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MULTIFUNCTIONAL ROLE OF CHITOSAN IN FARM ANIMALS: A COMPREHENSIVE REVIEW

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Abstract

The deacetylation of chitin results in chitosan, a fibrous-like material. It may be produced in large quantities since the raw material (chitin) is plentiful in nature as a component of crustacean (shrimps and crabs) and insect hard outer skeletons, as well as the cell walls of some fungi. Chitosan is a nontoxic, biodegradable, and biocompatible polyglucosamine that contains two essential reactive functional groups, including amino and hydroxyl groups. This unique chemical structure confers chitosan with many biological functions and activities such as antimicrobial, anti-inflammatory, antioxidative, antitumor, immunostimulatory and hypocholesterolemic, when used as a feed additive for farm animals. Studies have indicated the beneficial effects of chitosan on animal health and performance, aside from its safer use as an antibiotic alternative. This review aimed to highlight the effects of chitosan on animal health and performance when used as a promising feed additive.

Key words: chitosan polymer, antimicrobial activity, antioxidant activity, growth, reproduction, animal health

The increased demands for organic animal products and the emergence of the antibiotic resistance problem have evoked scientists to seek unconventional ways to upgrade farm animal performance while maintaining human, animal, and environmental health. Hence, in modern animal and poultry production systems, different feed additives are innovated to maintain the health and metabolic state and intensively improve the productive and reproductive performance of farm animals. Feed additives of natural origin, including probiotics, prebiotics, organic acids, feed enzymes, and phytochemicals, have been nominated to be safer antibiotic alternatives (Singla and Chawla, 2001; Świątkiewicz et al., 2015; Hashem et al., 2021; Madkour et al., 2021). Supplementation of prebiotics or probiotics can improve broiler growth performance (Rehman et al., 2020), growth and health status of fattening lambs (Mousa et al., 2022) as well as fertility (Hashem and Gonzalez-Bulnes, 2022). Alagawany et al. (2021) concluded that supplementing with enzymes, synbiotics, phytobiotics, and organic acids can promote immune system growth and elevation.

One of the new and less widely used feed additives is chitosan. Chitosan is derived from chitin (a component of the exoskeleton of shrimps, crabs, and insects). Chitin is a naturally abundant mucopolysaccharide with white, hard, inelastic, and nitrogenous compounds. It is a byproduct of the fishery industry and is considered a regenerating raw material second only to cellulose in terms of abundance (Bhuiyan et al., 2013; Muanprasat et al., 2015; Ahsan et al., 2018).

Shrimp is considered the major source of chitosan since it contains about 25% to 40% chitin, whereas the crab shell contains 15% to 20%. The availability of chitin, the raw material of chitosan, confers a bonus to the industry and the possibility of producing chitosan at upscale. In 2019, the global market for chitosan was valued at $6.8 billion, and it is expected to grow by almost 25% by 2027. (https://www.grandviewresearch.com/industry-analysis/global-chitosan-market). Chemically, unlike chitin, chitosan contains hydroxyl groups. Thus, chitosan has antimicrobial (Zheng and Zhu, 2003; Holappa et al., 2006), anti-inflammatory (Yoon et al., 2007; Ma et al., 2011), antioxidative (Kim and Thomas, 2007; Yin et al., 2008), antitumor (Qin et al., 2002; Shen et al., 2009), immunostimulatory (Zaharoff et al., 2007), and hypocholesterolemic (Liu et al., 2008 a) properties. Besides, chitosan is a nontoxic, biocompatible, and biodegradable substance. Based on these properties, chitosan has a great potential for a wide range of use in different fields including livestock production (Chou et al., 2015; Guan et al., 2019).

Some studies have shown that chitosan as a dietary supplement in animal feed improves the digestive system by absorbing accumulated toxins and treating chronic constipation and gastrointestinal ulcers (Suthongsa et al., 2017). In context, Ya-ping (2012) and De Souza (2018) reported that dietary chitosan supplementation improves health conditions and prevents diarrhea in growing animals. Furthermore, chitosan supplementation can enhance intestinal morphology and improve the villus structure and microflora, ileal digestibility of nutrients, and microbial protein synthesis in ruminants, monogastrics, and poultry (Huang et al., 2005; Świątkiewicz et al., 2015; Magalhaes et al., 2019; Osho and Adeola, 2020).

However, it is important to highlight that the effects of chitosan on animal health and growth performance depend on the dosage and molecular weight (MW) of chitosan (Walsh et al., 2012).

Chitosan not only benefits growing animals but also it has positive effects on adult animals and their reproductive performance. According to Wan et al. (2016), employing chitosan greatly boosts reproductive capacity and fetal survival in sows. The improvement in reproductive performance is related to the ability of chitosan to improve the histological structure and functions of the gonads and the synthesis of sex hormones and minimize the negative consequences of various types of stress, such as oxidative stress (Hernandez-Patlan et al., 2018).

Therefore, this review aimed to clarify the significant role of chitosan supplementation as a natural feed additive on its biological action and performance in animals.

Chitosan structure

Chitosan is a carbohydrate substance derived from chitin. Chitin is extracted from the outer shell of shellfish, oysters, marine shellfish, crabs, and shrimps (Nwe et al., 2009). Chitosan is more hydrophilic, possesses improved water solubility, and has more potential for chemical modifications due to its free amino group.

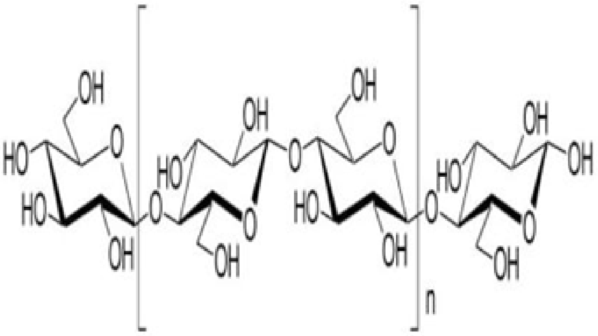
Chitosan is commercially produced by deacetylation or the removal of acetyl groups from the chitin polymer by treatment with alkali (Dutta et al., 2004). N-deacetylation of chitosan can be defined in two ways; degree of deacetylation (DDA) or degree of acetylation (DA). The more commonly used term is DA, which represents the ratio of N-acetylglucosamine monomers to the total number of polymer units. DA is an essential factor, as the improved properties of chitosan compared to native chitin result from N-deacetylation. The DA of the polymer can vary, but it is usually <50% (Benediktsdóttir et al., 2014).

The chemical structure of chitin and chitosan is very similar to that of cellulose which consists of several hundred to <1000 β-(1-4) linked D-glucosamine units (Bhuiyan et al., 2014; Islam et al., 2017) (Figure 1). In the chitin and chitosan structure, the hydroxyl at position C-2 of cellulose is replaced by an acetamide group. Chitosan, β-(1-4) linked 2-amino-2-deoxy-β-D-glucopyranose, is an N-deacetylated derivative of chitin obtained by transforming the acetamide groups into primary amino groups (Aranaz et al., 2009). However, deacetylation of chitin is almost never complete and chitosan or deacetylated chitin still contains acetamide groups to some extent. Unlike cellulose, chitin and chitosan contain 5% to 8% nitrogen, which in chitin is in the form of acetylated amine groups and in chitosan in the form of primary aliphatic amine groups, making chitin and chitosan suitable for typical reactions of amines (Kurita, 2001).

