



NUTRITIONAL SUPPLEMENTS FOR THE CONTROL OF AVIAN COCCIDIOSIS – A REVIEW

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Abstract

Coccidiosis is acclaimed as the most prevalent enteric parasitic ailment of poultry. It is caused by an apicomplexan protozoon of the genus *Eimeria*, which resides in chicken intestinal epithelium leading to intestinal damage. As a result, bloody droppings are there, feed efficiency is reduced, the growth rate is impaired, and egg production is temporarily decreased. Treatment and prevention of coccidiosis are primarily accomplished by inoculating live vaccines and administering anticoccidial drugs. Due to anticoccidials' continuous and excessive use, the mounting issue is drug resistant *Eimeria* strains. The poultry industry has managed resistance-related issues by suggesting shuttle and rotation schemes. Furthermore, new drugs have also been developed and introduced, but it takes a long time and causes cost inflation in the poultry industry. Moreover, government disallows growth promoters and drugs at sub-therapeutic doses in poultry due to increased concerns about the drug residues in poultry products. These constraints have motivated scientists to work on alternative ways to control coccidiosis effectively, safely, and sustainably. Using nutritional supplements is a novel way to solve the constraints mentioned above. The intriguing aspects of using dietary supplements against coccidiosis are that they reduce the risk of drug-resistant pathogen strains, ensure healthy, nutritious poultry products, have less reliance on synthetic drugs, and are typically considered environmentally safe. Furthermore, they improve productivity, enhance nonspecific immunity, preventing oxidation of fats (acting as antioxidants) and inflammation (acting as an anti-inflammatory). The present manuscript focuses on the efficacy, possible mechanism of action, applications, and different facets of nutrition supplements (such as organic acids, minerals, vitamins, probiotics, essential oils, amino acids, dietary nucleotides, feed enzymes, and yeast derivatives) as feed additive for treating poultry coccidiosis.

Key words: avian coccidiosis, nutrition, poultry, antioxidant, plant extract

Avian coccidiosis is a highly infectious parasitic disease of poultry (Du and Hu, 2004; Idris et al., 2017) caused by the intracellular protozoan parasite of the genus *Eimeria* (Abbas et al., 2012 a, b; Kiarie et al., 2013; 2016; 2019; Bortoluzzi et al., 2020). The global economic loss in the poultry industry due to coccidiosis and the preventive measures used against it amount to \$12.4 billion annually (Alagbe et al., 2022). Seven species of the genus *Eimeria* infect poultry (Kitandu and Juranova, 2006; Abbas et al., 2015) at different gastrointestinal tract sites. Most pathogenic strains are *Eimeria brunetti*, *E. maxima*, *E. tenella*, and *E. necatrix* (Quiroz-Castaneda and Dantán-González, 2015; Kiarie et al., 2019). These parasites reside in the intestinal epithelium, where they multiply and cause massive destruction of intestinal cells leading to dysentery (bloody diarrhea), hampered weight gain, and decreased feed conversion efficiency. The main concern that arises from coccidiosis in poultry is the economic loss due to stunted growth, suppressed immune system, reduced egg production, increased morbidity, and elevated level of mortality which is ultimately a great threat for food security (Dalloul and Lillehoj, 2006; Chapman et al., 2010).

For many years, the poultry industry has been dependent on anticoccidials (coccidiocidal and coccidiostats) for the control of coccidiosis. Commonly used anticoccidials are ionophores (salinomycin, sulphanilamide) and synthetic drugs (amprolium, clodolol, and halofuginone). Abbas et al. (2011 a) briefly reviewed their modes of action. Due to prolonged, continuous, and excessive use of anticoccidials, resistance has developed due to various biotic (e.g., alternation of membrane transport channels, altered pathogen metabolisms, etc.) and abiotic factors in different *Eimeria* strains (McDougald and Fitz-Coy, 2008; Abbas et al., 2011 a; Pop et al., 2019; Ur Rahman and Mohsin, 2019). Moreover, these drugs harm the bird's health due to accumulation of residues in various organs and possible interaction with other drugs (Kadykalo et al., 2018; Khater et al., 2020). The latest and innovative drugs have been developed to stop the appearance of drug resistance. These drugs are introduced regularly and rotationally with intensive shuttle programs. These programs eliminate the issue of drug resistance and allow the correct usage of drugs. However, this has increased the cost pressure on the poultry industry.

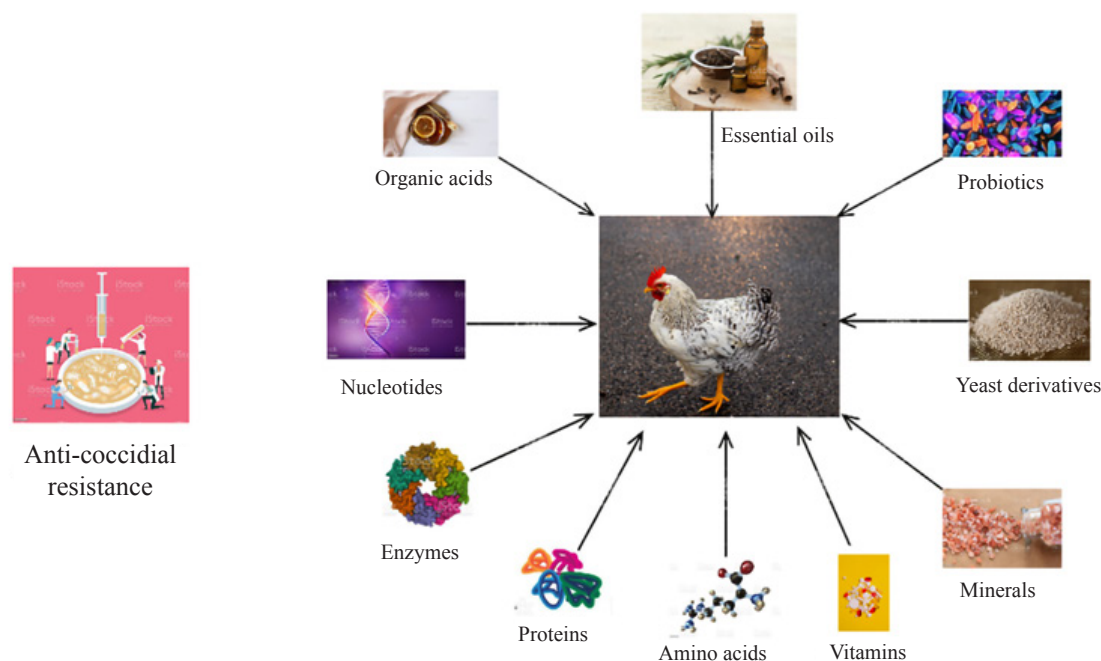


Figure 1. Graphical summary

Government agencies and consumers put pressure to ban or restrict the use of anticoccidials in poultry because the drug residues come in poultry products (meat and eggs) that have detrimental effects on human health. A chemical-free way to control coccidiosis is using vaccines (live or attenuated). Commonly used vaccines are Coccivac, Immucox, Paracox, and HatchPak Cocci III (Quiroz-Castaneda and Dantán-González, 2015). However, the issues with the vaccines are the high cost and complexity of *Eimeria* species (Zaheer et al., 2022). Live or attenuated vaccines have little protection against the continuously evolving *Eimeria* species (Dalloul and Lillehoj, 2005). It is also challenging to develop a cost-effective vaccine that is successful against all types of *Eimeria* species (Zaheer et al., 2022). This way, anticoccidials, and vaccines are the conventional strategies to control widely spread coccidiosis.

The arising problems with conventional control methods against parasites urge us to focus on measures and strategies that have less deleterious effects and prove to be more efficient in production and cost (Ahmad et al., 2022). Chemical-free nutritional supplementation is the best alternative in this regard. There are increased ongoing studies to find novel approaches and alternatives for poultry coccidiosis, such as organic acids, minerals, vitamins, probiotics, essential oils, amino acids, dietary nucleotides, feed enzymes, and yeast derivatives. The introduction of nutritional supplements improves productivity, enhances nonspecific immunity, and limits the use of anticoccidials and vaccines (Dalloul and Lillehoj, 2005). These additives occur naturally and are used as nutritional supplements for various effects, such

as stimulating the immune system, preventing oxidation of fats (acting as antioxidants), and preventing inflammation (acting as an anti-inflammatory). They have no metabolite or residue issue, are safe to use, and have multiple benefits i.e., not only can they be used against coccidiosis, but they can treat many diseases (Mohsin et al., 2021 a, b).

This review aims to broaden the current knowledge about using nutritional supplements (organic acids, minerals, vitamins, probiotics, essential oils, amino acids, dietary nucleotides, feed enzymes, and yeast derivatives) as alternative control measures in the prevention and treatment of coccidiosis as graphically summarized in Figure 1. These measures are inexpensive and safe to use.

Organic acids

Organic compounds with acidic pH have potential to act as anticoccidials at low pH. Acids like acetic acid, butyric acid, hydrochloric acid, and formic acid are efficacious in controlling avian coccidiosis (Shobha and Ravindranath, 1991; Garcia, 2007; Abbas et al., 2011 b, c; Zaman et al., 2012; Rani et al., 2021). Organic acids are used as feed additives and preservatives, preventing food deterioration (Hameed et al., 2022). These include saturated linear chain monocarboxylic acids and their corresponding by-products biologically referred to as volatile fatty acids (Ricke, 2003). Organic acids enhance the utilization of nutrients and promote feed conversion ratio in broiler chickens (Adil et al., 2010). Organic acids can decrease the pH of the digesta and have trophic effects on the mucosa of the gut wall (Adil et al., 2010). Acidification with various organic acids was reported to

reduce the production of free radicals (reactive oxygen/nitrogen species) by pathogens and decrease the settlement of pathogens in the intestine, thus, preventing damage to intestinal epithelial cells. The anticoccidial effect of acetic acid (ethanoic acid) is demonstrated by Abbas et al. (2011 c). They suggested that adding 3% of the acetic acid to the diet mitigates the negative impacts caused by *E. tenella* infection. It decreases the cecal pH, alleviates the impact of oocysts, and eventually reduces the intestinal lesion score (Abbas et al., 2011 c). Commercially available mixtures of organic acids, namely Lacplus® (fumaric acid, lactic acid, phosphoric acid, citric acid) and Acidomix (ammonium propionate, ammonium formate, formic acid) minimize the oocyst index in feces, lessen lesion scores, improve body weight, and enhance feed conversion ratio in chickens challenged with *E. tenella*. Ali et al. (2014) reported that adding butyric acid glycerides to the diet lowers the intestinal lesion score. It enhances the expression of intercellular junctions of the intestine, hence, reducing intestinal permeability to pathogens (Khater et al., 2020). Microencapsulated organic acids (Galli et al., 2021) and short-chain fatty acids (Ali et al., 2014) are used as potential natural alternatives to antibiotic growth promoters (AGP) in diets. Lactic acid produced by lactic acid fermenting bacteria inhibits the growth of specific pathogens such as *Clostridium perfringens*, *Escherichia coli*, and *Salmonella typhimurium* by lowering the pH (Adhikari et al., 2020). Moreover, feed enrichment of anacardic acid (0.2%) with cashew nutshell (0.4%) showed a successful effect in controlling coccidiosis (Abbas et al., 2012 a). This acid possesses the properties of ionophores, so besides being anticoccidial, it can also act as an anti-inflammatory drug (Abbas et al., 2012 a). Therefore, organic acids play a central role in the profitability of poultry production, providing people with wholesome and nutritive poultry products and control of avian coccidiosis.

Feed enzymes

The use of exogenous enzymes in avian nutrition was first suggested about 100 years ago (Ulo, 2022), but their use is limited because they are too expensive. In broilers, nutritional supplementation with protease minimizes the adverse impact of coccidiosis on the body mass gain but has no impact on lesions and oocyst spreading (Peek et al., 2009). Protease also increases the thickness of the mucus layer of the small intestine in broilers. In contrast, Parker et al. (2007) demonstrated that an enzyme mixture (protease, xylanase, and amylase) reduced lesion scores and altered microbial population profiles in coccidia-vaccinated chicks, but not the digestibility of ileal supplements. Intestinal damage by *Eimeria* species such as *E. maxima* and *E. acervulina*, which affect the duodenum and upper jejunum, is related to adverse bone health because these are the sites of mineral absorption (Van Der Klis et al., 1990). In this regard, the purpose of phytase enzymes in supplemented diets has been studied in the coccidial infection model (Watson et al., 2005; Mansoori et al., 2010). The normal pH of the duodenum of healthy birds is six or more significant than six, but it is reduced in birds infected with coccidiosis and becomes less than 5 (Fox et al., 1987). A decrease in the duodenal pH of infected birds increases the efficiency of the phytase enzyme (deterioration of phytate increases) which in turn improves absorption of the nutrients in the gut and improves gut health and repair. Watson et al. (2005) reported that phytase and xylanase enhance feed conversion ratio (FCR).

