and the biocompatibility for delivering system for biotech drugs. Liposomes had achieved its best success in the field of biology, biochemistry and medicine as

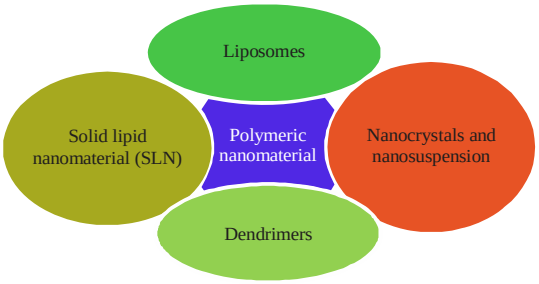

Fig. 2: Kinds of nanoparticles

the pharmacokinitics profile of the loaded drug can easily change by polyethylene glycol-units (PEG)[24].

Solid lipid nanomaterial: Solid Lipid Nanoparticles (SLN) is a carrier system to emulsions, liposomes while the polymeric nanoparticles are a colloidal carrier system for drug delivery so the main reason for the development of SLN as it combines the advantages of different carriers system as liposomes and polymeric nanoparticles[21]. Solid lipid nanoparticles is a solid lipid matrix so the drug can be incorporated in it, with a diameter <1 μm, so there is no aggregation and to ensure the dispersion, different surfactant can be used as long as it is accepted as GRAS (Generally recognized as safe) status. Also nanoparticles can be in a nanosuspensions form by high pressure homogenization. Figure 3 illustrates the digestion of SLN[24].

Dendrimers: Dendrimers are class polymers, there size and shape is depending on their highly branched macromolecules[13]. Dendrimers are polymerized monomers using either convergence or divergence. It has a defined structure, high stability, monodispersity of size with a functional surface making as an attractive candidate in drug carrying. Drug molecule is always incorporated inside either by complexation or encapsulation[24].

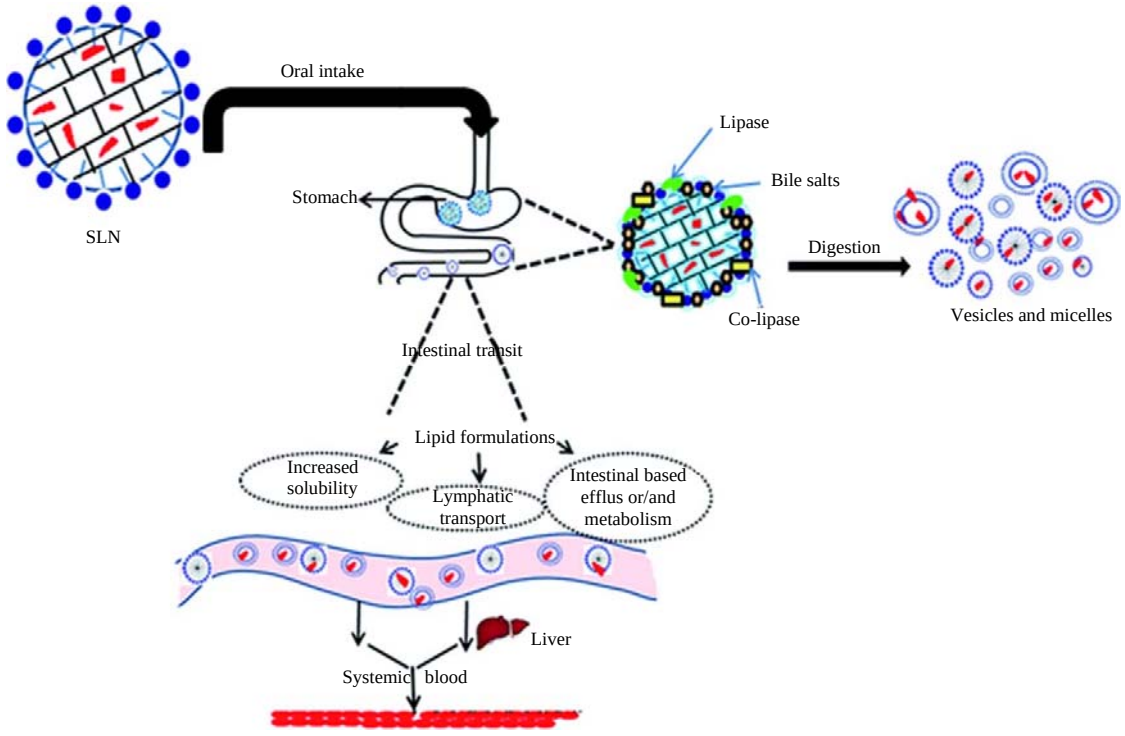

Fig. 3: Digestion of Solid Lipid Nanoparticles (SLN)