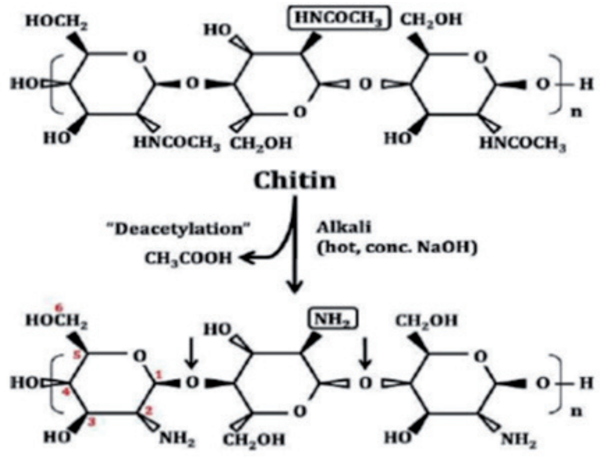
Yet, chitosan is chemically more active than chitin due to the primary and secondary hydroxyl groups on each repeat unit, and the amine group on each deacetylated unit (Figure 1). These reactive groups are readily subject to chemical modification to alter the mechanical and physical properties of chitosan.

The existence of amine groups in chitin and chitosan represents a great advantage because it enables distinctive biological functions and the application of modification reactions (Kumar, 2000). The excellent properties of these polysaccharides, such as biocompatibility, biodegradability, bioactivity, bioresorptivity, nontoxicity, and good adsorption properties, make them very suitable and essential biomaterials and draw a great deal of industrial attention as probable alternatives to synthetic polymers (Croisier and Jérôme, 2013; Tan et al., 2009).

In addition, Guan et al. (2019) indicated that chitosan as a feed additive has favorable biological effects, such as antimicrobial, antioxidative, cholesterol reducing, and immunomodulatory. The biological effects reviewed herein may provide a new appreciation for the future use of chitosan oligosaccharide (Chitosan).



Cellulose



Chitosan

Figure 1. Chemical structure of cellulose, chitin and chitosan showing the structural relationships between the three substances

Preparation of chitin and chitosan

Crab and shrimp shell wastes are currently the most common industrial biomass source for large-scale chitin and chitosan synthesis. Biowastes from marine food companies are processed to help recycle the waste and create derivatives or byproducts for use in other fields. Proteins, inorganic ions, chitin, and lipids are the main structural components of crustacean shell waste. Stepwise chemical techniques are primarily used to extract chitin and chitosan (Kim and Rajapakse, 2005).

The classic process for extracting chitin from crustacean shells involves two phases (Figure 2): deproteinization with alkali treatment at high temperatures and demineralization using diluted hydrochloric acid as the preferred reagent. Although the order of these two steps is interchangeable depending on the source and intended application of chitin (Synowiecki and Al-Khateeb, 2003), studies argued that demineralization should be done first to reduce residual mineral content (Tolaimate et al., 2003).

Shells are reduced to smaller sizes; minerals, primarily calcium carbonate, are extracted (demineralized, decalcified) using weak hydrochloric acid, and stirred at room temperature. Protein is extracted from the leftover material using diluted aqueous sodium hydroxide, protecting chitin products from becoming contaminated with proteins. The resultant chitin is deacetylated in 40% to 45% sodium hydroxide at 160°C for 1 to 3 h without oxygen before being purified to create cationic chitosan (Lamarque et al., 2005; Roberts, 1992). Deacetylation is the process of removing the acetyl group from chitin molecules, which influences the amount of free amine group ($-NH_2$) in chitosan. The repetition of the process can result in deacetylation levels of up to 98% without modification, this heterogeneous deacetylation process can never attain total deacetylation. Deacetylation is proportional to the degree of chitosan transformation from chitin, which is affected by NaOH concentration, reaction temperature, and duration (Kasaai, 2009). DDA varies from 56% to 99% depending on the production process and species. However, optimal chitosan solubility necessitates at least 85% deacetylation (No and Meyers, 1995).

Biological properties

Chitosan has unique qualities that allow it to be used in a variety of applications in livestock production. The biological properties of chitosan, such as antimicrobial, antioxidant, analgesic, anticancer, hemostatic, and hypocholesterolemic, have been confirmed in numerous studies (Figure 3) (Koide, 1998; Kumar, 2000; Klaykruayat et al., 2010).

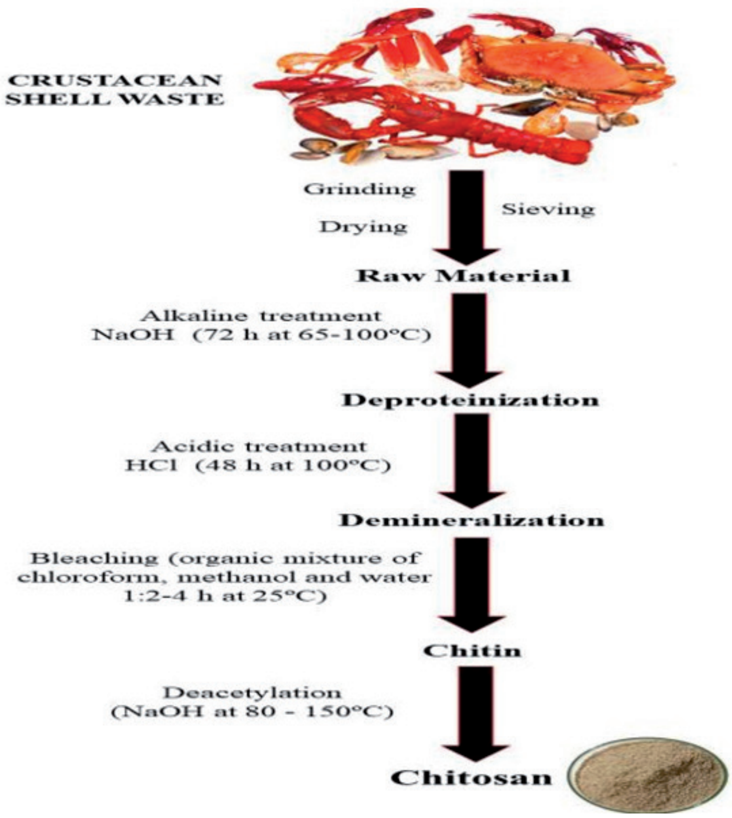


Figure 2. Scheme of chitin and chitosan preparation from crustacean shell waste using chemical methods

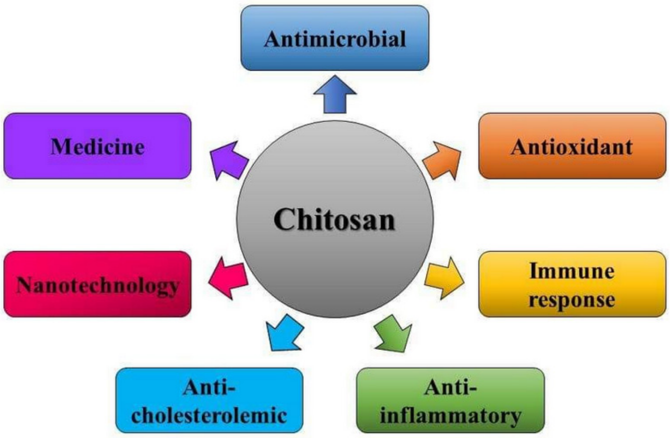


Figure 3. Scheme of summary of the biological activity of chitosan

The biological activity of chitosan is governed by several of its physichochemical properties. For example, the antibacterial and antifungal effects of chitosan depend on its molecular weight (MW) and functional groups. Compared to large MW chitosan, oligomeric chitosan (70–140 kDa) oligomeric chitosan may easily enter the bacterial cell membrane, limiting RNA transcription and preventing cell growth (Klaykruayat et al., 2010).