Vitamins

Vitamins are one of the main feed ingredients of poultry. Several vitamins are significant boosters for the immune system to protect against various infections, inflammations, and diseases. In the current scenario, a vitamins-incorporated diet is used as a treatment tool to mitigate severe poultry *Eimeria* infections.

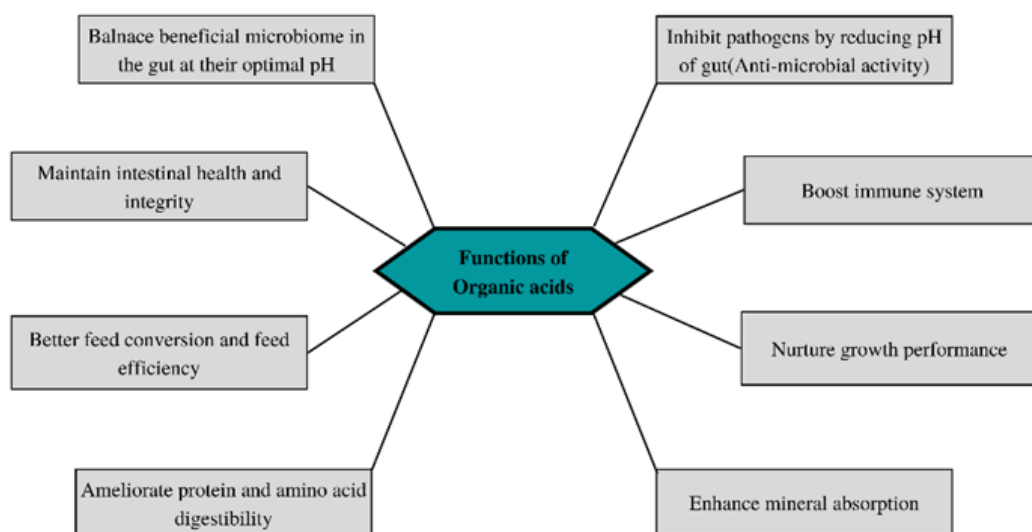


Figure 2. An overview of functions of organic acids

According to several investigations, the storage house of vitamin A is liver, which is responsible for the continuous supply of vitamin A during the active infection period (Moon et al., 2022). In the poultry field, the requirement for vitamin A is higher in infected chickens than in non-infected ones. Vitamin A deficient diet has a direct relationship to chick coccidial infection as it compromises the local immune system (Semba, 1998). A well-known statement is made experimentally: 'the more the vitamin A deficient diet is, the more is the coccidial mortality' (Singh and Donovan, 1973). Early studies declared that chickens infected with *E. tenella* fed with a diet containing 40% vitamin A and 20% vitamin B (above the normal requirements) had a consistent decrease in the excretion of oocysts. They further showed that high levels of vitamin A and proteins lower chick mortality from 25 to 5% during acute coccidiosis. Vitamin A is crucial for compromised poultry as it plays a magnificent role in maintaining intestinal epithelium integrity (Dalloul and Lillehoj, 2005; Alagawany et al., 2021). Vitamin A directly interferes with the biosynthesis of the mucopolysaccharide lining of the gut epithelium, which is a helpful tool against enteric pathogens (Mandal, 2022). In vitamin A deficiency, the epithelium becomes more susceptible to sporozoites, keratinization, and mucus degradation (Dalloul et al., 2002, 2003 b). Therefore, mucopolysaccharide coatings that protect the epithelial lining from coccidiosis are disrupted by the release of epithelial cells from the gut. It has been shown that vitamin A is effective in preventing poultry infections due to its ability to boost the cell-mediated immune system, improve growth, weight gain, and feed consumption, as well as prevent severe mortality, bloody discharge, and paleness in chick combs that occur during coccidial infections (Panda et al., 1964; Fekete and Kellems, 2007; Bedford and Apajalahti, 2022). Vitamin A supplementation increases the chick's resistance to *Eimeria* strains by humoral immunity (Abbas et al., 2012 a).

Ascorbic acid (commonly known as vitamin C) is an antioxidant and an anti-stress agent that is helpful for the maintenance and stability of poultry birds, especially when compromised with coccidiosis (Ahmadu et al., 2016). Generally, birds can synthesize vitamin C in the kidneys from glucose (Lohakare et al., 2005; Abidin and Khatoon, 2013). Ascorbic acid, however, may play an important role in combating stressful conditions, which can cause subclinical coccidiosis (Mohammed et al., 2016; Nahed et al., 2022). Vitamin C has a synergistic interrelationship with other vitamins. Reports from various experiments determined the tonic effects of vitamin C on birds infected with coccidiosis. Vitamin C added diet to growing infected chickens showed a positive response to hinder parasite reproduction, hemorrhagic events, wound healing, collagen, and connective tissue formation (Nahed et al., 2022; Penny et al., 2022). An important function of vitamin C is to regulate the endocrine system, which affects the bird's immune system (Fathima and Selvaraj, 2022). In addition, coccidia-challenged birds

showed improvement in egg mass, FCR, and intestinal health by affecting intestinal growth, mucosal immunity, and development of the intestinal microbiome (Abdel-Moneim et al., 2021). The ascorbic acid's antioxidant response controls any inflammation by optimizing intraepithelial leukocyte proliferation, mainly neutrophils (Shojadoost et al., 2021; Chodkowska et al., 2022; Imran et al., 2022).

Vitamin E is an essential dietary antioxidant for maintaining birds' health and immune system (Jeon et al., 2022). Marsh et al. (1981) demonstrated that the nutritional deficiency of vitamin E causes an impaired immune system which is measured by the humoral immune response to the sheep erythrocytes in broilers. It is used to attain various beneficial results under the *Eimeria*-challenged condition of chickens. During coccidiosis, vitamin E-rich diet is associated with lowering the mortality level, preventing oocyst shedding, increasing weight gain, immunity modulation, and phagocytic activity (Da Silva et al., 2009; Quiroz-Castañeda and Dantán-González, 2015). Further experiments revealed that *Eimeria* infected broilers produced high antibody levels in their serum (like IgA, IgG, and IgM) when fed vitamin E supplemented feed (Perez-Carbajal et al., 2010). Among them, IgG production was 3 to 4 times more, and it is considered the most active antibody against avian infections (Davison et al., 2008). Thus, vitamin E is a necessary supplemental part of the diet in coccidia-infected broilers for better immunity and productive performance.

Amino acids

Amino acids, which are protein components, modulate primary metabolic pathways for growth and immunity. Particular amino acids maintain gut integrity, improve immunity, and participate in the antioxidant defense system in broilers and combat with *Eimeria* species. In coccidiosis, the digestibility and absorption of all types of amino acids are reduced (Yazdanabadi et al., 2020). Low digestibility is due to the decreased gene expression of amino acid transporter molecules (Su et al., 2014, 2015; Chalvon-Demersay et al., 2021). Studies suggested that amino acids, e.g., glutamine, arginine, and threonine have an advantageous effect on broilers facing the problem of coccidiosis. The effects of supplementation of these amino acids on the performance, digestibility, and morphology of the intestine of coccidiosis infected broilers were evaluated by Chalvon-Demersay et al. (2021). The addition of these amino acids in the diet regenerates the mucosa of the intestine. Ultimately, feed conversion efficiency improves (Gottardo et al., 2016). These three trophic amino acids also regulate and maintain intestinal microbiota balance (Dong et al., 2017).

Arginine (essential)

Arginine has beneficial effects on oxidative stress, immunity, and gut health in poultry, as well as on body composition (fat, muscle, and bone metabolisms). Few experimentations reported that the supplementation of

arginine in the diet reduces oocyst excretion in feces (Allen, 1999; Laika and Jahanian, 2017) suggesting that arginine may affect the life cycle of *Eimeria* in a direct or indirect manner. It was found that a daily dose (once or twice a day) of L-arginine (500 mg/kg of body weight) can reduce the shedding of oocysts in *E. tenella* infections (Allen, 1999; Chalvon-Demersay et al., 2021).

Threonine (essential)

Mucin in the intestine is primarily composed of threonine, which is the third limiting amino acid (Faure et al., 2006; Corzo et al., 2007). Mucin comprises 28–35% of threonine out of all the amino acids (Nichols and Bertolo, 2008). So, threonine plays a significant role in the gut barrier and regulation of the immune system (Zhang et al., 2016). In 25X *Eimeria* vaccinated broilers, Zhang et al. (2016) found that threonine insufficiency notably increased oocyst shedding and gut leakage. In addition, they also demonstrated that supplementation of threonine from 0.48 to 0.96% was shown to be effective in improving intestinal integrity as well as reducing oocyst shedding. Increasing threonine supplementation from 0.6 to 0.8% markedly improves feed intake, feed efficiency, and body weight gain in broilers infected with 30,000 oocysts of *E. acervulina* (Kidd et al., 2003).

Glutamine (non-essential)

Glutamine addition to the diet improves feed conversion efficiency (Luquetti et al., 2016) and enhances growth performance in broiler chickens (Mussini et al., 2012; Oxford and Selvaraj, 2019). Glutamine serves as source of energy for enterocytes (Bortoluzzi et al., 2018) and takes part in the proliferation of intestinal cells and the repair mechanism of the intestine during challenging conditions particularly oxidative stress and inflammation. It is also an important component of glutathione that plays a key role in antioxidant system of poultry birds

(Rao and Samak, 2012). Figure 3 explains the use and noticeable effects of adding glutamine in diet.

Methionine (essential)

It is the first (sulfur-containing) limiting amino acid in broilers' growth (Lai et al., 2018) and stimulates the immune response. Methionine is essential for the proliferation of immune cells (Ren et al., 2020). Adding it to the diet is required to ensure the proper metabolism of proteins (Ren et al., 2020). The deficiency of methionine causes alleviation of feed utilization and decreases humoral immuno-competency (Zhang and Guo, 2008). Lai et al. (2018) proclaimed that methionine (0.56 and 0.68% of diet) boosts growth performance in medicated chicks. They also concluded that a higher level of methionine in diet augmented growth performance in chickens infected with *E. tenella* but not in vaccinated chickens. Methionine is oxidized into methionine sulfoxide and captures the reactive oxygen species. In the energy uptake mechanisms, methionine is metabolized into hydrogen disulfide, glutathione and taurine which are also antioxidant in nature (Yin et al., 2016). Hence it has possibility to control coccidiosis due to its antioxidant capacity.

Glycine (non-essential)

Glycine is an essential constituent of mucin, creatine, bile acids and glutathione and plays a substantial role in maintaining the integrity of the intestine and accelerating repair as the consequence of infection (Bedford and Apajalahti, 2022). Because of its vital role in the body, glycine is produced from threonine and serine. When a sufficient amount of dietary glycine is given, it not only enhances immune function, but also conserves serine and threonine for glycine requirements, facilitating an improved response against any *Eimeria* challenged infection (Siebert et al., 2015).

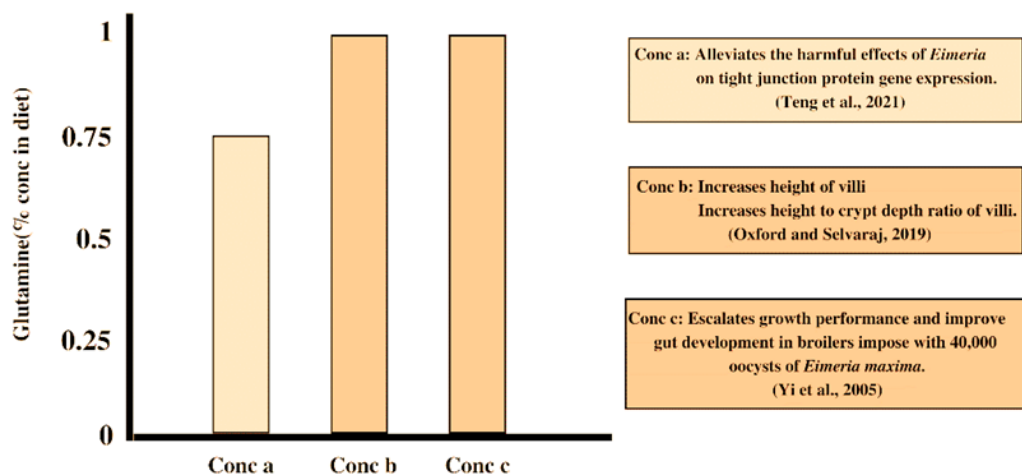


Figure 3. The practical outcome of different concentrations of glutamine used in poultry diet for the control of coccidiosis

Betaine (glycine derivative)

In coccidial infections, the methyl demand of the body increases (Metzler-Zebeli et al., 2009). So, to meet the body's demand, betaine (modified amino acid having glycine and three methyl groups) is given in the diet, which acts as a methyl donor. Betaine supplementation in diet minimizes duodenal lesion score, and, as a result, digestibility and absorption of nutrients are influenced in coccidia-challenged birds (Amerah and Ravindran, 2015). Enteric epithelial cells become osmotically destabilized as a result of stress caused by dehydration during coccidiosis. Betaine proves to be beneficial in this regard as it maintains the osmotic balance of enteric cells (Fabia et al., 2021).