Polymeric nanomaterial: Comparing SLN with polymeric nanoparticles (PNPs), consists of biodegradable polymers, also biocompatibility is one of the essential features in new vaccination, gene and drug delivery as most biodegradable polymers as poly (lactide acid) PLA or poly (lactide-co-glycolide). The latest development includes polymers as chitosan, gelatin and sodium alginate, so any toxicological problems can be avoided compared to the synthetic polymers[33,34]. Polymeric nanoparticles are a clear improvement over the previous traditional ways from the point of effectiveness and efficiency. Using PNP had many advantages, the most important is that they enhance the stability of any pharmaceutical volatile agents, easily and cheaply manufactured with different methodology. Also, they are specifically designed to deliver higher concentration to the target organ[12,35]. Nanosphere from the nanoparticle point of view is a matrix system that confirms dispersions. Also, it could be known as nanocapsules which is a polymeric membrane that surrounds the delivered drug in there matrix core. The ability of choosing polymer and to modify the drug release from the polymeric nanoparticle created the ideal way in certain areas as cancer therapy, delivery of vaccines, contraceptives and delivery of targeted antibiotic[36,37]. It could also be included in drug delivery and tissue engineering in human and animals, the expected that there will be huge development in the creating hydrophilic and hydrophobic polymers for better drug formulations[24].

NANOPARTICLES APPLICATIONS

Delivery of targeted drugs: One of the most important of any successful drug delivery is the accuracy of targeting and the control of fate of the drug entering the body[38,39]. Paul Ehrlich at the beginning of the 20th century had proposed a design that is called "Magic bullet", which is far away from what currently happening. Nanotechnology is offering a step ahead in that area to deliver the drug in the right place at the right time. Nanotechnology is promising a huge development in the next years in life sciences, especially drug delivery, nutraceuticals, diagnostics and the production of biomaterials[5,8,40,41]. Nanotechnology based therapy utilizes unique physical and chemical properties of nanomaterials to modulate the pharmacological value, dosage and targeted/efficacious delivery of various drugs and medicines[6,37,42-46]. Nanoparticles are also useful in drug targeting through improving the delivery of poorly soluble drugs. Also a great achievement is done in delivering anti-cancer drugs as doxorubicin 5-fluorouracil. Even glucocorticoid (dexamethasone) is encapsulated by polylactic/glycolic acid (PLGA) and polylactic acid (PLA) based nanoparticles to ensure there intracellular action so perform its anti-inflammatory effect. Several advantages in using NPs in site-specific-targeted drug delivery as it decrease the toxicity risk with minimum precipitation level in other organs, improved bioavailability leading to effective drug dose[12,24]. The hydrophobic and hydrophilic states are the key of the NP drug delivery controlling the route of delivery either oral, vascular or inhalation. Recently some new methods had been used to reach the best site-specific delivery of an effective dose as using polymeric micelles, dendrimers, iron oxide, proteins, ceramic NPs, covalent binding, conjugation, adsorption and encapsulation methods. Some Chinese research group had been using gold nanoparticles as a cancer cell detector in human blood, this is a sensitive approach according to those researchers, gold nanoparticles are a promising new technique as a probe in the biomedical application, they are easily prepared compared to probes such as quantum dots or organic dyes also they don't burn even after long exposure to light[32,47]. JicunRen and his colleagues at Shanghai Jiaotong University in China applied the nanoparticles to detect carcinoembryonic antigen (CEA) and Alpha Fetal Protein (AFP), they are used as biomarkers in the diagnosis of different cancer types. They simply attach their gold nanoparticle to the antibodies to measure the biomarker levels. Ovarian tumor can be suppressed by tiny particles carrying some killer gene in mice according to some research groups in MIT and Lankenau Institute. Those results can lead to a new ovarian cancer treatment, which cause more than 15,000 deaths each year in USA as it is always discovered in a late stage. A new treatment had been reported delivering gene that produces diphtheria toxin which kills the cell by preventing their ability to manufacture protein. Daniel Anderson, research associate in the David H. Koch Institute for Integrative Cancer Research at MIT and a senior researcher of the study that agreed that human clinical trial can start. They also agreed that this treatment is effective and in some cases more effective than traditional chemotherapy as didn't have the toxic effect of chemotherapy[24].

Animal and poultry nutrition: There are main four ways of using nanotechnology in animal nutrition, the first is administration of nutrients, supplements, probiotics and medication; the second way is the diagnosis and the treatment of certain disease so the veterinarians could avoid operating, the third way is registering to follow up animals case by case and the fourth way is management of reproduction with some hormonal immunosensors.