The length of the polymer chain and the distribution of acetyl groups affect the biodegradation kinetics of chitosan. Furthermore, the cationic behavior of chitosan persuades the biological characteristics and antibacterial activity of chitosan (Zhang and Neau, 2001). The positive charges of the chitosan molecule can interact with primarily anionic components of the cell membrane (e.g., microbe proteins), spoiling cell membrane permeability function and causing intracellular component leakage and cell death (Zheng and Zhu, 2003; Lim and Hudson, 2004).

Strong electrostatic contact is caused by a larger cationic charge density, and DDA of chitosan and its derivatives has a significant impact on the positive charge density. Also, chitosan with high deacetylation degree (DD) (97.5%) has a larger positive charge density, resulting in stronger antibacterial action than chitosan with moderate DD (83.7%) (Kong et al., 2010).

Regarding the antioxidant activity of chitosan, chitosan itself has antioxidant activity. Chitosan monomers have an amino group and two hydroxyl groups that react with free radicals, giving them free radical scavenging activity (Feng et al., 2008). However, this activity can be improved through the chemical modification of chitosan (Guo et al., 2006; Hu et al., 2014; Liu et al., 2017).

Sun (2007) reported that chitosan’s antioxidant activity is proportional to its MW, as low MW is associated with high antioxidant activity. Shorter chitosan chains are less likely to generate intramolecular hydroxyl bonds, resulting in more activated hydroxyl and amino groups, which aid in radical scavenging. Native chitosan (MW=307 kDa, DDA=80%) has negligible reducing power and insignificant scavenging potential against 2,2-diphenyl-1-picrylhydrazyl radicals (Schreiber et al., 2013). Aminoethyl-chitosan provides superior scavenging properties against hydroxyl and superoxide anion radicals (Je and Kim, 2006).

Table 1. Biological properties of chitosan and the main mode of action

Application field	Mode of action	References
Antimicrobial	The positively charged chitosan molecules engage with the negatively charged microbial cell membrane, causing it to pull apart. As a result, chitosan has antibacterial properties	(Dong et al., 2019; Klaykruayat et al., 2010)
Antioxidant	Antioxidant properties against hydroxyl, superoxide, and DPPH radicals	(Powell, 2000; Tomida et al., 2009; Xu et al., 2018)
Immune response	Chitosan can activate the complement system, humoral immunity, and CD4+ cells	(Sarwar et al., 2021; Zaharoff et al., 2007)
Anti-inflammatory	Considering the potentially deleterious implications of an inflammatory response that is exaggerated and protracted in several illnesses, chitosan offers powerful anti-inflammatory capabilities that have been frequently described	(Ma et al., 2011; Ngo et al., 2011; Villiers et al., 2009)
Anti-cholesterolemic	LDL cholesterol and triglycerides were reduced when chitosan and chitosan oligosaccharides were used	(Arslan and Tufan, 2018; Xu et al., 2020)
Nanotechnology	Chitosan has a great ability to charge positively charged nanoparticles, which improves its interaction with cell membranes and allows nanocapsules to enter cells	(Guo et al., 2013; Nagamoto et al., 2004)
Medicine	Different medications are delivered through different channels inside the body, such as oral, nasal	(Nagpal et al., 2010; Tiyaboonchai, 2013)

A summary of the biological activity and the main mode of action of chitosan is shown in Table 1. More details on the biological activities of chitosan and its effects on the farm animal health and performance are discussed in the next subsections.

Antimicrobial activity

Antibiotic growth boosters have been banned in animal production by the European Union and other nations due to potential negative consequences such as antibiotic residues in cattle, pollution, and the development of drug-resistant microorganisms. Chitosan is a potential antibiotic replacement. Chitosan exerts its antibacterial and antiparasitic actions by directly or indirectly promoting immunological activity. Cell lysis, cytoplasmic membrane penetration, and cation chelation are all part of the direct approach likely identical to that described for peptides (Park and Kim, 2010). Antimicrobial and antifungal actions could be explained by these pathways, but antiparasitic effects are less likely. Furthermore, preliminary research suggested that the antibacterial effect may be pathogen-specific, ruling out generic approaches (Dong et al., 2019). Chitosan may have similar qualities to fructo-oligosaccharides and mannan-oligosaccharides with prebiotic benefits (Gao et al., 2001). Several recent investigations have also demonstrated chitosan's antibacterial effectiveness against various microbes (*E. coli*, *S. aureus*) (Chung et al., 2003; Jayakumar et al., 2010).

In chicken farming, the search for safe and ecologically friendly alternatives to antibiotics to prevent disease and increase growth is necessary. Pathogen colonization is thwarted by the gut microbiota, epithelium, and immune system. When infections colonize the intestinal tract successfully, the immune system responds with an inflammatory or antibody response (Wu and Guo, 1997). Furthermore, broiler chicks are more susceptible to external stressors at a young age and thus have a greater disease incidence rate. *In vitro* and in broilers, adding 0.2% chitosan to the diet reduced *Salmonella typhimurium* colonization considerably (Menconi et al., 2014). According to Hernandez-Patlan et al. (2018), chitosan has antibacterial activity against Gram-positive and Gram-negative bacteria. The latter has stronger activity due to the ionic contact between the positively charged chitosan molecules and the negatively charged microbial cell membranes. The antibacterial activity of chitosan when supplied in the feed has been demonstrated in studies on hens and turkeys challenged with *Salmonella enteritidis* and *S. typhimurium*.

Li et al. (2019) found that dietary supplementation with chitosan at a dose of 30 mg/kg, as an alternative to antibiotics (chlortetracycline) improves broiler growth performance, intestinal morphology, barrier function, antioxidant capacity, and immunity. Chitosan supplementation suppressed the growth of intestine harmful bacteria and increased the density of small intestinal microvilli in broiler gut flora (Wang et al., 2003).

El-Sheikh et al. (2019) also revealed that chitosan nanoparticles and chitosan-propolis nanocomposite are viable alternative antibacterial agents. According to Enoka et al. (2020), garlic and onion aqueous extract can create stable chitosan nanoparticles with antibacterial activity similar to fosfomycin against *Staphylococcus aureus* and *Escherichia coli* and hence can be used as an alternative to antibiotics.

According to Hassanein et al. (2021), dietary chitosan and nanochitosan supplementation reduced pathogenic bacteria, such as *E. coli* and *Salmonella* spp. and increased the count of *Lactobacillus* as beneficial bacteria. The *Lactobacillus* index is a well-known sign of a healthy gut. Similarly, Nuengjamnong and Angkanaporn (2018) found that broilers fed chitosan at levels of 1 and 2 g/kg food boosted gut microbiota, such as *Bacillus* populations, but *E. coli* populations decreased ($P \leq 0.001$), suggesting that this may improve gut function. In addition, Tufan et al. (2015) found that *E. coli* concentrations were considerably lower in quails fed a diet containing 150 mg chitosan /kg diet than quails fed a control diet.