Probiotics

Probiotics are interpreted as live non-pathogenic microbial supplements that confer advantageous effects on the host by balancing the beneficial microbes in the gut (Fuller, 1989; Mohsin et al., 2021 a; Gul and Alsayeqh, 2022). Probiotics are widely used feed ingredients, especially during under-compromised conditions, and their classification (Liévin-Le Moal and Servin, 2014) is mentioned in Figure 4. They also explained the anti-infective activities of probiotics and probiotics as bio-therapeutic agents.

Probiotics are composed of single or multiple species of microorganisms. The mode of action of probiotics is comprehensively explained by Mohsin et al. (2021 a), as shown in Figure 5.

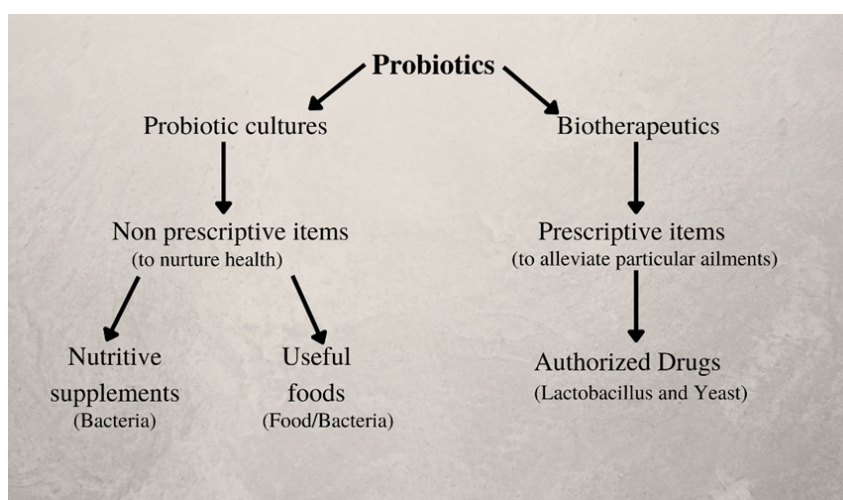


Figure 4. The broader classification of probiotics (Liévin-Le Moal and Servin, 2014)

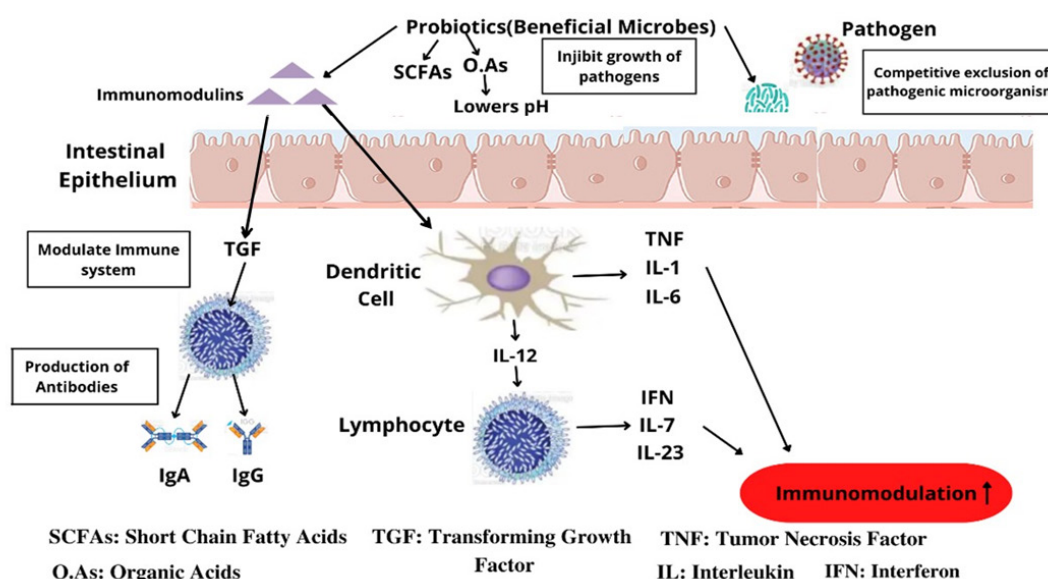


Figure 5. Diagrammatic illustration for mode of action of probiotics in controlling pathogens; probiotics meeting the intestinal epithelium have competition with the pathogens to occupy surface (physical barrier) as well as release short-chain fatty acids (SCFAs) and organic acids (OAs) which reduce the pH and lower the growth. Their contact triggers immune system to express an anti-inflammatory response which leads to activation of lymphocytes which kill the pathogens. SCFAs (short-chain fatty acids); TGF (transforming growth factors); IL (interleukin); TNF (tumor necrosis growth factor); IFN (interferons); Ig (immunoglobulin)

Probiotics were confined to viral and bacterial diseases but are also used to control parasitic diseases (Travers et al., 2011). Various microorganisms such as *Bacillus*, *Candida*, *Saccharomyces*, and *Lactobacillus* are used as probiotics that regulate the immune system, maintain intestinal microflora, enhance performance and inhibit pathogenic activity in poultry (Kabir et al., 2005; Pourakbari et al., 2016; Seidavi et al., 2017; Rashid et al., 2023). Probiotics can also be used as an alternative to drugs for poultry enteric diseases (Patterson and Burkholder, 2003; Rashid et al., 2023). Few *in-vivo* and *in-vitro* studies suggested that probiotics lessen the intestinal score in the chickens infected with *Eimeria* species (Lan et al., 2004). Stringfellow et al. (2011) investigated the effects of probiotics in coccidiosis-affected broilers and suggested that they can modulate immune responses. Interactivity between *Eimeria* and chicken isolated *Lactobacillus* strains was studied by Tierney et al. (2004). In *E. acervulina* infection, inoculation of *Lactobacillus*-based probiotics activates the defensive immunity (Dalloul et al., 2003 a). *Eimeria*-induced gut ulcers can be reduced by probiotics that contain four strains of lactic acid. This probiotic also reduces the gene expression of specific pro-inflammatory cytokines and significantly enhances the expression of anti-inflammatory cytokines (Chen et al., 2016).

PoultryStar®, a multi-species probiotic (*Pediococcus*, *Bifidobacterium animalis*, *Enterococcus faecium*, *Lactobacillus salivarius* based), also decreases the oocyst and lesion score in chickens infected with mixed *Eimeria* infections (Mohsin et al., 2021 b). Eimerial infection activates humoral immunity in birds, and the Mitogrow® probiotic (*Pediococcus acidilactici*) supplementation in the

diet of broilers elevates the level of anti-*Eimeria* antibodies. It also lessens the negative impact of coccidiosis (Lee et al., 2007). Wang et al. (2017) suggested that probiotics play a vital role as antioxidants in avian coccidiosis by decreasing oxidative stress. So, probiotic supplementation plays a significant role in diet against coccidiosis control. Further detail of commercial probiotics and their obvious effects are described in Table 1.

Yeast derivatives

Saccharomyces cerevisiae, known as yeast, is a single-celled microorganism associated with kingdom fungi and eukaryotic in nature (Bennett, 1998; Ingraham, 2010). It forms various mutualistic, parasitic, and symbiotic relationships with other microorganisms (Kiarie et al., 2019). A few known yeast species are used commercially, e.g., *Saccharomyces* (genus) species are notably used in industry to produce single cell protein (SCP), bread, and vitamins. Whey yeast (*Kluyveromyces marxianus*) plays a significant part in dairy production (Kiarie et al., 2019). Many yeast-related feed additives are manufactured, promoted, and applied in animal nutrition. Yeast is a reliable source of vitamins (especially vitamin B), proteins, minerals, and many other nutrients for animals and humans. Unique yeast products comprise *Phafia rhodozyma* yeast and yeast selenium, enhancing the flesh color in many fishes such as salmon and trout (Shurson, 2018). Nutritional yeast and its products are a rich source of micronutrients, proteins, and amino acids used in the feed industry. The functional elements of the cell contents of yeast to study are beta-glucans, chitin, and glycoproteins.

Table 1. Different commercial probiotics and their positive effects in birds challenged with various *Eimeria* strains

Commercial probiotics	Bacterial composition of probiotic	<i>Eimeria</i> species	Spotted effects	References
PoultryStar®	<i>Pediococcus</i> , <i>Bifidobacterium animalis</i> , <i>Enterococcus faecium</i> , <i>Lactobacillus salivarius</i>	Mixed <i>Eimeria</i> infection	Decreases oocysts and lesion score	Mohsin et al., 2021 b
Mitogrow®	<i>Pediococcus</i> based	<i>E. tenella</i> <i>E. acervulina</i>	Elevates level of anti- <i>Eimeria</i> antibodies. Minimizes oocyst shedding and increases body gain. Reduces negative impact concerned with coccidiosis.	Lee et al., 2007
Infant feces®	<i>Enterococcus faecium</i> , <i>Lactobacillus fermentum</i> , <i>L. acidophilus</i> , <i>L. plantarum</i>	Mixed	Reduces expression (cecal gene) of pro-inflammatory cytokines. Increases expression (cecal gene) of anti-inflammatory cytokines. Lessens cecal lesion score.	Chen et al., 2016
Primalac®	<i>Bifidobacterium thermophilum</i> , <i>L. acidophilus</i> , <i>E. faecium</i> , <i>L. casei</i>	<i>E. acervulina</i>	Decreases fecal oocyst shedding. Activates defensive immunity.	Dalloul et al., 2003 a

A few studies were conducted on yeast probiotics supplementation in broiler chickens (Patterson and Burkholder, 2003). The most common method is to use a mixture of yeast probiotics with bacterial microbic culture because multiple strains could be more beneficial than single-strain probiotics (Shim et al., 2012). Few experiments manifest that adding both (yeast and bacteria) probiotics has a synergistic effect on improving growth and survival rate in birds. Furthermore, an assemblage of yeast with *Lactobacillus* intensifies tolerance in gastric or intestinal juices (Xie et al., 2012). An amalgam of yeast with *L. acidophilus* and *Streptococcus faecium* boosts digestion and improves absorption of micro-nutrients; as a result, growth performance in broilers increases (Roto et al., 2015). The most explored yeast probiotic having beneficial effects in many human and animal GIT models was *Saccharomyces cerevisiae* var. *boulardii* (Foligné et al., 2010). The exact mechanism of yeast's action in controlling GIT diseases is still not precise. However, according to a few discussions among scientists, it alters inflammatory and immune responses. It liberates the anti-microbial peptides, causing acidification of the environment and leading to the deterioration of toxic factors. The latest experiment showed that the compound separated from *Meyerozyma guilliermondii* has anticoccidial activity against *E. tenella* oocysts (Dantán-González et al., 2015). *S. cerevisiae* has also been experimented with as an *Eimeria* vaccine delivery vehicle given orally (Lin et al., 2009). Yeast derivatives also called yeast cultures comprise a blend of yeast biomass and fermented products formed in a controlled fermentation process. Few remnants of viable remaining yeast cells are also included in it.

Minerals

Minerals are the micronutrient inorganic feed elements needed for average body growth and maintenance. Their presence is necessary for a healthy, balanced diet. Ozyilmaz et al. (2017) classified minerals as: microminerals or trace elements (required in small amount) and macrominerals (required in large amount). Microminerals or trace elements are minerals that are required in low amounts but essential for the body's proper and normal physiological functioning. In enzymatic reactions, these trace elements can act as catalysts to initiate metabolic reactions. The use of micro-elements as feed additives is a fundamental topic in the present-day poultry system. Recent studies indicate the positive impact of mineral supplements on the health of poultry birds as they maintain the intestine's epithelial integrity via antimicrobial, anti-inflammatory, and antioxidant responses (Bortoluzzi et al., 2020; Bedford and Apajalahti, 2022). Minerals act as activators of enzymes and hormones in poultry. They are also involved in the eggshell formation and replacement of older shells (Alagawany et al., 2021). The mineral requirement for high-producing laying hens and broilers is exceptionally high. They play a vital role in mitigating the adverse reactions of coccidiosis by modulation of the

compromised chick physiology, immunology, and normal intestinal microbiota (Bortoluzzi et al., 2020). Thus, mineral supplementation in poultry has positive results in preventing them from coccidiosis, which includes selenium, zinc, copper, and iron.