Xu *et al.*[48] confirmed the use of nanoparticles of noble metals (mainly silver) in animal nutrition as disinfectants and to minimize ammonia emissions and nitrogen oxides because of its antimicrobial properties. A study by Dobrzanski *et al.*[49] assured that the using nanosilver as a microbicidal preparation reduced the number of *Escherichia coli*, *Streptococcus* bacteria, harmful *Salmonella* and total number of mesophilic bacteria in the litter. Recent *in vivo*, *in ovo* and *in vitro* study on the using nanogold and nanosilver as feed additives to animal and poultry diets has been done[50,51]. These studies showed a positive selective impact of nanosilver on the count of bacteria in poultry digestive tract. This additive inhibited the pathogenic bacteria development. Jovanovic and Palic[52] and Xu *et al.*[48] theorized that the spectrum of action of nanoparticles (from various metals) on the redox or immune system can be quite broad from stimulation to suppression. This action is depending on size of nanoparticles, the dosage, the production method as well as the route and duration of application. Ahmadi[53] fed chickens diets supplemented with nanosilver (20, 40 and 60 ppm kg^{-1} of feed). Results revealed that this nanosilver could accumulate in the lymphatic organs, making an immunosuppressive impact on the organism. In another study, Ahmadi and Kurdestany[51] stated that broilers fed diet enriched with silver nanoparticles had lower RBC and WBC counts and a lower level of blood Hb. Gholami-Ahangaran and Zia-Jahromi[54] postulated that colloidal nanosilver activates erythropoiesis. Researchers illustrated that colloidal nanosilver administered with aflatoxin, which declines haemoglobin concentration and minimize chicken blood haematocrit, declined the negative influences of the aflatoxin on these blood indices. Sawosz *et al.*[50] found no impact of administration of nanosilver to broilers on the activity of ALP, ALT or AST. Authors reported a decrease in the activity of LDH in the plasma of chickens received AgL-nano and Ag-nano. Based on LDH activity, it is possible to clear the degree of cell membrane integrity under the impact of oxidative stress. Oxidative stress activated by nanosilver administration usually causes a depression in the function of mitochondrial, manifested as a depression in LDH activity[55]. A study of Ahmadi *et al.*[56] revealed that using lower doses like 4, 8 and 12 ppm kg^{-1} of feed had no impact on blood CHOL content; however, doses of 8 and 12 ppm kg^{-1} elevated LDL cholesterol and declined HDL cholesterol.

Andi *et al.*[57] reported an improvement in feed intake, weight gain and feed efficiency of broilers fed nanosilver nanoparticles. Researchers attributed this improvement to the impact of ionic silver on intestinal harmful bacteria and enhanced the health of hindgut and consequently better nutrients absorption. Shabani *et al.*[58] revealed that broilers fed a diet contaminated with aflatoxins (AF) without zeolite_hydrocolloidal silver nanoparticles (NZ) had lower weight gain and higher feed efficiency than other experimental groups. Utilizing NZ in diets contaminated by AF caused improved performance like the control diet. Broilers fed diet containing AF and free of NZ had a lower feed consumption compared with control diet.

Ahmadi *et al.*[59] investigated the impact of four treatments using 0, 300, 600 and 900 ppm of silver-nanoparticle levels on the intestine and liver structures of broilers. They recorded no significant differences among different levels of nanosilver for liver and intestine tissues. Loghman *et al.*[1] studied the toxicity of nanosilver and noticed morphological and pathological changes in broiler liver. Results revealed that control group had a healthy liver tissue without specific lesion. In the first treatment which received 4 ppm nanosilver, infrequent accumulations in hyperemia and the hepatocytes were observed. For second and third groups which received 8 and 12 ppm nanosilver, respectively revealed dilated central vein in addition to hyperemia with severe fatty change. In the third group (12 ppm), researchers found increased focal necrosis and connective tissue (fibroplasia) of hepatocytes. Lesions and apoptotic cells in groups 3 and 4 were more intensive than group 2. Researchers concluded that higher levels of nano-silver (8 and 12 ppm) may induce sever lesions in broiler liver.

NANOPARTICLES AS FOOD AND FEED SUPPLEMENTS

Minute micelles (nanocapsules) are acclimated as carriers for essential oils, flavor, antioxidant, coenzyme Q10, vitamins, minerals and phytochemicals to improve their bioavailability[60]. Encapsulating the nanoparticles of polyphenols, some minerals and some micronutrients is done to assure them from any oxidative actions and giving them an acceptable taste[61]. In food industry, appliance of liposomal nanovesicles for the encapsulation and supply of nutrients and other enzymes, flavors and antimicrobial compounds were conducted[62]. As the particle size decrease the better it is absorbed through the intestine, so minerals as feed additive in nanoparticle form will be absorbed easier. Nano-additives can be capsulated by protein or another nutritive ingredient. Micelles are spherical in shape with an inside layer that is fat soluble and out water soluble layer per the other way around if it will be suspended in oil such as nanocapsules having omega 3 fish oil with an un pleasant taste. The wet milling for feedstock and silicon nanoparticle alliance as feed additive releases orthosilicic acid in the GIT, which is the bioavailable