Šimůnek et al. (2006) also found that adding 75 or 150 mg/kg chitosan to the diet reduced the number of intestinal pathogen microorganisms (*E. coli*). Similarly, Li et al. (2007) reported that adding 100 mg chitosan to broiler chicken diets reduced the number of *E. coli* in the cecum. In several experiments, dietary chitosan supplementation enhanced *Lactobacillus* populations but decreased *E. coli* numbers in poultry intestines (Spring et al., 2000; Xu et al., 2013; Tufan et al., 2015).

Tufan et al. (2015) found that adding chitosan to quail meals at 75 or 150 mg/kg diet resulted in lower *Lactobacillus* spp. levels than the control group. Chitosan is classified as either bactericidal, which means it can kill live bacteria, or bacteriostatic, which means it can prevent bacteria from growing but not kill them (Goy et al., 2009). In this regard, one of the mechanisms for chitosan's antibacterial potential is its binding to microbial DNA, which activates the suppression of mRNA and protein production via chitosan penetration into the microorganism's nuclei (Sebti et al., 2005; Shaltout et al., 2019).

In pigs, chitosan enhances intestinal function after weaning by having a positive effect on the intestinal microbial community, increasing *Lactobacilli* and decreasing *E. coli* (Kong et al., 2014; Suthongsa et al., 2017). Dietary supplementation of chitosan increased the growth performance, apparent digestibility, and diarrheal incidence of weaned piglets (Han et al., 2007 b; Liu et al., 2008 b). Similarly, Tang et al. (2005) found that feeding weaned piglets a diet containing 250 mg/kg chitosan increased the serum levels of growth hormone and insulin-like growth factor-I. Compared to the control litter group without chitosan, the addition of 10% w/w chitosan to the broiler litter reduced total and organic nitrogen loss as well as concentrations of ammonia-producing bacteria and fungi (Cook et al., 2011).

Antioxidant activity

Antioxidants are substances that prevent or reduce oxidative stress (Brewer, 2011). Oxidative stress can be induced by various environmental factors, such as heat stress, pollutants, radiation, and medications (Blokhina et al., 2003; Sindhi et al., 2013). Furthermore, oxidative stress can be induced following some farm practices, such as early weaning, or some physiological events, such as pregnancy and lactation (Yin et al., 2014). Chitosan has demonstrated significant scavenging action against a variety of radical species, indicating that it has a wide range of applications, the scavenging ability of chitosan derivatives against free radicals is based on hydrogen atom donation via different mechanisms: (1) The polysaccharide unit's hydroxyl groups can react with hydroxyl radicals via the H-abstraction process, (2) The residual-free amino groups NH_2 can combine with OH to create stable macromolecule radicals, and (3) By absorbing H+ from the solution, NH_2 groups can create ammonium groups NH_3, which then react with OH via addition reactions (Xie et al., 2001). Thus, farm animals may need supplements that aid their antioxidant defense system to neutralize all these stresses.

The function of broilers could be improved by food supplementation with an appropriate amount of chitosan (Liu et al., 2011). Hernawan et al. (2017) found that adding 150 mg/g chitosan to the diet of laying hens at 28 weeks reduced blood cholesterol and malondialdehyde (MDA) levels. Moreover, chitosan possesses antioxidant characteristics and can be a potent antioxidant source for broiler chickens (Anraku et al., 2018). Dietary chitosan may enhance broiler hens' intestinal health by reducing the negative effects of stress (Osho and Adeola, 2020). Dietary chitosan supplementation reduced MDA levels and elevated glutathione peroxidase (GSH-Px) activity in the duodenum and jejunum mucosa, implying that chitosan supplementation can reduce heat stress-induced oxidative stress in the gut mucosa (Li et al., 2019; Lan et al., 2020). Chitosan supplementation increased the antioxidant capacity of the intestinal mucosa of heat stressed broilers, according to chitosan's antioxidant potential (Naveed et al., 2019).

Hassan et al. (2021) reported that chitosan and nanochitosan supplementation improved the antioxidative status of Japanese quails and increased the activity of catalase (CAT) as an antioxidant enzyme, a representative enzymatic antioxidant in poultry. To preserve body health, Xu et al. (2020) found that chitooligosaccharide supplementation might lower serum lipids, increase antioxidant activity, and improve hens' immune function during the late laying season.

Ren (2008) reported that chitosan can improve the antioxidative function of dairy cattle by increasing the activity of total superoxide dismutase (T-SOD) and total antioxidant capability. In contrast, Li et al. (2015) found that 500 mg/kg chitosan increased T-SOD levels and decreased MDA levels in serum to improve antioxidative function in beef cattle, which was especially helpful for fatteners because meat quality is linked to antioxidative capacity (Ouali et al., 2006).

Xu et al. (2018) found that dietary supplementation with chitosan increased serum SOD, GSH-Px, and CAT activities, which are representative enzymatic antioxidants in the body, improved performance and antioxidative function, and regulated the immunological response of weaned pigs. According to Xie et al. (2016), adding chitosan to a sow's diet during late gestation increased antioxidant defense capability and accelerated placental amino acid transport, which may improve sows' health and fetal development.

Immunomodulatory properties

Some researchers have suggested that chitosan has immunoenhancing effects and can be employed as an immune stimulant for animals (Yoon et al., 2008; Kong et al., 2014).

Based on *in vivo* and *in vitro* studies, dietary chitosan is a potent and promising immunostimulator. Chitosan's immunostimulatory characteristics are mediated via interactions with membrane receptors on the macrophage surface and dependent on Toll-like receptor 4 (Zhang et al., 2014).

In broiler chicks, chitosan increased humoral and cellular immunological activities (Liu et al., 2007). Furthermore, chitosan is thought to affect immune function, with the index of immune organs reflecting the developing thymus and spleen, which was used to measure the immune condition of birds (Li et al., 2015). Supporting these roles, giving a low dose dietary chitosan to broilers can enhance the weight of immunological organs and body weight-adjusted lymphoid organ weights (Wang et al., 2003; Zhu et al., 2003; Shi et al., 2005; Shi-bin and Hong, 2012). Similarly, Jan et al. (2012) reported that chitosan and its derivatives have strong potential in immune enhancement, such as increased Newcastle disease antibody titers and CD4+ T cell levels, and disease control, such as improved diarrhea and respiratory symptoms and reduced bird mortality, suggesting that it could be used as a feed additive.

Chitosan increased the weight of immunological organs and the blood concentrations of immunoglobulins, complements, hormones, and cytokines, and improved immune function in the growing Huoyan geese (Miao et al., 2020). Furthermore, Xiaofeng et al. (2017) noted that chitosan increased the relative weights of immunological organs and the percentages of G2/M phase thymocytes in broilers. In addition, nutritional supplementation with 100 mg/kg chitosan improved serum IgA, IgG, and IgM concentrations, and immunological organ development in broilers (Huang et al., 2007). In contrast, serum IgG, IgA, and IgM concentrations in Fengda-1 laying hens were not affected by chitosan treatment at 0.075 and 0.125 g/kg food (Xu et al., 2020). In addition, Hamady and Farroh (2020) found that chitosan treatments up to 200 mg/kg diet had no significant differences in IgA and IgM among all treatments, but IgY and intestinal *Lacto-*

bacillus count significantly increased, and *E. coli* count significantly decreased in Bábolna TETRA-SL hens compared to the control group.