Selenium is a potential trace mineral that combines with proteins to form seleno-proteins which act as essential antioxidant enzymes (Abbas et al., 2013). In poultry, the importance of selenium is due to its direct relationship with the glutathione system, where glutathione peroxidases (antioxidants) are selenium-dependent that protect the cell from damage and free radicals (Hafeez et al., 2020 b). It is also observed that selenium supplements in the feed of animals have a protective mechanism in case of lipid peroxidation during several parasitic diseases. The organic form of selenium is more easily absorbed than the inorganic one (Choct et al., 2004). Its central portion is digested in the duodenum (anterior part of the intestine). Hence, as *Eimeria* species cause extensive damage here, it results in low selenium absorption and utilization, ultimately ending with severe coccidiosis in poultry.

Zinc is a trace mineral found in more than 200 enzymes and takes part in many cellular activities due to its catalytic solid and adsorbing ability. The zinc-rich diet increases the goblet cell count, enhancing the innate immunity to *E. papillata* (Dkhil et al., 2015), and activates the antioxidant system and intestinal absorptivity in *E. maxima* challenged broilers (Bortoluzzi et al., 2020). Furthermore, Fekete and Kellems (2007) reviewed that zinc is also responsible for lymphocyte maturation and prevents them from apoptotic deaths. Zinc supplements significantly decrease the damage to jejunum structure and gastrointestinal tract (GIT) lesion score in birds with *Eimeria* infection (Zaghari et al., 2022).

Copper is an essential antioxidant mineral for synthesizing antibodies, secretions (mainly IgG), cellular immunity, and anti-inflammatory actions. Overbeck et al. (2008) found that copper and zinc together showed additive effects, such as uptake of redox mechanisms, and excellent antioxidant activity corresponding to the activation of specific enzymes, such as superoxide dismutase (Richards et al., 2005).

Sodium. In the control of coccidiosis, sodium salts are more practical and beneficial than sodium in its isolated form. Supplementing the diet with sodium sources (sodium bisulfate) notably improves weight uniformity and breast meat yield and minimizes mortality and coccidial lesion score (Hooge et al., 1999). Bird health and rearing are improved by sodium bisulfate, which binds to ammonia and improves litter quality (Pope and Cherry, 2000; Hunolt et al., 2015). It also improves feed conversion efficiency in broilers (Ruiz-Feria et al., 2011). Adding sodium bisulfate to feed will help coccidia-challenged birds to maintain intestinal integrity and enhance

their growth but does not affect parasite oocyst shedding (Chadwick et al., 2020).

Sulfur. The use of sulfur in controlling parasitic diseases of poultry has gained enormous interest for many past years. Herrick and Holmes (1936) pointed out that flowers of sulfur hold much promise in preventing coccidiosis. Carpenter (1939) declared that sulfur flour gave better defense against coccidia than sulfur flowers because of their fineness. The sulfur containing amino acids inoculation in poultry diet proved as best for growth performance and constant immunity (Adhikari et al., 2022). According to Goff and Upp (1940), no matter what sulfur grade chickens were fed, they would sporulate and produce clear signs of the disease after they were inoculated with coccidia. After this, the use of sulfur became limited and further use of sulfur grades for controlling coccidiosis is still in the experimental stages.

Calcium is the most crucial macromineral nutrient, and its absorption is pivotal to the growth of poultry birds, eggshell quality, and egg production in laying hens (Turk, 1973; An et al., 2016). They also concluded that intestinal coccidial infection changes and decreases calcium absorption, while cecal coccidial infection does not affect its absorption. So, it is necessary to supplement Ca in the diet to enhance broilers' growth during intestinal coccidial infection.

All these microminerals have no direct anticoccidial activity but they have their role in capturing reactive oxygen species, boosting immunity, gut wall repair and recovery, so, their addition in the poultry diets along with other dietary materials can help bird to fight against coccidiosis.

Dietary nucleotides

Nucleotides are a series of bioactive agents with low molecular weight and are considered intracellular compounds that have a significant role in several animal biological and physiological activities (Superchi et al., 2012). The molecular structure of a nucleotide is composed of sugar (ribose or deoxyribose), nitrogenous bases (adenine, guanine, cytosine, thymine, and uracil), and one or more phosphate groups. They participate in various biological processes such as lipid metabolism, protein synthesis, mediate humoral response, reproduction, nucleic acid synthesis, injury recovery, intestinal growth, and development (Carver and Walker, 1995; Carver, 1999). Dietary nucleotides play a vital role in the poultry industry regarding health and productivity. Their major documented concerns are immunity boosters (Dil and Qureshi, 2002), antibody formation, body weight gain, gut integrity (Wu et al., 2018), and meat quality (Zhang et al., 2008; ChioFalo et al., 2011). Adding nucleotides to the diet optimizes the overall body weight gain (BWG), improves feed consumption and absorption, and results in better feed conversion ratio (Rafique et al., 2020). Khedr and Ahmed (2020) have depicted that a nucleotide-added

diet has achieved more beneficial economic outputs per kg body weight in chickens. Wu et al. (2018) showed that nucleotide supplementation resulted in an immediate and potent immune response to routine vaccination in poultry. It is experimentally concluded that nucleotide supplementation expresses a healthier gut and improves intestinal feed absorption capacity due to increased villus height to crypt depth of intestinal villi (Jung and Batal, 2012; Abd El- Wahab et al., 2019).

Nucleotide-yeast extract

The products and by-products of yeast cell wall greatly influence the GIT system for modulating the richness and diversity of intestinal microbiota. Till now, several experiments showed the favorable combination of a rich nucleotides diet with yeast extracts against various enteric pathogens, including *Eimeria* species (Perricone et al., 2022). Specifically, yeast-nucleotide (YN) supplements are investigated for increased growth performance, jejunal histomorphology, and cecal antimicrobial activities during the *Eimeria*-challenged course of broiler chickens. The necropsied study by Kiarie et al. (2019) showed that YN added to the diet in bird's feed has improved the body weight gain (BWG), intestinal lesion score, feed conversion ratio (FCR), short-chain fatty acids (SCFA), and cecal digestibility when infected by *E. acervulina* and *E. maxima*. Yeast-nucleotide nutrition is also beneficial for better gut and immune functioning, intestinal repair, and enhanced chicken digestion capacity and performance. Jung and Batal (2012) reported a yeast nucleotide named torula yeast RNA with multiple beneficial effects during poultry enteric diseases like coccidiosis. They mentioned that torula yeast RNA increases chick growth, cecal villi height, and lymphocyte proliferation which are responsible for protection against various enteric pathogens. With the limited information, a YN-rich diet has an adequate response for broiler growth and development of digestive capabilities regardless of *Eimeria* outbreaks.

Plant-derived compounds

Herbal extracts have been used for flavorings, beverages, fragrances, cosmetics, agriculture, and medicine as insecticides, antiparasitics, bactericides, fungicides, since ancient times (Bakkali et al., 2008; Abbas et al., 2010; Djilani and Dicko, 2012; Hanif et al., 2019; Zaman et al., 2020; Ashraf et al., 2021; Bosila et al., 2021; Sobhy et al., 2021; Sayyar et al., 2021; Štrbac et al., 2021; Ali et al., 2022; Nawaz et al., 2022; Okonkwo and Achilike, 2022). Recently, the utilization of herbal extracts, especially essential oils as a treatment alternative gained massive importance in the medical field (Turek and Stintzing, 2013; Baz et al., 2021; Rizwan et al., 2022; Salman and Imran, 2022). In light of current avian coccidiosis outbreaks, herbal extracts are considered potential anticoccidial agents (Chand et al., 2016; Idris et al., 2017; Hafeez et al., 2020 a; Wajiha and Qureshi, 2021; Khan et al., 2022). *In-vivo* and *in-vitro* studies have found that most plant derived extracts have potential anticoccidial properties

(Abbas et al., 2010, 2012 b; Moryani et al., 2021; Wajiha and Qureshi, 2021). Some important examples of potential plants with anticoccidial activity include oregano oil (Giannenas et al., 2003), thyme (Ibrir et al., 2001), clove, carvacrol, tea tree (Remmal et al., 2011), lemon (Evans, 2001), lavender (Küçükyılmaz et al., 2012), laurel leaf oil (Christaki et al., 2004), peppermint oil, grapevine oil, cinchona oil, aloe-based oils (Yim et al., 2011; Ahmad et al., 2020), *Beta vulgaris* extracts (Abbas et al., 2017), *Vitis vinifera* extract (Abbas et al., 2020), *Ageratum conyzoides* and *Artemisia brevifolia* extracts (Hussain et al., 2021 a, b) *Citrus sinensis* essential oils (Imran and Alsayeqh, 2022), *Glycyrrhiza glabra* extract (Hussain et al., 2022).

Among all discussed plant derived compounds, oregano oils have an excellent mechanism of action. Research has shown that oregano oils prevent avian coccidiosis by disrupting the life cycle of *Eimeria* species (Mohiti-Asli and Ghanaatparast-Rashti., 2015). It is based on the splitting of the cell membrane, release of intracellular ATP (adenosine triphosphate), and alteration of cell membrane permeability (Lambert et al., 2001; Oussalah et al., 2006; Giannenas et al., 2013) as explained schematically in Figure 6. They contain two main hydrophobic components, thymol and carvacrol, which help to lower the drooping level and gastrointestinal lesion score in chickens, especially those infected by *E. tenella* (Giannenas et al., 2003), *E. acervulina* (Ibrir et al., 2009), and mixed *Eimeria* infections. Oregano oils were also observed to add to the litter of broilers during coccidiosis. They dry the diarrheal wet litter with reduced levels of pH and oocyst per gram of the litter (Hafez, 2008; Abd El-Wahab et al., 2012). Additionally, oregano oils enhance the broiler's growth and performance by improvement in the nutrient absorption capacity (Mohiti-Asli and Ghanaatparast-Rashti, 2015).

Recent studies disclosed that using aloe-based products drops the fecal oocyst count and gut lesions in birds

infected by *E. maxima* (Yim et al., 2011). The oils extracted from the Echinacea plant (*E. purpurea*) are proven to have impactful results as anti-inflammatory, antimicrobial, and antioxidant in *Eimeria* ailments (Abbas et al., 2012 b). Barbour et al. (2015) explored that the essential oils obtained from eucalyptus and peppermint plants are effective anticoccidial against the most pathogenic strains of *Eimeria*. These oil blends improved chick production and reduced the oocyst discharge in feces and intestinal lesions during severe coccidiosis. Despite the enormous beneficial characteristics, scientists suggest the controlled use of essential oils due to side effects such as feed toxicity, impaired drug response, resistance development, and some anti-nutritional and economic losses (Idris et al., 2017). Moreover, essential oil supplementation does not affect young, vaccinated broilers suffering from coccidiosis (Oviedo-Rondón et al., 2006).