form of silicon, which has a great role in the prevention of osteoporosis[63]. Vitamin E sensitivity to light makes it lose its function, also storage for a long time can do the same. Synthetic versions of vitamin E are less expensive but with lower biological activity. Assimilation of the top bendability aqueous anatomy (vitamin E 97%) was adjourned gravimetrically by weight increase. Mesoporous silicon segments of 65% porosity and 158 μm array were absorbed for capricious times at room temperature and balance aqueous on the alien apparent removed by burden assimilate clarify paper. The capillary armament are abundantly ample to accomplish fractional loading in abbreviate periods[63]. Polyunsaturated fatty acids are necessary for cardiovascular health. A commercial product (Vertese™-Omega 3, 6 and 9) was acclimated for incorporation. The oil alloy contained alpha-linoleic acid, linoleic acid, oleic acid, palmitic acerbic and stearic acid. Capsules were torn and the oils extracted and pooled. Immersion of the silicon membranes was agitated out for 1 h and at allowance temperature. After balance oil abatement by clarify paper, the weight access was agnate to a boilerplate of 41 wt% loading throughout the silicon. Cross-sectional EDX spectra accepted the accord throughout and top akin of loading into the silicon structure, with an actual top carbon to oxygen arrangement constant with the actinic agreement of such oils[63]. When nano-Se supplemented to sheep at amount of 3 ppm in basal diet luminal pH (range of 6.68-6.80) and ammonia N absorption (range of 9.95-12.49 mg/100 mL) was decreased ($p<0.01$) and absolute VFA absorption (range of 73.63-77.72mM) was added linearly ($p<0.01$) and quadratically ($p<0.01$) with accretion nano-Se supplementation[64]. The arrangement of acetate to propionate was linearly ($p<0.01$).

IMPACT ON NUTRITIONAL VALUES AND FEED QUALITY

Nano-sized self-assembled liquid structures (NSLS) is a liquid droplet technology involves encapsulation and absolution particles in the cells. The micelle particles are acclimated to encapsulate nutraceuticals (beta-carotene, CoQ10, docosahexaenoic acid/eicosapentaenoic acerbic (DHA/EPA) and added compounds) into 30 nm diameter spheres. Micelles are nanoparticulates that can be accumulated by the thermodynamically apprenticed action accepted as self-assembly. Micelles fabricated in this way accept the adeptness to abbreviate non-polar molecules such as lipids, flavors, antimicrobials, antioxidants and vitamins[32].

Compounds that are commonly soluble or just water soluble can be fabricated as water soluble and extend their use in foods/feeds and potentially alteration their bioavailability just after ingestion. The micelles are about fabricated from lipid with hydrophilic interior and hydrophobic exterior. The NSLS particles act as vehicles for compounds to be captivated into the bloodstream from the gut added readily, accretion their bioavailability. Liposomes are an addition archetype of micelles and can be acclimated to abbreviate both water and lipid soluble compounds[65].

The dissolution of fat-soluble nutrients in water-based drinks is one of the key applications of liposomes. Liposomes can be produced to differing sizes (10-500 nm) to have different stability under different environmental conditions. Liposome technology can be acclimated potentially to be specific for certain sites. Manipulation of amount at the nano level opens up the door for the improvement of the product quality. Dziechciarek *et al.*[66] had succeeded in developing starch-based nanoparticles that behave like colloids in aqueous solution and can be acclimated in food/feed applications such as mixing, emulsification and imparting specific archeology to foods/feeds[24].

Another aspect to be advised is the assuming of the nanoparticles beneath a ambit of accordant biological conditions, such as in food/feed products, interacting with proteins, lipids, sugars or added biomolecules. This may accept after-effects for the apparent agreement of the nanoparticles and their aggregation behavior as the adsorbed proteins and biomolecules may accept altered hydrophobicity, allegation and allegation administration than the as-synthesized nanoparticles. The adsorbed proteins and added biomolecules advise a "Biological identity[67]" to the nanoparticles as it is these adsorbed molecules that are amenable for the primary alternation with alive systems. Additionally, the nanoparticles can adapt the action of the adsorbed biological molecules, e.g., agitator activity, abasement and added properties, authoritative them added or beneath alive than the absolved anatomy[68]. An added aspect of the adsorption of biomolecules to the nanoparticles is the after effect on the anatomy of proteins such as enzymes and as well on their function, stability, action and accession state, a part of added properties. There are an amount of examples of added agitator adherence and action afterward adsorption to nanoparticles, e.g., the lifetime of the enzymes trypsin and peroxidase was apparent to access dramatically, from a few hours to weeks, by adhering them to alluring adamant nanoparticles[69].