In pigs, dietary chitosan supplementation enhanced serum immunoglobulins and compensated for a loss caused by early weaning (Yin et al., 2008; Li et al., 2013). Likewise, Xiao et al. (2013) fed weaned piglets 50 mg/kg chlortetracycline or 300 mg/kg chitosan and found that jejunal mucosal secretory IgA protein expression was higher in the chitosan group than in the control and chlortetracycline groups, indicating that chitosan may improve intestinal mucosal immune function. In the same way, dietary chitosan stimulates a cell-mediated immune response in early weaned piglets by influencing antibody and cytokine production (Yin et al., 2008).

Wan et al. (2017) found that giving pigs 100 mg/kg dietary chitosan increased their SOD and CAT activities, total antioxidant capacity, and serum levels of interleukin (IL)-6, IgG, and tumor necrosis factor-α (TNF-α).

Chitosan helped beef cattle grow faster by improving their immune status and animal health (Shi-bin and Hong, 2012). The addition of chitosan at a dose of 500 mg/kg boosted serum IgA significantly and improved IgM to a minor level, but the benefits were diminished as the dose of chitosan increased (Li et al., 2015).

Anti-inflammatory properties

The anti-inflammatory capabilities of chitosan have widely been reported in light of potentially harmful implications of an inflammatory response that is disproportionate and extended in various disorders (Villiers et al., 2009; Ma et al., 2011; Ngo et al., 2011).

Many potential processes have been proposed to explain the anti-inflammatory activities of chitosan, including acid hydrolysis of chitosan to glucosamine hydrochloride, sulfate, phosphate, or other salts, via salt conversion. Besides, chitosan can reduce lipopolysaccharide (LPS)-induced inflammatory responses by reducing gene expression of the nuclear factor κB light-chain enhancer of activated B cells (Li et al., 2011). As a result, chitosan successfully decreases inflammation caused by a wide range of farm animal infectious microorganisms, such as enterotoxigenic *E. coli* (Liu et al., 2016; Xiao et al., 2016). Several studies confirmed this effect when chitosan was used as a dietary supplement in the diets of farm animals.

In weaned pigs, supplementation with 300 mg/kg chitosan improved the mRNA expression of IL-1β and IL-6 in the jejunal mucosa, showing similar effects to antibiotics in boosting growth and lowering intestinal inflammation (Xiao et al., 2013, 2014). Similarly, Li et al. (2017) found that dietary chitosan (100, 500, 1000, and 2000 mg/kg feed) enriched the linear or quadratic levels of prostaglandin E2, leukotriene B4, and arachidonic acid in piglets given dietary chitosan, which could help explain how chitosan affects the anti-inflammatory function of weaned piglets.

The addition of 300 mg/kg chitosan significantly reduced LPS-induced intestinal damage by reducing serum IL-6, IL-8, and TNF-α levels, decreasing intestinal levels of proinflammatory cytokine mRNA, and increasing anti-inflammatory cytokine mRNA, levels in an LPS-challenged piglet model (Huang et al., 2016).

Magalhaes et al. (2021) reported that chitosan can reduce inflammation in rumen histological segments of sheep fed whole cottonseed supplemented with chitosan, indicating that chitosan possesses anti-inflammatory properties.

In adult animals, Xie et al. (2016) reported that maternal dietary supplementation with chitosan protected sows from oxidative stress by increasing plasma antioxidants and blocking the inflammatory response. Therefore, chitosan supplementation during late gestation may be an effective means of regulating the health of pregnant sows and nutrition transport from sows to the fetus.

Anticholesterolemic properties

Hematobiochemical attributes are good indicators for the safety of any feed additives and the animal's health status. Many studies have confirmed the safety of chitosan as a dietary supplement and its positive effects on animal health or at least lack of negative or hazardous effects (Arslan and Tufan, 2018; Gorelik et al., 2021; Hassan et al., 2021; Kamal, 2021). Interestingly, one of the most important effects of chitosan on blood metabolites attributes is the reduction of cholesterol levels, specifically low-density lipoprotein (LDL). This effect is important especially when animals are fed high energy/fat diets, such as those containing high content of seed oil and/or fat supplements (e.g., protected fat). Feeding high fat content diets may disrupt hepatic function. In this context, the inclusion of chitosan in the diets of meat chickens reduced LDL cholesterol (LDL-C) levels (Keser et al., 2012) and lowered hepatic triglyceride synthesis (Kobayashi et al., 2006). In addition, Xu et al. (2020) discovered that adding chitosan to the diet at a dose of 0.125 g/kg significantly increased serum albumin content and significantly decreased serum cholesterol and triglyceride levels in laying hens compared to birds fed the control diet, without negative effects on total protein, glucose, glutamate oxaloacetate transaminase, and glutamate pyruvate transaminase. El-Ashram et al. (2020) found that adding chitosan to the diet of Japanese quails at a dose of 0.2 g/kg enhanced total serum protein and high-density lipoprotein but decreased serum triglyceride and had no effect on serum albumin, cholesterol, or LDL. Similar effects were also seen in ruminants. Gorelik et al. (2021) found that feeding cows chitosan succinate of various MWs benefited their body's physiological state and metabolism. Low-molecular-weight chitosan had a stronger effect on the hematopoietic process (enhanced red blood cells, white blood cells, and hemoglobin). In contrast, some studies have shown that the addition of chitosan to the diets of farm animals, did not affect their hematobiochemical attributes and did not exert harmful effects on these attributes (Zhou et al., 2009; Nuengjamnong and Angkanaporn, 2018; Hassan et al., 2021; Kamal, 2021).

Antitoxic properties

In modern livestock production systems, feeding diets rich in grains and seeds is crucial for animal growth under intensive production systems. One of the major challenges associated with feeding such feed sources is the contamination with mycotoxins. Mycotoxins are classified as normally occurring pollutants produced by specific types of fungi, causing toxicity and hazardous to animal and human health. Mycotoxins represent a serious health threat factor, especially in developing countries where environmental conditions, high temperature, and relative humidity aid fungal growth and their toxin synthesis. These fungi can attack grains and other crops in the field or during storage, thereby causing real economic losses and affecting the quality of animal products (meat, milk, and egg). The major toxins of concern include aflatoxins (AFB_1, AFB_2, AFG_1, AFG_2), ochratoxin A (OTA), fumonisins (FB_1 and FB_2), and trichothecenes (ZEA, HT-2, T-2, and DON), which are placed in group 1 to 3, respectively (Vila-Donat et al., 2018).

Many attempts have been carried out to attenuate the effect of mycotoxins, either by suppressing fungal growth or reducing the bioavailability of mycotoxins after consumption of contaminated diets. Chitosan is one of the antitoxin candidates. Chemically, due to the cationic nature of chitosan, it can interact and bind with the negative charges of oxygen found in mycotoxins (Juarez-Morales et al., 2017).