Concluding remarks

Using nutritional supplements for the control of avian coccidiosis as an alternative to anticoccidials would be a revolutionary approach to eliminate problems such as anticoccidial drug resistance, people's concern about drug residues in poultry, and ensuring nutritive poultry products. The demand for using nutritional supplements against coccidiosis is increasing remarkably, so it is important to understand their mechanism of action and other favorable effects. The present review recapitulates the beneficial effects, use, and probable mechanism of actions of different nutritional supplements in coccidiosis control. Nutritional supplements act as antioxidant, immuno-modulatory, and anti-inflammatory agents as they avert oxidative stress, modulate the immune system, and prevent inflammation, respectively. For the above-mentioned reasons, it could be suggested that nutritional supplements are used as a complementary approach in coccidiosis to reduce the severity and incidence of disease, anticoccidials use, and subsequently prevalence of

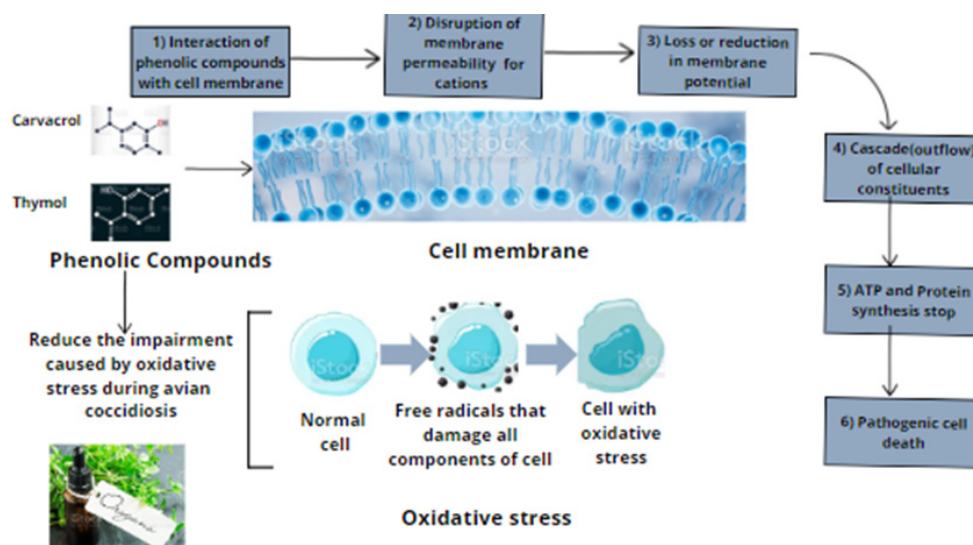


Figure 6. The mechanism of cell lysis in oregano oil treatment

Eimeria species resistance. Nutritional supplements have several benefits when used as anticoccidials, but several issues still need to be addressed properly in some of the nutritional supplements before extensive applications can be made. These issues include product efficacy, toxicity, recognition of active compounds, the exact mechanism of action, and cost-effectiveness. It is, therefore, necessary to conduct deeper investigations on nutritional supplements using more defined protocols to determine the proper efficacy and appropriate mechanism of action and target *Eimeria* species. Furthermore, integrated alternative control strategies should be the focus of future studies so that farmers will be able to control coccidiosis with minimal use of drugs.

References

- Abbas A., Iqbal Z., Abbas R.Z., Khan M.K., Khan J.A. (2015). *In-vitro* anticoccidial potential of *Saccharum officinarum* extract against *Eimeria* oocysts. Bol. Latinoam. Caribe. Plant., 14: 456–461.
- Abbas A., Iqbal Z., Abbas R.Z., Khan M.K., Khan J.A., Sindhu Z.U.D., Mahmood M.S., Saleemi M.K. (2017). *In vivo* anticoccidial effects of *Beta vulgaris* (sugar beet) in broiler chickens. Microb. Path., 111: 139–144.
- Abbas R., Iqbal Z., Mansoor M., Sindhu Z., Zia M., Khan J. (2013). Role of natural antioxidants for the control of coccidiosis in poultry. Pak. Vet. J., 33: 401–407.
- Abbas R.Z., Iqbal Z., Khan M.N., Zafar M.A., Zia M.A. (2010). Anticoccidial activity of *Curcuma longa* L. in broiler chickens. Braz. Arch. Biol. Technol., 53: 63–67.
- Abbas R.Z., Iqbal Z., Blake D., Khan M.N., Saleemi M.K. (2011 a). Anticoccidial drug resistance in fowl coccidia: the state of play revisited. Worlds Poult. Sci. J., 67: 337–350.
- Abbas R.Z., Manzoor Z., Munawar S.H., Iqbal Z., Khan M.N., Saleemi M.K., Zia M.A., Yousaf A. (2011 b). Anticoccidial activity of hydrochloric acid (HCl) against *Eimeria tenella* in broiler chickens. Pesq. Vet. Brasil. 31: 425–429.
- Abbas R.Z., Munawar S.H., Manzoor Z., Iqbal Z., Khan M.N., Saleemi M.K., Zia M.A., Yousaf A. (2011 c). Anticoccidial effects of acetic acid on performance and pathogenic parameters in broiler chickens challenged with *Eimeria tenella*. Pesq. Vet. Brasil., 31: 99–103.
- Abbas R.Z., Iqbal Z., Khan A., Sindhu Z.U.D., Khan J.A., Khan M.N., Raza A. (2012 a). Options for integrated strategies for the control of avian coccidiosis. Int. J. Agric. Biol., 14: 1014–1020.
- Abbas R.Z., Colwell D.D., Gilleard J. (2012 b). Botanicals: an alternative approach for the control of avian coccidiosis. Worlds Poult. Sci. J., 68: 203–215.
- Abbas R.Z., Abbas A., Iqbal Z., Raza M.A., Hussain K., Ahmed T., Shafi M.U. (2020). *In vitro* anticoccidial activity of *Vitis vinifera* extract on oocysts of different *Eimeria* species of broiler chicken. J. Hellenic Vet. Med. Soc., 71: 2267–2272.
- Abd El-Wahab A., Visscher C.F., Wolken S., Reperant J.M., Beineke A., Beyerbach M., Kamphues J. (2012). Foot-pad dermatitis and experimentally induced coccidiosis in young turkeys fed a diet without anticoccidials. Poult. Sci. J., 91: 627–635.
- Abd El-Wahab A., Mahmoud R., Marghani B., Gadallah H. (2019). Effects of yeast addition to the diet of Japanese quails on growth performance, selected serum parameters and intestinal morphology as well as pathogens reduction. Pak. Vet. J., 40: 219–223.
- Abdel-Moneim A.M.E., Shehata A.M., Khidr R.E., Paswan V.K., Ibrahim N.S., El-Ghoul A.A., Ebeid T.A. (2021). Nutritional manipulation to combat heat stress in poultry – A comprehensive review. J. Therm. Biol., 98: 102915.
- Abidin Z., Khatoon A. (2013). Heat stress in poultry and the beneficial effects of ascorbic acid (vitamin C) supplementation during periods of heat stress. Poult. Sci. J., 69: 135–152.
- Adhikari P., Kiess A., Adhikari R., Jha R. (2020). An approach to alternative strategies to control avian coccidiosis and necrotic enteritis. J. Appl. Poult. Res., 29: 515–534.
- Adhikari P.A., Castro F.L.D.S., Liu G., Kim W.K. (2022). Effects of total sulfur amino acids on growth performance, immunity, and meat yield in broilers fed diets with and without antibiotics. Front. Vet. Sci., 9: 903901.
- Adil S., Banday T., Bhat G.A., Mir M.S., Rehman M. (2010). Effect of dietary supplementation of organic acids on performance, intestinal histomorphology, and serum biochemistry of broiler chicken. Vet. Med. Int., 2010: 479485.
- Ahmad S., Rizwan M., Saeed Z. (2022). Alternative therapeutic strategies for histomonosis: A Review. Int. J. Agri. Biosci., 11: 238–245.
- Ahmad Z., Hafeez A., Ullah Q., Naz S., Khan R.U. (2020). Protective effect of *Aloe vera* on growth performance, leucocyte count and intestinal injury in broiler chicken infected with coccidiosis. J. Appl. Anim. Res., 48: 252–256.
- Ahmadu S., Mohammed A.A., Buhari H., Auwal A. (2016). An overview of vitamin C as an antistress in poultry. Malays. J. Vet. Res., 7: 9–22.
- Alagawany M., Elnesr S.S., Farag M.R., Tiwari R., Yatoo M.I., Karthik K., Dhama K. (2021). Nutritional significance of amino acids, vitamins and minerals as nutraceuticals in poultry production and health – a comprehensive review. Vet. Q., 41: 1–29.
- Alagbe E.O., Schulze H., Adeola O. (2022). Dietary enzymatically treated yeast and coccidia challenge effects on the growth performance, nutrient digestibility, and intestinal health of broiler chickens. Res. Squ., 2022. DOI: 10.21203/rs.3.rs-2090446/v1.
- Ali A.I.D.Y., Bahmani M., Pirhadi M., Kaviar V., Karimi E., Abbasi N. (2022). Phytochemical analysis and antimicrobial effect of essential oil and extract of *Loranthus europaeus* Jacq. on *Acinetobacter baumannii*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. Kafkas Üni. Vet. Fakül. Dergisi., 28: 161–167.
- Ali A.M., Seddiek S.A., Khater H.F. (2014). Effect of butyrate, clopidol and their combination on the performance of broilers infected with *Eimeria maxima*. Br. Poult. Sci., 55: 474–482.
- Allen P.C. (1999). Effects of daily oral doses of L-arginine on coccidiosis infections in chickens. Poult. Sci. J., 78: 1506–1509.
- Amerah A.M., Ravindran V. (2015). Effect of coccidia challenge and natural betaine supplementation on performance, nutrient utilization, and intestinal lesion scores of broiler chickens fed suboptimal level of dietary methionine. Poult. Sci. J., 94: 673–680.
- An S.H., Kim D.W., An B.K. (2016). Effects of dietary calcium levels on productive performance, eggshell quality and overall calcium status in aged laying hens. Asian-Australas. J. Anim. Sci., 29: 1477–1482.
- Ashraf F., Sajid A., Khan B., Rahman H.U., Khan S., Ullah S., Ullah Q., Rafiullah, Anwar M. (2021). Antiviral activity of *Withania somnifera* and *Curcuma longa* against foot and mouth disease virus. Cont. Vet. J., 1: 25–31.
- Bakkali F., Averbeck S., Averbeck D., Idaomar M. (2008). Biological effects of essential oils – a review. Food Chem. Toxicol., 46: 446–475.
- Barbour E.K., Bragg R.R., Karrouf G., Iyer A., Azhar E., Harakeh S., Kumosani T. (2015). Control of eight predominant *Eimeria* spp. involved in economic coccidiosis of broiler chicken by a chemically characterized essential oil. J. Appl. Microbiol., 118: 583–591.
- Baz M.M., Hegazy M.M., Khater H.F., El-Sayed Y.A. (2021). Comparative evaluation of five oil-resin plant extracts against the mosquito larvae, *Culex pipiens* Say (Diptera: Culicidae). Pak. Vet. J., 41: 191–196.
- Bedford M.R., Apajalahti J.H. (2022). The influence of nutrition on intestinal disease with emphasis on coccidiosis. Avian Pathol., 51: 504–520.
- Bennett J.W. (1998). Mycotechnology: the role of fungi in biotechnology. J. Biotechnol., 66: 101–107.
- Bortoluzzi C., Rochell S.J., Applegate T.J. (2018). Threonine, arginine, and glutamine: Influences on intestinal physiology, immunology, and microbiology in broilers. Poult. Sci. J., 97: 937–945.
- Bortoluzzi C., Vieira B.S., Applegate T.J. (2020). Influence of dietary zinc, copper, and manganese on the intestinal health of broilers under *Eimeria* challenge. Front. Vet. Sci., 7: 13.