APPLICATIONS IN FEED PROCESSING

Nanoparticles with their fine size have a high surface area so they function more effective than the macro-scale structure. They shared in the new technology of nano-sieves

or micro-sieves that can be applied in food processing. The pores size is in nanometer range. They also used in capsulating valuable food ingredients that could be lost during processing. Nanotechnology is already leading an appulse on the development of the foods/feeds industry, for supplying the body's requirements and to deliver nutrient more efficiently[24]. Various researchers are as well working to advance new "On demand" foods/feeds, which will abide in the body and give nutrients to the cells when needed. A key aspect in this area is the development of nanocapsules that can be part of food/feed to bear nutrients. Other developments in food/feed processing cover the accession of nanoparticles to absolute foods to enhance the absorption of nutrients. Nanocochleates, which are 50 nm coiled nanoparticles and can be acclimated to bear nutrients such as vitamins, lycopene and omega blubbery acids added calmly to cells, without affecting the color or after taste of food/feed[23].

HAZARDS AND RISKS

The risk assessment includes four sides, the hazard identification then the hazard characterization then exposure assessment and the risk characterization. These four stages are so important for the risk assessment[24]. If substance is with high risk hazard but with little exposure potential the risk will be small, while others with limited risk and high exposure for a long period could be with greater risk. So, it is important to characterize both the nature and the exposure time[23]. Feeding of nanoparticle include the increased bioavailability of nanoparticle, the nanoparticle initiate the ROS in the inflammatory digestive disease, the effect of nanoparticle on protein and enzyme stability may be disrupted and the clear effect of nanoparticle on storage and heating[23].

CONCLUSION

Nanotechnology is a novel pathway for improving the pathway of improving digestion and absorption in livestock by improving food ingredients, feed additives, food safety and quality control. The study of nanotechnology is still so limited although it carries huge promises for a better livestock production. Nanoparticle in animal nutrition enhances the efficiency of growth and animal production. A huge amount of studies is still required to support the effectiveness and safety of nanotechnology, avoiding any harm transferring to animals or humans. Also nanotechnology has been used in drug delivery, discovery and in disease diagnosis. Nanotechnology can be part of smarter surfaces and systems. They already had been used in manufacturing glass proof glasses, crack resistant paints, transparent sunscreens, self-cleaning windows, ceramic coatings for solar cells and stain-repellent fabrics.

SIGNIFICANCE STATEMENT

Nanotechnology is a new strategy to improve the pathway of improving the digestion, absorption and metabolism in animal and poultry by improving the utilization of feedstuffs, feed additives, food safety and quality control. The study of nanotechnology is still so limited although it carries huge promises for a better livestock production. Use of nanoparticle in livestock nutrition enhances the efficiency of growth, production and health.

ACKNOWLEDGMENTS

All the authors of the manuscript are immensely grateful to their respective universities and institutes for their technical assistance and valuable support in the completion of this research project.

REFERENCES

1. Loghman, A., S.H. Iraj, D.A. Naghi and M. Pejman, 2012. Histopathologic and apoptotic effect of nanosilver in liver of broiler chickens. Afr. J. Biotechnol., 11: 6207-6211.
2. Ognik, K., A. Stepniowska, E. Cholewinska and K. Kozłowski, 2016. The effect of administration of copper nanoparticles to chickens in drinking water on estimated intestinal absorption of iron, zinc and calcium. Poult. Sci., 95: 2045-2051.
3. Otles, S. and B. Yalcin, 2008. Smart food packaging. Elektroniczne Czasopismo Naukowe z Dziedziny Logistyki, 4: 1-7.
4. Mohapatra, P., R.K. Swain, S.K. Mishra, T. Behera and P. Swain *et al*., 2014. Effects of dietary nano-selenium supplementation on the performance of layer grower birds. Asian J. Anim. Vet. Adv., 9: 641-652.
5. Dhama, K., M. Mahendran, S. Tomar and S. Nandi, 2008. Nanotechnology and its applications in biomedicine, biotechnology and animal health. Livest. Line, 2: 21-26.
6. Blecher, K., A. Nasir and A. Friedman, 2011. The growing role of nanotechnology in combating infectious disease. Virulence, 2: 395-401.
7. Stephen, B.J., M. Jain, K. Dhama, S.V. Singh and M. Datta *et al*., 2015. Nanotechnology based therapeutics, drug delivery mechanisms and vaccination approaches for countering *Mycobacterium avium* subspecies *paratuberculosis* (MAP) associated diseases. Asian J. Anim. Vet. Adv., 10: 830-842.