In an *in vitro* study, the addition of chitosan to palm kernel-based diet resulted in 94.35%, 45.90%, 82.11%, 84.29%, 90.03%, 51.30%, 90.53% and 90.18% maximum removal rate for AFB_1, AFB_2, AFG_1, AFG_2, OTA, ZEA, $FB_{1,}$ and FB_2, respectively (Abbasi Pirouz et al., 2020).

In another study, copper-chitosan nanocomposite hydrogel is employed to induce plant defense against toxigenic fungi. In this study, copper-chitosan nanocomposite hydrogel inhibited *aflP* and *aflA* genes of various strains of *Aspergillus flavus* involved in the synthetic track of aflatoxin when incubated with peanut meal and cotton seeds (Abd-Elsalam et al., 2020).

The other study was conducted to assess the efficacy of nanocomposite magnetic graphene oxide with chitosan (MGO-CTS) adsorbents against feed contaminated with ~20 ng/g (ppb) aflatoxin on 300 one-day-old chicks. This study indicated that a higher concentration of MGO-CTS (0.50%) effectively improved the overall performance of broiler chickens by preventing the adverse effects associated with aflatoxicosis (Saminathan et al., 2018).

Benefits of chitosan for growing animals

For growing animals (weaned pigs), boosting their digestive system function and maintaining their general health status are the key factors that control the growth performance of these animals at the early growing stages (Xu et al., 2014).

Chitosan is a proper feed additive for growing animals, as it can increase the release of digestive enzymes from the stomach, pancreas, and intestinal mucosa (Hou and Gao, 2001). Furthermore, chitosan can improve the digestibility of ileal contents, increase absorption capacity, and boost cell division, implying that chitosan might be used as a dietary addition to improve digestive efficiency and stimulate nutrient absorption in weaned pigs (Suthongsa et al., 2017). Chitosan also improves intestinal morphology, villus structure and microbiota, and nutritional digestion and absorption and reduces diarrhea in poultry, weaned pigs, and rabbits, respectively (Świątkiewicz et al., 2015; Suthongsa et al., 2017; De Souza, 2018). Interestingly, positive effects of chitosan on the digestive system's functions have been confirmed in ruminants, whose rumen plays a great role in their growth and health. Chitosan has positive effects on ruminal fermentation and fiber digestibility in beef (Dias et al., 2017) and improved ruminal fermentation products by increasing propionic acid synthesis over methane synthesis (Belanche et al., 2016).

Several studies confirmed the positive effects of dietary chitosan supplementation in different farm animals. Chitosan improved the growth performance of growing piglets (Liu et al., 2008 a; Yin et al., 2010; Yang et al., 2012; Hu et al., 2018; Duan et al., 2020), rabbits (Kamal, 2021), lambs (Magalhaes et al., 2019; Pereira et al., 2020), chicks and quails (Khambualai et al., 2009; Kong et al., 2010; Shi-bin and Hong, 2012; El-Ashram et al., 2020; Osho and Adeola, 2020).

A summary of some studies on the beneficial effects of chitosan on growing farm animals is presented in Table 2.

Benefits of chitosan for adult animals

Reproduction in farm animals is an important physiological event that determines to a far extent the sustainability of production and economic revenue. Thus, breeders should always ensure the efficiency of this event. Adding chitosan to the diets of adult farm animals can improve and support many reproductive events, such as pregnancy and its outcomes, milk production, and egg production in dairy cows, swine, and laying hens (Del Valle et al., 2017; Wan et al., 2018; Hamady and Farroh, 2020). The positive effects of chitosan on the reproductive performance of farm animals have been related to many modes of action. Chitosan can create an ideal environment for fetal growth and survival by increasing the immunity and antioxidant capacity of dams (Wan et al., 2016), improving placental functions (Wan et al., 2018) and nutrient utilization by either dams or offspring (Del Valle et al., 2017).

Table 2. Summary of some studies on the beneficial effects of chitosan on growing farm animals

Species	Additive/dose	Finding	References
1	2	3	4
Ruminants (Beef cattle, Lamb)	1.0% of diet DM	Chitosan enhanced total tract digestibility of NDF in a high-roughage diet when fed at 1% (DM basis).	(Henry et al., 2015)
	150 g/100 kg	Chitosan improved dry matter intake and digestibility. Increased ruminal propionate concentration and estimated microbial crude protein synthesis.	(Dias et al., 2017)
	136 mg/kg	Whole cottonseed combined with chitosan increased ether extract ADC and microbial protein production.	(Magalhaes et al., 2019)
	2 g/kg of DM	Chitosan increased performance and quality of lamb carcass dressing by altering muscle metabolism.	(Pereira et al., 2020)
Monogastric (Pigs, Rabbits)	1.0, 2.0 g/kg	Chitosan improved feed efficiency and reduced the formation of dangerous microorganisms.	(Han et al., 2007 a)
	0.1, 0.2 g/kg	Increased FI, BWG, FCR, nutrient digestibility.	(Liu et al., 2008 b)
	250, 500 mg/kg	Chitosan improved BWG, as well as dry matter and nitrogen digestibility. Chitosan had no effect on blood indices. Reduced rectal temperature and cortisol blood levels.	(Chen et al., 2009)
	160 mg/kg	Chitosan lowered the occurrence of diarrhea and improved certain other infection-related symptoms.	(Liu et al., 2010)
	100, 500, 1,000 and 2,000 mg/kg	Chitosan ability to boost growth could be attributable to an increase in serum GH concentration and an improvement in the morphological structure of the small intestine.	(Xu et al., 2013)
	100, 500, 1,000 and 2,000 mg/kg	Chitosan improved digestibility of key nutrients and higher jejunum amylase activity were likely responsible for the growth-promoting effect.	(Xu et al., 2014)
	75, 150 or 225 mg/kg	Chitosan improved weaner health or performance through a combination of increased nutrient bioavailability and increased gut absorption.	(Suthongsa et al., 2017)
	50 mg/kg	Chitosan improved growth performance, improved intestinal barrier function, and reduced intestinal inflammation in weaned pigs.	(Hu et al., 2018)
	30 mg/kg	Chitosan boosted immunological response, and piglet diets including chitosan increased growth rate.	(Duan et al., 2020)
	0.1, 0.5, and 1.0 g/kg	Rabbits' diarrhea was prevented when chitosan was added to the feed.	(Ya-ping, 2012)
	0.2 g/kg	The inclusion of chitosan in the diet improved the health of growing rabbits.	(De Souza, 2018)
	0.2, 0.4, and 0.6 g/kg	Chitosan enhanced final body weight, weight gain, and feed conversion ratio.	(Kamal, 2021)

Table 2. – contd.