- Bosila M.A., Mekky H.M., Fedawy H.S., Elbayomi K.M., Amer M.M. (2021). Histopathological lesion of arthritis in *Mycoplasma synoviae* naturally infected breeder chicken in Egypt. *Int. J. Vet. Sci.*, 10: 72–74.
- Carpenter C.D. (1939). A study of aqueous colloidal sulphur in the control of fowl coccidiosis caused by *Eimeria tenella*. *Poult. Sci. J.*, 18: 403.
- Carver J.D. (1999). Dietary nucleotides: effects on the immune and gastrointestinal systems. *Acta Paediatr.*, 88: 83–88.
- Carver J.D., Walker W.A. (1995). The role of nucleotides in human nutrition. *J. Nutr. Biochem.*, 6: 58–72.
- Chadwick E., Rahimi S., Grimes J., Pitts J., Beckstead R. (2020). Sodium bisulfate feed additive aids broilers in growth and intestinal health during a coccidiosis challenge. *Poult. Sci. J.*, 99: 5324–5330.
- Chalvon-Demersay T., Yamphet T., Srinongkote S., Ohara H., Lambert W. (2021). Supplementing functional amino acids and polyphenols at low dose can restore performance and amino acid digestibility in broilers challenged with coccidiosis. *Livest. Sci.*, 254: 104769.
- Chand N., Faheem H., Khan R.U., Qureshi M.S., Alhidary I.A., Abudabos A.M. (2016). Anticoccidial effect of mananoligosaccharide against experimentally induced coccidiosis in broiler. *Environ. Sci. Pollut. Res.* 23: 14414–14421.
- Chapman H.D., Jeffers T.K., Williams R.B. (2010). Forty years of monensin for the control of coccidiosis in poultry. *Poult. Sci. J.*, 89: 1788–1801.
- Chen C.Y., Chuang L.T., Chiang Y.C., Lin C.L., Lien Y.Y., Tsean H.Y. (2016). Use of a probiotic to ameliorate the growth rate and the inflammation of broiler chickens caused by *Eimeria tenella* infection. *Anim. Nutr.*, 1:10.
- ChioFalo B., Presti V.L., Samoini G., Chiofalo V., Liotta L. (2011). Nucleotides in broiler chicken diet: effect on breast muscles quality. *Czech J. Food Sci.*, 29: 308–317.
- Choct M., Naylor A.J., Reinke N. (2004). Selenium supplementation affects broiler growth performance, meat yield and feather coverage. *Br. Poult. Sci.*, 45: 677–683.
- Chodkowska K.A., Abramowicz-Pindor P.A., Tuśnio A., Gawin K., Taciak M., Barszcz M. (2022). Effect of phytobiotic composition on production parameters, oxidative stress markers and myokine levels in blood and pectoral muscle of broiler chickens. *Animals*, 12: 2625.
- Christaki E., Florou-Paneri P., Giannenas I., Papazahariadou M., Bot-soglou N.A., Spais A.B. (2004). Effect of a mixture of herbal extracts on broiler chickens infected with *Eimeria tenella*. *J. Anim. Res.*, 53: 137–144.
- Corzo A., Kidd M.T., Dozier III W.A., Pharr G.T., Koutsos E.A. (2007). Dietary threonine needs for growth and immunity of broilers raised under different litter conditions. *J. Appl. Poult. Res.*, 16: 574–582.
- Da Silva I.C.M., Ribeiro A.L., Canal C.W., Pinheiro C.C., de Moraes Vieira M., Gonçalves T.A., Lacerda L. (2009). Broiler chicken responses to immunological stimuli as mediated by different levels of vitamin E in the diet. *J. Appl. Poult. Res.*, 18: 752–760.
- Dalloul R.A., Lillehoj H.S. (2005). Recent advances in immunomodulation and vaccination strategies against coccidiosis. *Avian Dis.*, 49: 1–8.
- Dalloul R.A., Lillehoj H.S. (2006). Poultry coccidiosis: recent advancements in control measures and vaccine development. *Expert Rev. Vaccines.*, 5: 143–163.
- Dalloul R.A., Lillehoj H.S., Shellem T.A., Doerr J.A. (2002). Effect of vitamin A deficiency on host intestinal immune response to *Eimeria acervulina* in broiler chickens. *Poult. Sci. J.*, 81: 1509–1515.
- Dalloul R.A., Lillehoj H.S., Shellem T.A., Doerr J.A. (2003 a). Enhanced mucosal immunity against *Eimeria acervulina* in broilers fed a *Lactobacillus*-based probiotic. *Poult. Sci. J.*, 82: 62–66.
- Dalloul R.A., Lillehoj H.S., Shellem T.A., Doerr J.A. (2003 b). Intestinal immunomodulation by vitamin A deficiency and *Lactobacillus*-based probiotic in *Eimeria acervulina*-infected broiler chickens. *Avian Dis.*, 47: 1313–1320.
- Dantán-González E., Quiroz-Castañeda R.E., Cobaxin-Cárdenas M., Valle-Hernández J., Gama-Martínez Y., Tinoco-Valencia J.R., Ortiz-Hernández L. (2015). Impact of *Meyerozyma guilliermondii* isolated from chickens against *Eimeria* sp. protozoan, an *in vitro* analysis. *BMC Vet. Res.*, 11: 1–11.
- Davison F., Magor K.E., Kaspers B., Fred D., Karel A.S. (2008). Structure and evolution of avian immunoglobulins. *Avian Immunol.*, 1: 107–127.
- Dil N., Qureshi M.A. (2002). Differential expression of inducible nitric oxide synthase is associated with differential Toll-like receptor-4 expression in chicken macrophages from different genetic backgrounds. *Vet. Immunol. Immunopathol.*, 84: 191–207.
- Djilani A., Dicko A. (2012). The therapeutic benefits of essential oils. *J. Nutr. Health.*, 7: 155–179.
- Dkhil M.A., Al-Quraishy S., Wahab R. (2015). Anticoccidial and antioxidant activities of zinc oxide nanoparticles on *Eimeria papillata*-induced infection in the jejunum. *Int. J. Nanomedicine.*, 10: 1961.
- Dong X.Y., Azzam M.M.M., Zou X.T. (2017). Effects of dietary threonine supplementation on intestinal barrier function and gut microbiota of laying hens. *Poult. Sci. J.*, 96: 3654–3663.
- Du A., Hu S. (2004). Effects of a herbal complex against *Eimeria tenella* infection in chickens. *J. Vet. Med., Series B*, 51: 194–197.
- Evans J.W. (2001). Effect of an essential oil blend on coccidiosis in broiler chicks. *Poult. Sci. J.*, 80: 258.
- Fabia K., Wolski D., Bienko M., Radzki R.P., Szymanczyk S. (2021). The problem of coccidiosis in broiler chickens and laying hens: Selected control methods and alternative solutions. *Med. Weter.*, 77: 25–29.
- Fathima S., Selvaraj R.K. (2022). Application of nutritional immunology in the mitigation of economic and production losses in the poultry industry associated with food-borne pathogens, coccidiosis, and necrotic enteritis. *Proc. Arkansas Nutrition Conference*, 1: 5.
- Faure M., Mettraux C., Moennoz D., Godin J.P., Vuichoud J., Rochat F., Corthésy-Theulaz I. (2006). Specific amino acids increase mucin synthesis and microbiota in dextran sulfate sodium-treated rats. *J. Nutr.*, 136: 1558–1564.
- Fekete S.G., Kellems R.O. (2007). Interrelationship of feeding with immunity and parasitic infection: a review. *Vet. Med. (Praha)*, 52: 131.
- Foligné B., Dewulf J., Vandekerckove P., Pignède G., Pot B. (2010). Probiotic yeasts: anti-inflammatory potential of various non-pathogenic strains in experimental colitis in mice. *World J. Gastroenterol.*, 16: 2134.
- Fox M.C., Brown D.R., Southern L.L. (1987). Effect of dietary buffer additions on gain, efficiency, duodenal pH, and copper concentration in liver of *Eimeria acervulina*-infected chicks. *Poult. Sci. J.*, 66: 500–504.
- Fuller R. (1989). Probiotics in man and animals. *J. Appl. Bacteriol.*, 66: 365–378.
- Galli G.M., Anicevski E., Petrolli T.G., da Rosa G., Boiago M.M., Simões C.A., Da Silva A.S. (2021). Growth performance and meat quality of broilers fed with microencapsulated organic acids. *Anim. Feed Sci. Technol.*, 271: 114706.
- Garcia M. (2007). *Seminavis atlantica* Garcia, a new psammic diatom (Bacillariophyceae) from southern Brazilian sandy beaches. *Braz. J. Biol.*, 67: 765–769.
- Giannenas I., Florou-Paneri P., Papazahariadou M., Christaki E., Bot-soglou N.A., Spais A.B. (2003). Effect of dietary supplementation with oregano essential oil on performance of broilers after experimental infection with *Eimeria tenella*. *Arch. Anim. Nutr.*, 57: 99–106.
- Giannenas I., Bonos E., Christaki E., Florou-Paneri P. (2013). Essential oils and their applications in animal nutrition. *Int. J. Med. Aromat. Plants.*, 2: 2167–2412.
- Goff O.E., Upp C.W. (1940). Effect of four grades of sulphur upon artificially produced coccidiosis: Preliminary Report. *Poult. Sci. J.*, 19: 180–186.
- Gottardo E.T., Prokoski K., Horn D., Viott A.D., Santos T.C., Fernandes J.I.M. (2016). Regeneration of the intestinal mucosa in *Eimeria* and *E. coli* challenged broilers supplemented with amino acids. *Poult. Sci. J.*, 95: 1056–1065.
- Gul S.T., Alsayeqh A.F. (2022). Probiotics as an alternative approach