8. Iqbal, H.M., A. Villalba, R. Khandia, A. Munjal and K. Dhama, 2016. Recent trends in nanotechnology-based drugs and formulations for targeted therapeutic delivery. Recent Patents Inflamm. Allergy Drug Discov., Vol. 10.10.2174/18722 13X10 666161213162823.
9. Lambe, U., P. Minakshi, B. Brar, M. Guray and K. Ranjan *et al*., 2016. Nanodiagnostics: A new frontier for veterinary and medical sciences. J. Exp. Biol. Agric. Sci., 4: 307-320.
10. Yang, L., W. Li, M. Kirberger, W. Liao and J. Ren, 2016. Design of nanomaterial based systems for novel vaccine development. Biomater. Sci., 4: 785-802.
11. Moraru, C.I., C.P. Panchapakesan, Q. Huang, P. Takhistov, S. Liu and J.L. Kokini, 2003. Nanotechnology: A new frontier in food science. Food Technol., 57: 24-29.
12. Mahmoud, U.T., 2012. Silver nanoparticles in poultry production. J. Adv. Vet. Res., 2: 303-306.
13. Fondevila, M., 2010. Potential Use of Silver Nanoparticles as an Additive in Animal Feeding. INTECH Open Access Publisher, USA., ISBN: 9789533070285.
14. Tiwari, R., S. Chakraborty, K. Dhama, S. Rajagunalan and S.V. Singh, 2013. Antibiotic resistance-an emerging health problem: Causes, worries, challenges and solutions-A review. Int. J. Curr. Res., 5: 1880-1892.
15. Hahn, J.D. and D.H. Baker, 1993. Growth and plasma zinc responses of young pigs fed pharmacologic levels of zinc. J. Anim. Sci., 71: 3020-3024.
16. Smith, J.W., M.D. Tokach, R.D. Goodband, J.L. Nelssen and B.T. Richert, 1997. Effects of the interrelationship between zinc oxide and copper sulphate on growth performance of early-weaned pigs. J. Anim. Sci., 75: 1861-1866.
17. Liu, J.H., X. Ma, Y. Xu, H. Tang and S.T. Yang *et al*., 2017. Low toxicity and accumulation of zinc oxide nanoparticles in mice after 270-day consecutive dietary supplementation. Toxicol. Res. 10.1039/C6TX00370B
18. Jensen-Waern, M., L. Melin, R. Lindberg, A. Johannisson, L. Petersson and P. Wallgren, 1998. Dietary zinc oxide in weaned pigs-effects on performance, tissue concentrations, morphology, neutrophil functions and faecal microflora. Res. Vet. Sci., 64: 225-231.
19. Broom, L.J., H.M. Miller, K.G. Kerr and J.S. Knapp, 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.
20. Fathi, M., M. Haydari and T. Tanha, 2016. Effects of zinc oxide nanoparticles on antioxidant status, serum enzymes activities, biochemical parameters and performance in broiler chickens. J. Livest. Sci. Technol., 4: 7-13.
21. Hill, G.M., G.L. Cromwell, T.D. Crenshaw, C.R. Dove and R.C. Ewan *et al*., 2000. Growth promotion effects and plasma changes from feeding high dietary concentrations of zinc and copper to weanling pigs (regional study). J. Anim. Sci., 78: 1010-1016.
22. Zhao, C.Y., S.X. Tan, X.Y. Xiao, X.S. Qiu, J.Q. Pan and Z.X. Tang, 2014. Effects of dietary zinc oxide nanoparticles on growth performance and antioxidative status in broilers. Biol. Trace Elem. Res., 160: 361-367.
23. FSAI., 2008. Zoonotic Tuberculosis and Food Safety. 1st Edn., Food Safety Authority of Ireland, Dublin, Ireland.
24. Bunglavan, S.J., A.K. Garg, R.S. Dass and S. Sameer, 2014. Use of nanoparticles as feed additives to improve digestion and absorption in livestock. Livest. Res. Int., 2: 36-47.
25. Al-Beitawi, N.A., M.M. Shaker, K.N. El-Shuraydeh and J. Blaha, 2017. Effect of nanoclay minerals on growth performance, internal organs and blood biochemistry of broiler chickens compared to vaccines and antibiotics. J. Applied Anim. Res., 45: 543-549.
26. Rastogi, I.D., 2012. Nanotechnology: Safety paradigms. J. Toxicol. Environ. Health Sci., 4: 1-12.
27. Hoet, P.H., I. Bruske-Hohlfeld and O.V. Salata, 2004. Nanoparticles-known and unknown health risks. J. Nanobiotechnol., Vol. 2. 10.1186/1477-3155-2-12
28. Florence, A.T. and N. Hussain, 2001. Transcytosis of nanoparticle and dendrimer delivery systems: Evolving vistas. Adv. Drug Deliv. Rev., 50: S69-S89.
29. Taylor, S., L. Qu, A. Kitaygorodskiy, J. Teske, R.A. Latour and Y.P. Sun, 2004. Synthesis and characterization of peptide-functionalized polymeric nanoparticles. Biomacromolecules, 5: 245-248.
30. Stanley, S.L. and L.L. Doris, 2000. Glyconutritionals: Implications in antimicrobial activity. GlycoScience, 1: 1-4.
31. Cinco, M., E. Banfi, E. Ruaro, D. Crevatin and D. Crotti, 1984. Evidence for L-fucose (6-deoxy-L-galactopyranose)-mediated adherence of *Campylobacter* spp. to epithelial cells. FEMS Microbiol. Lett., 21: 347-351.
32. Chen, H., J. Weiss and F. Shahidi, 2006. Nanotechnology in nutraceuticals and functional foods. Food Technol., 3: 30-36.
33. Eliasof, S., D. Lazarus, C.G. Peters, R.I. Case and R.O. Cole *et al*., 2013. Correlating preclinical animal studies and human clinical trials of a multifunctional, polymeric nanoparticle. Proc. Nat. Acad. Sci. USA., 110: 15127-15132.
34. Zuckerman, J.E., I. Gritli, A. Tolcher, J.D. Heidel and D. Lim *et al*., 2014. Correlating animal and human phase Ia/Ib clinical data with CALAA-01, a targeted, polymer-based nanoparticle containing siRNA. Proc. Natl. Acad. Sci. USA., 111: 11449-11454.
35. Liu, Y., V. Gunda, X. Zhu, X. Xu and J. Wu *et al*., 2016. Theranostic near-infrared fluorescent nanoplatform for imaging and systemic siRNA delivery to metastatic anaplastic thyroid cancer. Proc. Natl. Acad. Sci. USA., 113: 7750-7755.
36. Bertrand, N., J. Wu, X. Xu, N. Kamaly and O.C. Farokhzad, 2014. Cancer nanotechnology: The impact of passive and active targeting in the era of modern cancer biology. Adv. Drug Deliv. Rev., 66: 2-25.