1	2	3	4
Poultry (Broiler chicks, Ducks, Japanese quail)	0.2, 0.5, 1.0, 3.0, and 5.0 g/kg	Positive effect of chitosan (0.5, 1.0g) on BWG, FCR and nitrogen retention.	(Shi et al., 2005)
	50, 100 mg/kg	Chitosan improved BWG and FCR. Increased nutrient digestibility, caecal *Lactobacillus* concentration, and serum protein and HDL.	(Liu et al., 2007)
	0.1, 0.3, and 0.6 g/kg	Chitosan improved BWG, FCR, and breast meat weight.	(Khambualai et al., 2008; Khambualai et al., 2009)
	0.2, 0.4 g/kg	Chitosan reduced abdominal fat, and increased RBC and HDL in blood.	(Zhou et al., 2009)
	0.25 g/kg	Reduced blood LDL concentration in birds fed a chitosan-supplemented meal, with no effect on triglyceride, total cholesterol, or HDL levels, or growth performance.	(Keser et al., 2012)
	0.1 g/kg	Chitosan had a positive influence on BWG, FCR, dry matter, organic matter, and nitrogen-free extract digestibility.	(Świątkiewicz et al., 2013)
	0.5, 1. and 2 g/kg	Chitosan in broiler diets could be employed as an alternative to antibiotics.	(Nuengjamnong and Ang-kanaporn, 2018)
	30 mg/kg	Dietary chitosan inclusion (30 mg/kg) had favorable impacts on growth performance, intestinal morphology, barrier function, antioxidant capacity, and immunology as an alternative to antibiotics.	(Li et al., 2019)
	1 g/kg	Dietary chitosan increased broiler chick growth and immunological function.	(Osho and Adeola, 2020)
	200 mg chitosan/kg, 50–200 mg ChNP/kg	Nano-chitosan supplementation in the diet of Japanese quail enhanced final body weight, weight gain.	(El-Ashram et al., 2020)

DM = Dry matter, NDF = Neutral detergent fiber, ADC = Apparent digestibility coefficient, FI = Feed intake, BWG = Body weight gain, FCR = Feed conversion ratio, GH = Growth hormone, HDL = High-density lipoprotein, LDL = Low-density lipoprotein, RBC = Red blood cells, ChNP = Chitosan nanoparticle.

Table 3. Summary of some studies on the beneficial effects of chitosan on adult farm animals

Species	Type	Additive/dose	Finding	References
Ruminants	Dairy cows	Chitosan 50, 100, 150 mg/kg	Increased nutritional digestibility without affecting productive efficiency or the mid-lactation milk fatty acid composition.	(Mingoti et al., 2016)
	Dairy cows	Chitosan 75, 150, 225 mg/kg	In dairy cow diets, chitosan, rather than ionophores, can be used as a rumen modulator.	(de Paiva et al., 2016)
	Dairy cows	Chitosan 4 g/kg	Increased long chain fatty acid concentrations improved animal performance, improved nutrition utilization efficiency.	(Del Valle et al., 2017)
	Dairy cows	Chitosan 4 g/kg	Boosted feed efficiency, increased the amount of unsaturated fatty acids in milk.	(Zanferari et al., 2018)
Monogastric	Sows	Chitosan 100 mg/kg	Chitosan supplementation during pregnancy improved the health of sows.	(Wan et al., 2016)
	Sows	Chitosan 100 mg/kg	A chitosan diet during late pregnancy and lactation resulted in increased progeny growth.	(Wan et al., 2018)
	Gilts	Chitosan 0.12 and 0.24 g/gilt/day	Improved pig production, Improved milk production, Improved health of pregnant and breastfeeding sows and their piglets.	(Ho et al., 2020)
	Rabbit bucks	Chitosan 0.2, 0.4, and 0.6 g/kg	Promoted sexual behavior, Improved semen quality and reproductive efficiency.	(Kamal, 2021)
Poultry	Hens	Chitosan 100, 200 mg/kg	Improved egg weight, yolk color, and Haugh units. Raised RBC, WBC, and lymphocyte concentrations	(Yan et al., 2010)
	Hens	Chitosan 200, 400 mg/kg	Improved laying performance, Haugh units, dry matter and nitrogen digestibility, and WBC and total protein blood concentration.	(Meng et al., 2010)
	Hens	Chitosan 100 mg/kg	Chitosan had a positive influence on egg mass and laying performance. Reduced cholesterol levels in the egg yolks of hens fed a chitosan-supplemented diet.	(Świątkiewicz et al., 2013)
	Ducks	Chitosan 1.20 and 2.40 g/kg	Chitosan had a positive effect on BWG, FI, and FCR, as well as immune organ weights and lymphocyte proliferation.	(Shi-bin and Hong, 2012)
	Geese	Chitosan 100, 200, 400 mg/kg	Chitosan supplementation enhanced immune organ weight, immunoglobulin, complement, hormone, and cytokine concentrations in the blood, and improved immune function.	(Miao et al., 2020)
	Hens	200 mg chitosan/kg, 50–200 mg ChNP/kg	Adding 200 mg/kg chitosan, and chitosan nanoparticles to the diet of laying hens improved egg quality, egg yolk composition, immunity, and gut bacteria.	(Hamady and Farroh, 2020)

FI = Feed intake, BWG = Body weight gain, FCR = Feed conversion ratio, HDL = High-density lipoprotein, LDL = Low-density lipoprotein, RBC = Red blood cells, WBC = White blood cells, ChNP = Chitosan nanoparticle.

Chitosan and its derivatives have been proven to have a beneficial biological function in the change of gut flora. Because of its antibacterial properties, chitosan has recently been used as a silage inoculant (Gandra et al., 2016) and as a rumen modulator in confined beef steers (Araújo et al., 2015) and nursing dairy cows (de Paiva et al., 2016) with promising results. Henry et al. (2015) studied the effects of chitosan supplementation on neutral detergent fiber, acid detergent fiber, and dry matter digestibility in beef heifers fed a high forage diet. When comparing the effects of chitosan on *in vitro* batch cultures, these scientists found that batches with chitosan produced more exceptional total volatile fatty acid synthesis than those with monensin. Furthermore, Belanche et al. (2016) found that chitosan altered the fermentation pattern from acetate to propionate synthesis in rumen simulation research.

Chitosan can also improve milk production and quality, as observed in many farm animals, such as dairy cows (de Paiva et al., 2016) and sows (Ho et al., 2020).

In poultry, chitosan can improve egg production by laying hens (Yan et al., 2010), egg weight, yolk color, and egg yolk composition (Meng et al., 2010; Świątkiewicz et al., 2013; Hamady and Farroh, 2020). Kamal (2021) found that, using chitosan at doses of 0.2 and 0.4 g/kg diet was effective in enhancing sexual behavior and improving semen quality and reproductive efficiency in New Zealand White rabbit bucks.

A summary of some studies on the beneficial effects of chitosan on adult farm animals is presented in Table 3.

The emerging applications of chitosan as a nanocarrier in farm animals

Recently, nanotechnology and its applications in livestock production have gained attention (Hashem and Gonzalez-Bulnes, 2021). Many nanoparticles, such as nanominerals, nanoantibiotics, nanophytogenics, nanohormones, and other substances, have been engineered to improve farm animals' productive and reproductive performance and health. Nanoparticles are particles with a diameter of 1 to 100 nm, with different physicochemical properties compared to the original substances and thus different biological activities (Khan et al., 2019). Several techniques are used to create nanoparticles; of these techniques chemical fabrication with polymers is the most important (Abdelnour et al., 2021). In this context, due to the biodegradability, low toxicity, and high affinity properties of chitosan, it is considered one of the most used nanocarriers (Malmiri et al., 2012; Guo et al., 2013).

Chitosan nanoparticles have a wide range of use due to their unique characteristics. Various types of nanoparticles have been researched for use in the poultry business for feeding, watering, and other ways to promote chicken health (Anwar et al., 2019). The use of nanotechnologies and the introduction of nanoparticles into chicken feed is increasing because they increase feed quality, nutritional availability, and pathogen removal (Amenta et al., 2015).