- to antibiotics for safe poultry meat production. Pak. Vet. J., 42: 285–291.
- Hafeez A., Ullah Z., Khan R.U., Ullah Q., Naz S. (2020 a). Effect of diet supplemented with essential coconut oil on performance and intestinal injury in broiler exposed to avian coccidiosis. Trop. Anim. Health Prod., 52: 2499–2504.
- Hafeez M.A., Sattar A., Ashraf K., Mehdi M., Rafique A., Mahmood M.S., Zia M.R. (2020 b). Effect of ibuprofen alone and in conjugation with vitamin E and selenium on experimentally induced coccidiosis in broilers. J. Anim. Plant Sci., 30: 627–633.
- Hafez H.M. (2008). Poultry coccidiosis: Prevention and control approaches. Arch. Geflügelkd., 72: 2–7.
- Hameed U., Shabbir S., Bello A. (2022). Synergistic effects of organic acids with different solute concentrations on *Bacillus cereus* isolated from raw meat. Cont. Vet. J., 2: 118–126.
- Hanif M.A., Nisar S., Khan G.S., Mushtaq Z., Zubair M. (2019). Essential oils. In: Essential oil research. Springer, Cham., pp. 3–17.
- Herrick C.A., Holmes C.E. (1936). Effects of sulphur on coccidiosis in chickens. Vet. Med., 31: 390–391.
- Hooge D.M., Cummings K.R., McNaughton J.L. (1999). Evaluation of sodium bicarbonate, chloride, or sulfate with a coccidiostat in corn-soy or corn-soy-meat diets for broiler chickens. Poultry Sci., 78: 1300–1306.
- Hunolt A.E., Maguire R.O., Ogejo J.A., Badgley B.D., Frame W.H., Reiter M.S. (2015). Multiple applications of sodium bisulfate to broiler litter affect ammonia release and litter properties. J. Environ. Qual., 44: 1903–1910.
- Hussain K., Abbas R., Abbas A., Samiullah K., Ahmed T., Siddique F., Mohsin M., Rehman A., Rahman A.U.L., Waqas M. (2021 a). Anticoccidial potential of *Ageratum conyzoides* and its effect on blood parameters of experimentally infected broiler chickens. J. Hellenic Vet. Med. Soc., 72: 3085–3090.
- Hussain K., Abbas R.Z., Abbas A., Rehman M.A., Raza M.A., Rehman T., Hussain R., Mahmood M.S.V., Imran M., Zaman M.A.V., Sindhu Z.D., Khan M.K., Ali S. (2021 b). Anticoccidial and biochemical effects of *Artemisia brevifolia* extract in broiler chickens. Braz. J. Poult. Sci., 23: 1–6.
- Hussain K., Alsayeqh A.F., Abbas A., Abbas R.Z., Rehman A., Waqar Z.A.I.B., Rehman T.U., Mahmood M.S. (2022). Potential of *Glycyrrhiza glabra* (licorice) extract an alternative biochemical and therapeutic agent against coccidiosis in broiler chickens. Kafkas Üni. Vet. Fakül. Dergisi, 28: 585–591.
- Ibrir F., Greathead H.M.R., Forbes J.M. (2001). The effect of thymol/carvacrol on the performance of broiler chickens infected with *Eimeria acervulina*. In: Proceedings of workshop on alternatives to feed antibiotics and anticoccidials in the pig and poultry meat production, Oslo, Norway.
- Ibrir F., Greathead H.M.R., Forbes J.M. (2009). Effect of dietary thymol/carvacrol mixture at a range of concentrations on coccidial infection in broiler chickens. Proc. 2nd Mediterranean Summit of WPSA, Antalya, Turkey, pp. 309–317.
- Idris M., Abbas R.Z., Masood S., Rehman T., Farooq U., Babar W., Riaz U. (2017). The potential of antioxidant rich essential oils against avian coccidiosis. Worlds Poult. Sci. J., 73: 89–104.
- Imran A., Alsayeqh A. (2022). Anticoccidial efficacy of *Citrus sinensis* essential oil in broiler chicken. Pak. Vet. J., 42: 461–466.
- Imran M., Umer T., Rehman H.U., Saleem M., Farooq H., Bhutta Z.A., Kulyar M.F.A., Shabbir S., Boruah P., Abbas J. (2022). Anti-inflammatory, immunomodulatory and antioxidant activities of alliin, vitamin C and doxycycline, or their combination against *Pasteurella multocida* infection in rabbits. Cont. Vet. J., 2: 112–117.
- Ingraham J.L. (2010). March of the microbes: sighting the unseen. Harvard University Press.
- Jeon Y.S., Kim Y.B., Lee H.G., Park J., Heo Y.J., Chu G.M., Lee K.W. (2022). Effect of dietary organic and inorganic sulfur on the performance of coccidiosis vaccine challenged broiler chickens. Animals, 12: 1200.
- Jung B., Batal A.B. (2012). Effect of dietary nucleotide supplementation on performance and development of the gastrointestinal tract of broilers. Br. Poult. Sci., 53: 98–105.
- Kabir S.M.L., Rahman M.M., Rahman M.B., Hosain M.Z., Akand M.S.I., Das S.K. (2005). Viability of probiotics in balancing intestinal flora and effecting histological changes of crop and caecal tissues of broilers. J. Biotechnol., 4: 325–330.
- Kadykalo S., Roberts T., Thompson M., Wilson J., Lang M., Espeisse O. (2018). The value of anticoccidials for sustainable global poultry production. Int. J. Antimicrob. Agents., 51: 304–310.
- Khan M., Chand N., Naz S., Khan R.U. (2022). Dietary tea tree (*Melaleuca alternifolia*) essential oil as alternative to antibiotics alleviates experimentally induced *Eimeria tenella* challenge in Japanese quails. J. Anim. Physiol. Anim. Nutr., 2022: 1–7.
- Khater H.F., Ziam H., Abbas A., Abbas R.Z., Raza M.A., Hussain K., Selim A. (2020). Avian coccidiosis: Recent advances in alternative control strategies and vaccine development. Agrobiol. Rec., 1: 11–25.
- Khedr N., Ahmed T. (2020). Effect of dietary nucleotide supplementation on broiler intestinal histomorphology. Benha Med. J., 39: 127–131.
- Kiarie E., Romero L.F., Nyachoti C.M. (2013). The role of added feed enzymes in promoting gut health in swine and poultry. Nutr. Res. Rev., 26: 71–88.
- Kiarie E., Walsh M.C., Nyachoti C.M. (2016). Performance, digestive function, and mucosal responses to selected feed additives for pigs. J. Anim. Sci., 94: 169–180.
- Kiarie E.G., Leung H., Akbari M.K.R., Patterson R., Barta J.R. (2019). Utility of feed enzymes and yeast derivatives in ameliorating deleterious effects of coccidiosis on intestinal health and function in broiler chickens. Front. Vet. Sci., 6: 473.
- Kidd M.T., Pote L.M., Keirs R.W. (2003). Lack of interaction between dietary threonine and *Eimeria acervulina* in chicks. J. Appl. Poult. Res., 12: 124–129.
- Kitandu A., Juranova R. (2006). Progress in control measures for chicken coccidiosis. Acta. Vet. Brno., 75: 265–276.
- Küçükyılmaz K., Bozkurt M., Selek N., Güven E., Eren H., Atasever A., Çınar M. (2012). Effects of vaccination against coccidiosis, with and without a specific herbal essential oil blend, on performance, oocyst excretion and serum IBD titers of broilers reared on litter. Ital. J. Anim. Sci., 11: e1.
- Lai A., Dong G., Song D., Yang T., Zhang X. (2018). Responses to dietary levels of methionine in broilers medicated or vaccinated against coccidia under *Eimeria tenella*-challenged condition. BMC Vet. Res., 14: 1–11.
- Laika M., Jahanian R. (2017). Increase in dietary arginine level could ameliorate detrimental impacts of coccidial infection in broiler chickens. Livest. Sci., 195: 38–44.
- Lambert R.J.W., Skandamis P.N., Coote P.J., Nychas G.J. (2001). A study of the minimum inhibitory concentration and mode of action of oregano essential oil, thymol and carvacrol. J. Appl. Microbiol., 91: 453–462.
- Lan Y., Xun S., Tamminga S., Williams B.A., Verstegen M.W.A., Erdi G. (2004). Real-time PCR detection of lactic acid bacteria in cecal contents of *Eimeria tenella*-infected broilers fed soybean oligosaccharides and soluble soybean polysaccharides. Poult. Sci. J., 83: 1696–1702.
- Lee S., Lillehoj H.S., Park D.W., Hong Y.H., Lin J.J. (2007). Effects of *Pediococcus*- and *Saccharomyces*-based probiotic (MitoMax®) on coccidiosis in broiler chickens. Comp. Immunol. Microbiol. Infect. Dis., 30: 261–268.
- Liévin-Le Moal V., Servin A.L. (2014). Anti-infective activities of *Lactobacillus* strains in the human intestinal microbiota: from probiotics to gastrointestinal anti-infectious biotherapeutic agents. Clin. Microbiol. Rev., 27: 167–199.
- Lin G.J., Liu T.Y., Tseng Y.Y., Chen Z.W., You C.C., Hsuan S.L., Huang C. (2009). Yeast-expressed classical swine fever virus glycoprotein E2 induces a protective immune response. Vet. Microbiol., 139: 369–374.
- Lohakare J.D., Kim J.K., Ryu M.H., Hahn T.W., Chae B.J. (2005). Effects of vitamin C and vitamin D interaction on the performance, immunity, and bone characteristics of commercial broilers. J. Appl. Poult. Res., 14: 670–678.
- Luquetti B.C., Alarcon M.F.F., Lunedo R., Campos D.M.B., Furlan R.L., Macari M. (2016). Effects of glutamine on performance and intestinal mucosa morphometry of broiler chickens vaccinated against coccidiosis. Sci. Agric., 73: 322–327.

- Mandal A.B. (2022). Feeding and nutrient requirements of ducks. In: Duck production and management strategies. Springer, Singapore, pp. 303–337.
- Mansoori B., Modirsanei M., Nodeh H., Rahbari S. (2010). The interactive effect of phytase and coccidia on the gross lesions as well as the absorption capacity of intestine in broilers fed with diets low in calcium and available phosphorous. *Vet. Parasitol.*, 168: 111–115.
- Marsh J.A., Dietert R.R., Combs Jr G.F. (1981). Influence of dietary selenium and vitamin E on the humoral immune response of the chick. *Proceed. Soc. Exp. Biol. Med.*, 166: 228–236.
- McDougald L.R., Fitz-Coy S.H. (2008). Coccidiosis (Chapter 28 – Protozoal Infections). *Diseases of Poultry* (12th Ed.), Saif Y.M. et al. (eds). Wiley-Blackwell Publishing, Ames, Iowa.
- Metzler-Zebeli B.U., Eklund M., Mosenthin R. (2009). Impact of osmoregulatory and methyl donor functions of betaine on intestinal health and performance in poultry. *Worlds Poult. Sci. J.*, 65: 419–442.
- Mohammed A.A., Ahmadu S., Buhari H., Auwal A. (2016). An overview of vitamin C as an antistress in poultry. *Malays. J. Vet. Res.*, 7: 9–22.
- Mohiti-Asli M., Ghanaatparast-Rashti M. (2015). Dietary oregano essential oil alleviates experimentally induced coccidiosis in broilers. *Prev. Vet. Med.*, 120: 195–202.
- Mohsin M., Abbas R.Z., Yin G., Sindhu Z.U.D., Abbas A., Huang Z., Shoaib M. (2021 a). Probiotics as therapeutic, antioxidant and immunomodulatory agents against poultry coccidiosis. *Worlds Poult. Sci. J.*, 77: 331–345.
- Mohsin M., Li L., Huang X., Aleem M.T., Habib Y.J., Ismael A. (2021 b). Immunogenicity and protective efficacy of probiotics with EtIMP1C against *Eimeria tenella* challenge. *Pak. Vet. J.*, 41: 274–278.
- Moon J., Ramkumar S., von Lintig J. (2022). Genetic dissection in mice reveals a dynamic crosstalk between the delivery pathways of vitamin A. *J. Lipid. Res.*, 100215.
- Moryani A.A., Rajput N., Naeem M., Shah A.H., Jahejo A.R. (2021). Screening of the herbs and evaluation of their combined effects on the health and immunity of coccidiosis challenged broiler chickens. *Pak. Vet. J.*, 41: 228–234.
- Mussini F.J., Goodgame S.D., Lu C., Bradley C.D., Fiscus S.M., Walddroup P.W. (2012). A nutritional approach to the use of anticoccidial vaccines in broilers: glutamine utilization in critical stages of immunity acquisition. *Int. J. Poult. Sci.*, 11: 243–246.
- Nahed A., Abd El-Hack M.E., Albaqami N.M., Khafaga A.F., Taha A.E., Swelum A.A., Elbestawy A.R. (2022). Phytochemical control of poultry coccidiosis: a review. *Poult. Sci. J.*, 101: 101542.
- Nawaz M., Zhou J., Khalid I., Shamim A., Hussain A., Ahmed Z., Waqas M., Ahmed I., Malik M.I. (2022). Antiparasitic activity of plants extract against gastrointestinal nematodes and *Rhipicephalus microplus*. *Int. J. Vet. Sci.*, 11: 474–478.
- Nichols N.L., Bertolo R.F. (2008). Luminal threonine concentration acutely affects intestinal mucosal protein and mucin synthesis in piglets. *J. Nutr.*, 138: 1298–1303.
- Okonkwo I.F., Achilike K.M. (2022). Comparative assessment of antimicrobial activities of *Allium cepa* (onions) extracts. *Agrobiol. Record.*, 9: 73–79.
- Oussalah M., Caillet S., Lacroix M. (2006). Mechanism of action of Spanish oregano, Chinese cinnamon, and savory essential oils against cell membranes and walls of *Escherichia coli* O157: H7 and *Listeria monocytogenes*. *J. Food Prot.*, 69: 1046–1055.
- Overbeck S., Rink L., Haase H. (2008). Modulating the immune response by oral zinc supplementation: a single approach for multiple diseases. *Arch. Immunol. Ther. Exp.*, 56: 15–30.
- Oviedo-Rondón E.O., Clemente-Hernández S., Salvador F., Williams P., Losa R., Stephan F. (2006). Essential oils on mixed coccidia vaccination and infection in broilers. *Int. J. Poult. Sci.*, 5: 723–730.
- Oxford J.H., Selvaraj R.K. (2019). Effects of glutamine supplementation on broiler performance and intestinal immune parameters during an experimental coccidiosis infection. *J. Appl. Poult. Res.*, 28: 1279–1287.
- Ozyilmaz A., Demirci A., Konuskan D.B., Demirci S. (2017). Macro minerals, micro minerals, heavy metal, fat, and fatty acid profiles of European hake (*Merluccius merluccius* Linnaeus, 1758) caught by gillnet. *J. Entomol. Zool. Stud.*, 5: 272–275.
- Panda B., Combs G.F., DeVolt H.M. (1964). Studies on coccidiosis and vitamin A nutrition of broilers. *Poult. Sci. J.*, 43: 154–164.
- Parker J., Oviedo-Rondón E.O., Clack B.A., Clemente-Hernandez S., Osborne J., Remus J.C., Pierson E.M. (2007). Enzymes as feed additive to aid in responses against *Eimeria* species in coccidia-vaccinated broilers fed corn-soybean meal diets with different protein levels. *Poult. Sci. J.*, 86: 643–653.
- Patterson J.A., Burkholder K.M. (2003). Application of prebiotics and probiotics in poultry production. *Poult. Sci. J.*, 82: 627–631.
- Peek H.W., Van der Klis J.D., Vermeulen B., Landman W.J.M. (2009). Dietary protease can alleviate negative effects of a coccidiosis infection on production performance in broiler chickens. *Anim. Feed Sci. Technol.*, 150: 151–159.
- Penny H., Flores R., Pennington E., Pedersen A., Tran S. (2022). The role of macronutrients and micronutrients in wound healing: a narrative review. *J. Wound Care.*, 31: S14–S22.
- Perez-Carbajal C., Caldwell D., Farnell M., Stringfellow K., Pohl S., Casco G., Ruiz-Feria C.A. (2010). Immune response of broiler chickens fed different levels of arginine and vitamin E to a coccidiosis vaccine and *Eimeria* challenge. *Poult. Sci. J.*, 89: 1870–1877.
- Perricone V., Sandrini S., Irshad N., Savoini G., Comi M., Agazzi A. (2022). Yeast-derived products: The role of hydrolyzed yeast and yeast culture in poultry nutrition – a review. *Animals*, 12: 1426.
- Pop L.M., Varga E., Coroian M., Nedişan M.E., Mircean V., Dumitrache M.O., Györke A. (2019). Efficacy of a commercial herbal formula in chicken experimental coccidiosis. *Parasites Vectors*, 12: 1–9.
- Pope M.J., Cherry T.E. (2000). An evaluation of the presence of pathogens on broilers raised on poultry litter treatment-treated litter. *Poult. Sci. J.*, 79: 1351–1355.
- Pourakbari M., Seidavi A., Asadpour L., Martínez A. (2016). Probiotic level effects on growth performance, carcass traits, blood parameters, cecal microbiota, and immune response of broilers. *An. Acad. Bras. Cienc.*, 88: 1011–1021.
- Quiroz-Castañeda R.E., Dantán-González E. (2015). Control of avian coccidiosis: future and present natural alternatives. *Biomed. Res. Int.*, Article ID 430610.
- Rafique K., Rahman A., Mahmood M. (2020). Effect of dietary supplementation of different levels of *Saccharomyces cerevisiae* on growth performance and hematology in broiler. *Indian J. Anim. Res.*, 54: 59–64.
- Rani Z., Abbas R.Z., Abbas A., Saeed Z., Rehman T., Hussain, Mehmood K., Rehman A., Hussain K. (2021). *In vitro* and *in vivo* anticoccidial effects of butyric acid and its impact on blood and serum chemistry of broiler chickens. *Kafkas Univ. Vet. Fak. Derg.*, 27: 583–588.
- Rao R., Samak G. (2012). Role of glutamine in protection of intestinal epithelial tight junctions. *J. Epithel. Biol. Pharmacol.*, 5: 47.
- Rashid S., Alsayeqh A.F., Akhtar T., Abbas R.Z., Ashraf R. (2023). Probiotics: Alternative of antibiotics in poultry production. *Int. J. Vet. Sci.*, 12: 45–53.
- Remmal A., Achahbar S., Bouddine L., Chami N., Chami F. (2011). *In vitro* destruction of *Eimeria* oocysts by essential oils. *Vet. Parasitol.*, 182: 121–126.
- Ren Z., Bütz D.E., Whelan R., Naranjo V., Arendt M.K., Ramuta M.D., Cook M.E. (2020). Effects of dietary methionine plus cysteine levels on growth performance and intestinal antibody production in broilers during *Eimeria* challenge. *Poult. Sci. J.*, 99: 374–384.
- Richards J.D., Hampton T.R., Wuelling C.W., Wehmeyer M.E., Parker D., Dibner J.J. (2005). MINTREX™ Zn and MINTREX™ Cu organic trace minerals improve intestinal strength and immune response to coccidiosis infection and/or vaccination in broilers. *Proc. 15th European Symposium on Poultry Nutrition, Balatonfüred, Hungary, 25–29.09.2005*, World's Poultry Science Association (WPSA), pp. 257–259.
- Ricke S.C. (2003). Perspectives on the use of organic acids and short chain fatty acids as antimicrobials. *Poult. Sci. J.*, 82: 632–639.
- Rizwan H.M., Khan M.K., Mughal M.A.S., Abbas Z., Abbas R.Z., Sajid M.S., Abbas A. (2022). A new insight in immunomodulatory impact of botanicals in treating avian coccidiosis. *J. Parasit. Dis.*, 46: 1164–1175.