37. Shi, J., P.W. Kantoff, R. Wooster and O.C. Farokhzad, 2017. Cancer nanomedicine: Progress, challenges and opportunities. Nat. Rev. Cancer, 17: 20-37.
38. Mochalin, V.N., A. Pentecost, X.M. Li, I. Neitzel and M. Nelson *et al*., 2013. Adsorption of drugs on nanodiamond: toward development of a drug delivery platform. Mol. Pharm., 10: 3728-3735.
39. Smith, D.M., J.K. Simon and J.R. Baker Jr., 2013. Applications of nanotechnology for immunology. Nat. Rev. Immunol., 13: 592-605.
40. Wang, Y., P. Li, T.T.D. Tran, J. Zhang and L. Kong, 2016. Manufacturing techniques and surface engineering of polymer based nanoparticles for targeted drug delivery to cancer. Nanomaterials, Vol. 6. 10.3390/nano6020026.
41. Gontero, D., M. Lessard-Viger, D. Brouard, A.G. Bracamonte, D. Boudreau and A.V. Veglia, 2017. Smart multifunctional nanoparticles design as sensors and drug delivery systems based on supramolecular chemistry. Microchem. J., 130: 316-328.
42. Chakravarthi, V.P. and N. Balaji, 2010. Applications of nanotechnology in veterinary medicine. Vet. World, 3: 477-480.
43. Manuja, A., B. Kumar and R.K. Singh, 2012. Nanotechnology developments: opportunities for animal health and production. Nanatechnol. Dev., 2: 17-25.
44. Num, S.M. and N.M. Useh, 2013. Nanotechnology applications in veterinary diagnostics and therapeutics. Sokoto J. Vet. Sci., 11: 10-14.
45. Svenson, S., 2014. What nanomedicine in the clinic right now really forms nanoparticles? Wiley Interdisciplin. Rev.: Nanomed. Nanobiotechnol., 6: 125-135.
46. Liu, L. and C. Jiang, 2017. Drug delivery strategies based on nanotechnology for cancer immunotherapy. Curr. Organ. Chem., 21: 34-44.
47. Zhu, L., Z. Zhou, H. Mao and L. Yang, 2017. Magnetic nanoparticles for precision oncology: Theranostic magnetic iron oxide nanoparticles for image-guided and targeted cancer therapy. Nanomedicine, 12: 73-87.
48. Xu, Y., H. Tang, J.H. Liu, H. Wang and Y. Liu, 2013. Evaluation of the adjuvant effect of silver nanoparticles both *in vitro* and *in vivo*. Toxicol. Lett., 219: 42-48.
49. Dobrzanski, Z., K. Zygadlik, B. Patkowska-Sokola, P. Nowa-kowski, M. Janczak, A. Sobczak and R. Bodkowski, 2010. The effectiveness of nanosilver and mineral sorbents in the reduction of ammonia emissions from livestock manure. Przem. Chem., 4: 348-351, (In Polish).
50. Sawosz, E., M. Grodzik, M. Zielinska, T. Niemiec, B. Olszanska and A. Chwalibog, 2009. Nanoparticles of silver do not affect growth, development and DNA oxidative damage in chicken embryos. Arch. Geflugelkunde, 73: 208-213.
51. Ahmadi, F. and A.H. Kurdestany, 2010. The impact of silver nano particles on growth performance, lymphoid organs and oxidative stress indicators in broiler chicks. Global Veterinaria, 5: 366-370.
52. Jovanovic, B. and D. Palic, 2012. Immunotoxicology of non-functionalized engineered nanoparticles in aquatic organisms with special emphasis on fish-review of current knowledge, gap identification and call for further research. Aquat. Toxicol., 118: 141-151.
53. Ahmadi, F., 2012. Impact of different levels of silver nanoparticles (Ag-NPs) on performance, oxidative enzymes and blood parameters in broiler chicks. Pak. Vet. J., 32: 325-328.
54. Gholami-Ahangaran, M. and N. Zia-Jahromi, 2014. Effect of nanosilver on blood parameters in chickens having aflatoxicosis. Toxicol. Ind. Health, 30: 192-196.
55. Carr, A., M.R. McCall and B. Frei, 2000. Oxidation of LDL by myeloperoxidase and reactive nitrogen species: Reaction pathways and antioxidant protection. Arterioscler Thromb. Vasc. Biol., 20: 1716-1723.
56. Ahmadi, F., M.M. Khah, S. Javid, A. Zarneshan and L. Akradi *et al*., 2013. The effect of dietary silver nanoparticles on performance, immune organs and lipid serum of broiler chickens during starter period. Int. J. Biosci., 3: 95-100.
57. Andi, M.A., M. Hashemi and F. Ahmadi, 2011. Effects of feed type with/without nanosil on cumulative performance, relative organ weight and some blood parameters of broilers. Global Veterinaria, 7: 605-609.
58. Shabani, A., B. Dastar, M. Khomeiri, B. Shabanpur and S. Hassani, 2010. Effects of zeolite-hydrocolloidal silver nanoparticles on the performance and serum biochemical parameters in broiler during experimental aflatoxicosis. Proceedings of the 28th Biennial Conference of the Australian Society of Animal Production, July 11-15, 2010, Armidale, NSW, Australia, pp: 98.
59. Ahmadi, J., M. Irani and M. Choobchian, 2009. Pathological study of intestine and liver in broiler chickens after treatment with different levels of silver nanoparticles. World Applied Sci. J., 7: 28-32.
60. Ognik, K., E. Cholewinska, A. Czech, K. Kozlowski and L. Wlazlo *et al*., 2016. Effect of silver nanoparticles on the immune, redox and lipid status of chicken blood. Czech J. Anim. Sci., 61: 450-461.
61. Heller, L., 2006. Flavor firm uses nanotechnology for new ingredient solutions. Food Navigator News, 10 July, 2006. http://www.foodnavigator-usa.com/Suppliers2/Flavor-firm-uses-nanotechnology-for-new-ingredient-solutions.
62. Wen, H.W., T.R. DeCory, W. Borejsza-Wysocki and R.A. Durst, 2006. Investigation of NeutrAvidin-tagged liposomal nanovesicles as universal detection reagents for bioanalytical assays. Talanta, 68: 1264-1272.