Chitosan has a role in the development of antiviral vaccines due to its adjuvant properties (Van der Weken et al., 2021). Additionally, the use of chitosan in the development of nanoparticle vaccines to treat arbovirus disease has been suggested by de Souza et al. (2021). In recent years, nanotechnology has been used to improve the efficiency of chitosan as an antiviral agent (Rikta, 2019; Singh et al., 2019). Chitosan nanoparticles have better physical properties and can be employed as carrier molecules to boost the antiviral effectiveness of antiviral drugs.

Chitosan nanoparticles are natural antifungal agents that may be manufactured and employed (Yien et al., 2012). Several studies were undertaken to improve the growth performance, immunological state, and microbiota of commercial poultry birds using nanochitosan, a natural substance with good physicochemical qualities. Nanochitosan effectively delayed fungal activity at concentrations between 3.0 and 4.5 µg/ml (Abdeltwab et al., 2019). Xu et al. (2018) found that iron-loaded chitooligosaccharide nanoparticles in broiler chickens diminish the incidence of bacterial chondronecrosis with osteomyelitis.

Regarding the application of chitosan-loaded nanocomposites on adult animals, Hassanein et al. (2021) compared multiple routes of administration and doses of gonadotropin hormone-releasing hormone (GnRH)-loaded chitosan nanoparticles (GnRH-ChNPs) to promote ovulation in rabbits, demonstrating their utility in reducing GnRH dose, handling animals, and enhancing *in vitro* fertilization outcomes. Using GnRH-ChNPs allowed the standard intramuscular GnRH dose to be cut in half without affecting fertility. However, despite its efficacy in triggering ovulation, the addition of GnRH-ChNPs to semen has harmful effects on fertility. Also, the presence of chitosan dextran sulfate nanoparticles did not affect rabbit semen motility, vitality, or membrane functioning. Nevertheless, acrosome integrity was considerably higher than control (Fernández-Serrano et al., 2017).

Hashem and Sallam, (2020) found that giving goats chitosan tripolyphosphate conjugated GnRH nanoparticles resulted in a three- to four-fold reduction in GnRH dose without affecting fertility or prolificacy. In a recent study by Hashem et al. (2022), in goats, delivering hormones (GnRH and prostaglandin $F_{2\alpha}$) of the Ovsynch estrous synchronization protocol using chitosan-tripolyphosphate nanoparticles as carrier material improved the efficiency of the protocol compared to the common protocol. Nanodelivered Ovsynch protocol hormones improved ovarian blood flow and therefore ovarian response and steroidogenesis, specifically when half doses of common hormones were used.

Chitosan safety for human and animals

Chitosan's nontoxic, biodegradable, and antibacterial qualities make it useful in various situations, including biomedical research, agriculture, genetic engineering, food industry, pollution control, and water treatment, among other applications (Cheba, 2011).

Jiménez-Ocampo et al. (2019) indicated that chitosan is a promising agent with methane-mitigating effects, improved animal performance and nutrient utilization efficiency, increased propionate production, reduced acetate to propionate ratio, and increased unsaturated fatty acid concentration in milk, but more studies are needed with *in vivo* models to establish effective daily doses without harming the animal. According to Jayanegara et al. (2021), chitosan helps mitigate the problem of global warming caused by the accumulation of greenhouse gases, such as methane in the rumen system.

Chitosan lowers serum cholesterol in humans and serum and liver cholesterol in animals (Gallaher, 2003). Although the exact process of cholesterol reduction is unknown, micelle entrapment is a potential possibility. Chitosans can help people lose weight faster if they eat a low-calorie diet, but they will not help them lose weight if they eat their regular diet. In addition to its effects on the gut microbiota, where it promotes gastrointestinal health due to its prebiotic potential (Selenius et al., 2018), chitin and its derivatives are the functional dietary fiber that can lower LDL-C levels in the blood when taken in foods (Choi et al., 2012; Caparros Megido et al., 2014). Antiviral, anticancer, and antifungal characteristics, antibacterial qualities, and a bacteriostatic effect on Gram-negative bacteria such as *E. coli*, *Vibrio cholerae*, and *Shigella dysenteriae*, are demonstrated by chitin or its derivatives (Piccolo et al., 2017).

Chitosan has antioxidant, anticancer, anti-inflammatory, immunostimulant, wound healing, coadjutant (in aquatic animals), cholesterol-lowering, antibacterial, and antifungal effects and can be used as an active component of the diet to help people lose weight. Chitosan is also linked to reduced blood pressure, arthritis control, diabetes mellitus treatment, and immunostimulation (Lee et al., 2002; Geerlings et al., 2018). Chitosan limits the digestion and absorption of visceral fats and interferes with bile acid synthesis and lipid metabolism, resulting in cholesterol-lowering effects. This suggests that combining chitosan and *Ganoderma* polysaccharides in the mouth can help with lipid metabolism (Lamas et al., 2016; Shang et al., 2017).

Due to the gradual growth in the consumption rates of these goods, contamination of milk and dairy products with various species of fungi and mycotoxins is quite common, posing a public health risk. As a result, Sayed-Elahl et al. (2019) proposed that chitosan nanoparticles be added to the coating of kareish cheese to improve quality and lengthen shelf life. Likewise, Sorour et al. (2021) discovered that chitosan and its nanoparticles could be utilized to lengthen the shelf life and improve the microbiological quality of tilapia fish.

There is evidence of the effect of chitosan on the health benefits for animals, wherein Ya-ping (2012), De Souza (2018) and Kamal (2021) reported that dietary chitosan enhanced the health of rabbits and increased FBW and FCR. Chitosan has been used in various drug delivery systems, as indicated by the fact that using GnRH-ChNPs allowed a reduction in the standard intramuscular GnRH dose without impacting fertility (Fernández-Serrano et al., 2017; Hashem and Sallam, 2020; Hassanein et al., 2021). Chitosan, rather than ionophores, can be used as a rumen modulator and increases long-chain fatty acid concentrations. This increased the amount of unsaturated fatty acids in milk, improved nutrition utilization efficiency and boosted feed efficiency from cows to pigs (de Paiva et al., 2016; Mingoti et al., 2016; Del Valle et al., 2017; Zanferari et al., 2018). Dietary chitosan improved the health of poultry by lowering blood LDL levels and increasing RBC and HDL levels (Zhou et al., 2009; Keser et al., 2012; Nuengjamnong and Angkanaporn, 2018; Osho and Adeola, 2020).

Conclusion

Chitosan has a wide spectrum of biological properties, suggesting that it could be used for various economic purposes. The usage of chitosan and its derivatives as an animal feed additive has shown antibacterial, antioxidative, immunoregulatory, and blood cholesterol-lowering properties. Nonetheless, different chitosan structures have varied biological features, and no single form of chitosan has all of them. Most studies have shown that chitosan has favorable effects, such as improved nutrient digestibility and animal and poultry growth performance. However, the molecular processes of these bioactivities and the specific effects of the physicochemical qualities of these compounds on their varied bioactivities, remain unknown. Existing experimental data implied that the growth-promoting effects of chitosan are comparable to those of dietary antibiotics in most published research. As a result, chitosan is a viable and effective antibiotic substitute.

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