- Roto S.M., Rubinelli P.M., Ricke S.C. (2015). An introduction to the avian gut microbiota and the effects of yeast-based prebiotic-type compounds as potential feed additives. *Front. Vet. Sci.*, 2: 28.
- Ruiz-Feria C.A., Larrison E., Davis M., Farnell M., Carey J., Grimes J.L., Pitts J. (2011). Supplementation of feed grade sodium bisulfate in broiler diets improves feed efficiency. *Int. J. Poult. Sci.*, 10: 670–676.
- Salman M., Imran A. (2022). *In vitro* anticoccidial evaluation of *Citrus sinensis* essential oil against *Eimeria* oocysts. *Agrobiol. Record.*, 10: 15–18.
- Sayyar H.T., Afroz S., Assad T. (2021). Evaluation of phytochemical screening, antimicrobial and antioxidant activities of ethanol extracts of *Cucumis flexuosus* and *Cucumis reticulatus* seeds. *Pak. Vet. J.*, 41: 142–146.
- Seidavi A., Dadashbeiki M., Alimohammadi-Saraei M.H., van den Hoven R., Payan-Carreira R., Laudadio V., Tufarelli V. (2017). Effects of dietary inclusion level of a mixture of probiotic cultures and enzymes on broiler chickens immunity response. *Environ. Sci. Pollut. Res.*, 24: 4637–4644.
- Semba R.D. (1998). The role of vitamin A and related retinoids in immune function. *Nutr. Rev.*, 56: S38–S48.
- Shim Y.H., Ingale S.L., Kim J.S., Kim K.H., Seo D.K., Lee S.C., Kwon I.K. (2012). A multi-microbe probiotic formulation processed at low and high drying temperatures: effects on growth performance, nutrient retention and caecal microbiology of broilers. *Br. Poult. Sci.*, 53: 482–490.
- Shobha S.V., Ravindranath B. (1991). Supercritical carbon dioxide and solvent extraction of the phenolic lipids of cashew nut (*Anacardium occidentale*) shells. *J. Agric. Food Chem.*, 39: 2214–2217.
- Shojadoost B., Yitbarek A., Alizadeh M., Kulkarni R.R., Astill J., Boodhoo N., Sharif S. (2021). Centennial review: Effects of vitamins A, D, E, and C on the chicken immune system. *Poult. Sci. J.*, 100: 100930.
- Shurson G.C. (2018). Yeast and yeast derivatives in feed additives and ingredients: Sources, characteristics, animal responses, and quantification methods. *Anim. Feed Sci. Technol.*, 235: 60–76.
- Siebert W., Ahmadi H., Rodehutschord M. (2015). Meta-analysis of the influence of dietary glycine and serine, with consideration of methionine and cysteine, on growth and feed conversion of broilers. *Poult. Sci. J.*, 94: 1853–1863.
- Singh S.P., Donovan G.A. (1973). A relationship between coccidiosis and dietary vitamin A levels in chickens. *Poult. Sci. J.*, 52: 1295–1301.
- Sobhy H., AboElnaga T.R., Behour T.S., Razin E.A. (2021). *In vitro* trypanocidal activity of essential oils of some plants against *Trypanosoma evansi*. *Int. J. Vet. Sci.*, 10: 191–195.
- Štrbac F., Bosco A., Amadesi A., Rinaldi L., Stojanović D., Simin N., Orčić D., Pušić I., Krnjajić S., Ratajac R. (2021). Ovicidal potential of five different essential oils to control gastrointestinal nematodes of sheep. *Pak. Vet. J.* 41: 353–358.
- Stringfellow K., Caldwell D., Lee J., Mohl M., Beltran R., Schatzmayr G., Farnell M. (2011). Evaluation of probiotic administration on the immune response of coccidiosis-vaccinated broilers. *Poult. Sci. J.*, 90: 1652–1658.
- Su S., Miska K.B., Fetterer R.H., Jenkins M.C., Wong E.A. (2014). Expression of digestive enzymes and nutrient transporters in *Eimeria acervulina*-challenged layers and broilers. *Poult. Sci. J.*, 93: 1217–1226.
- Su S., Miska K.B., Fetterer R.H., Jenkins M.C., Wong E.A. (2015). Expression of digestive enzymes and nutrient transporters in *Eimeria*-challenged broilers. *Exp. Parasitol.*, 150: 13–21.
- Superchi P., Saleri R., Borghetti P., De Angelis E., Ferrari L., Cavalli V., Sabbioni A. (2012). Effects of dietary nucleotide supplementation on growth performance and hormonal and immune responses of piglets. *Animals*, 6: 902–908.
- Teng P.Y., Choi J., Tompkins Y., Lillehoj H., Kim W. (2021). Impacts of increasing challenge with *Eimeria maxima* on the growth performance and gene expression of biomarkers associated with intestinal integrity and nutrient transporters. *J. Vet. Res.*, 52: 1–12.
- Tierney J., Gowing H., Van Sinderen D., Flynn S., Stanley L., McHardy N., Mulcahy G. (2004). *In vitro* inhibition of *Eimeria tenella* invasion by indigenous chicken *Lactobacillus* species. *Vet. Parasitol.*, 122: 171–182.
- Travers M.A., Florent I., Kohl L., Grellier P. (2011). Probiotics for the control of parasites: an overview. *J. Parasitol. Res.*, Article ID 610769.
- Turek C., Stintzing F.C. (2013). Stability of essential oils: a review. *Compr. Rev. Food Sci. Food Saf.*, 12: 40–53.
- Turk D.E. (1973). Calcium absorption during coccidial infections in chicks. *Poult. Sci. J.*, 52: 854–857.
- Ulo Y.B. (2022). Fundamental role of supplanting enzymes in poultry diet. *World Sci. News.*, 166: 100–115.
- Ur Rahman S., Mohsin M. (2019). The under reported issue of antibiotic-resistance in food-producing animals in Pakistan. *Pak. Vet. J.*, 1: 1–16.
- Van der Klis J.D., Verstegen M.W.A., De Wit W. (1990). Absorption of minerals and retention time of dry matter in the gastrointestinal tract of broilers. *Poult. Sci. J.*, 69: 2185–2194.
- Wajiha and Qureshi N.A. (2021). *In vitro* anticoccidial, antioxidant activities and biochemical screening of methanolic and aqueous leaves extracts of selected plants. *Pak. Vet. J.*, 41: 57–63.
- Wang Y., Sun J., Zhong H., Li N., Xu H., Zhu Q., Liu Y. (2017). Effect of probiotics on the meat flavour and gut microbiota of chicken. *Sci. Rep.*, 7: 1–13.
- Watson B. C., Matthews J.O., Southern L.L., Shelton J.L. (2005). The interactive effects of *Eimeria acervulina* infection and phytase for broiler chicks. *Poult. Sci. J.*, 84: 910–913.
- Wu C., Yang Z., Song C., Liang C., Li H., Chen W., Xie Q. (2018). Effects of dietary yeast nucleotides supplementation on intestinal barrier function, intestinal microbiota, and humoral immunity in specific pathogen-free chickens. *Poult. Sci. J.*, 97: 3837–3846.
- Xie N., Zhou T., Li B. (2012). Kefir yeasts enhance probiotic potentials of *Lactobacillus paracasei* H9: the positive effects of coaggregation between the two strains. *Int. Food Res. J.*, 45: 394–401.
- Yazdanabadi F.I., Mohebalian H., Moghaddam G., Abbasabadi M., Sarir H., Vashan S.J.H., Haghparsat A. (2020). Influence of *Eimeria* spp. infection and dietary inclusion of arginine on intestine histological parameters, serum amino acid profile and ileal amino acids digestibility in broiler chicks. *Vet. Parasitol.*, 286: 109241.
- Yim D., Kang S.S., Kim D.W., Kim S.H., Lillehoj H.S., Min W. (2011). Protective effects of *Aloe vera*-based diets in *Eimeria maxima*-infected broiler chickens. *Exp. Parasitol.*, 127: 322–325.
- Yin J., Li T., Yin Y. (2016). Methionine and antioxidant potential. *J. Antioxid. Act.*, 1: 12–17.
- Zaghari M., Pouraghaali S., Zhandi M., Abbasi M. (2022). Effect of monovalent copper oxide and potentiated zinc oxide on growth performance and gut morphology of broiler chickens challenged with coccidiosis. *Biol. Trace Elem. Res.*, doi: 10.1007/s12011-022-03339-8.
- Zaheer T., Abbas R.Z., Imran M., Abbas A., Butt A., Aslam S., Ahmad J. (2022). Vaccines against chicken coccidiosis with particular reference to previous decade: progress, challenges, and opportunities. *Parasitol. Res.*, 121: 2749–2763.
- Zaman M.A., Iqbal Z., Abbas R.Z., Khan M.N. (2012). Anticoccidial activity of herbal complex in broiler chickens challenged with *Eimeria tenella*. *Parasitology*, 139: 237–243.
- Zaman M.A., Abbas R.Z., Qamar W., Qamar M.F., Mehreen U., Shahid Z., Kamran M. (2020). Role of secondary metabolites of medicinal plants against *Ascaridia galli*. *Worlds Poult. Sci. J.*, 76: 639–655.
- Zhang L.B., Guo Y.M. (2008). Effects of liquid DL-2-hydroxy-4-methylthio butanoic acid on growth performance and immune responses in broiler chickens. *Poult. Sci. J.*, 87: 1370–1376.
- Zhang G.Q., Ma Q.G., Ji C. (2008). Effects of dietary inosinic acid on carcass characteristics, meat quality, and deposition of inosinic acid in broilers. *Poult. Sci. J.*, 87: 1364–1369.
- Zhang Q., Chen X., Eicher S.D., Ajuwon K.M., Applegate T.J. (2016). Effect of threonine deficiency on intestinal integrity and immune response to feed withdrawal combined with coccidial vaccine challenge in broiler chicks. *Br. J. Nutr.*, 116: 2030–2043.

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