63. Canham, L.T., 2007. Nanoscale semiconducting silicon as a nutritional food additive. Nanotechnology, 18: 1857-1864.
64. Shi, L., W. Xun, W. Yue, C. Zhang and Y. Ren *et al*., 2011. Effect of elemental nano-selenium on feed digestibility, rumen fermentation and purine derivatives in sheep. Anim. Feed Sci. Technol., 163: 136-142.
65. Taylor, T.M., J. Weiss, P.M. Davidson and B.D. Bruce, 2005. Liposomal nanocapsules in food science and agriculture. Crit. Rev. Food Sci. Nutr., 45: 587-605.
66. Dziechciarek, Y., R.J.G. van Schijndel, K.F. Gotlieb, H. Feil and J.J.G. van Soest, 1998. Development of starch-based nanoparticles: Structure, colloidal and rheological properties. Proceedings of the Meeting of Dutch Society of Rheology, October 22, 1998, Prentice Hall, Upper Saddle River, New Jersey, pp: 784.
67. Lynch, I., T. Cedervall, M. Lundqvist, C. Cabaleiro-Lago, S. Linse and K.A. Dawson, 2007. The nanoparticle-protein complex as a biological entity; a complex fluids and surface science challenge for the 21st century. Adv. Colloid Interface Sci., 134: 167-174.
68. Palocci, C., L. Chronopoulou, I. Venditti, E. Cernia, M. Diociaiuti, I. Fratoddi and M.V. Russo, 2007. Lipolytic enzymes with improved activity and selectivity upon adsorption on polymeric nanoparticles. Biomacromolecules, 8: 3047-3053.
69. Sharma, A., Y. Qiang, J. Antony, D. Meyer, P. Kornacki and A. Paszczynski, 2007. Dramatic increase in stability and longevity of enzymes attached to monodispersive iron nanoparticles. IEEE Trans. Magn., 43: 2418-2420.