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REVIEW ARTICLE

Role of Natural Antioxidants for the Control of Coccidiosis in Poultry

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ABSTRACT

Avian coccidiosis is thought to be the one of the most expensive infectious diseases of poultry. Thus far, chemoprophylaxis and anticoccidial feed additives have controlled the disease but situation has been complicated by the emergence of drug resistant strains against commonly used drugs. Immunization by using vaccines has been another effective approach, but, in poorly managed poultry production systems particularly in case of broiler birds, vaccines may result in the onset of severe reactions. The other drawback of using vaccines is diversity of *Eimeria* strains in different geographical distributions. Therefore, vaccine strain, effective in one geographical area may not be effective in other area. A solution to these problems could be the use of antioxidant rich plant products that function by mechanisms other than those of chemotherapeutics, with the additional advantage of a natural origin. Antioxidant compounds could hold promise for the control of *Eimeria* infections due to the association of coccidial infection with lipid peroxidation of the intestinal mucosa. This paper reviews the research on naturally occurring antioxidants including botanical antioxidants effective against avian coccidiosis. Information regarding antioxidant activity, doses and mechanism of action of vitamin A, vitamin E, Zinc, Selenium and herbal complexes such as saponins, flavonoids, tannins, aromatic plants and their essential oils is provided in this paper, which may serve as new beneficial anticoccidial compounds and an essential component of alternative strategies for control of resistant *Eimeria* strains.

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INTRODUCTION

Avian coccidiosis is a parasitic disease of intestinal tract caused by single cell protozoan parasite belonging to genus *Eimeria*. It causes massive destruction of the epithelial cells, which leads to bloody diarrhea, reduced weight gain and temporary reduction in egg production (Dalloul and Lillehoj, 2005; Razzaq *et al*., 2011). Seven species have been recognized to infect poultry and each specie has its own characteristics according to site of infection, immunogenicity and pathogenicity (Williams, 1998; Akhtar *et al*., 2012). Coccidiosis has been considered as a very harmful disease affecting growth and performance of birds in the intense poultry (Lin *et al*., 2006; Mujahid *et al*., 2007; Bachaya *et al*., 2012) and contributory factor in the pathogenesis of several diseases (Kris-Etherton *et al*., 2004; Shahzad *et al*., 2012). According to a recent estimate (Chapman, 2009), coccidiosis may cost the US chicken industry about $127 million annually and likewise similar losses may occur worldwide. Thus coccidiosis is probably the most expensive and wide spread infectious disease in commercial poultry systems.

Control of coccidiosis mostly depends upon the chemoprophylaxis by using anticoccidial drugs, however, managerial skills are also important to get maximum anticoccidial effect of these drugs (Tewari and Maharana, 2011). Chemical anticoccidial feed additives has played a vital role in the growth of the poultry industry and has also facilitated better availability of affordable and good quality poultry meat and other products to the consumers during last 50 years. But due to frequent and irrational use of these anticoccidial drugs, varying degree of resistance has been developed against almost all the available anticoccidial drugs in various parts of the world (Chapman, 1998; Abbas *et al*., 2008, 2011a). Moreover, drug residues in poultry products may be potentially toxic to human beings. To overcome the alarming situation of resistance, integrated approaches such as immunity enhancement and reduction in the ingestion of coccidial oocysts may be the required practices for the control of coccidiosis in poultry.

In order to enhance the immunity of birds, use of vaccines has been a valid approach to prevent the disease. These vaccines have led to induction of an immune response in birds challenged with virulent strains of *Eimeria* (Chapman *et al.,* 2005). In the field, appealing results have been achieved by using combinations of anticoccidial drugs and vaccines. But live vaccines need good management otherwise they can cause severe reactions and use of attenuated vaccines is not economical. Feeding drug-dietary supplements or probiotics to birds is another novel approach to improve their intrinsic defense mechanisms. It can effectively decrease the need for treatment of enteric parasitic infections (Alfaro *et al*., 2007; Hafez, 2011). Use of botanicals, natural products and other alternatives to anticoccidial drugs have proved much better and economical approach for the control of coccidiosis in the age of drug resistance (Anthony *et al*., 2005; Abbas *et al*., 2010; 2011 b & c, 2012 a & b; Zaman *et al*., 2012).

Nutrition/diet also plays a significant role in maintaining health of the animals and preventing them from various diseases. Among all dietary factors, antioxidant rich diets have gained special importance for growth, survival and maintenance, productive and reproductive health of the animals (Surai, 2002). Antioxidants are those molecules that inhibit oxidation and reduce oxidative stress caused by increased level of reactive oxygen species (ROS) and free radicals that can start chain reactions in the cell, resulting in death or damage to the cell. Free radicals react with polyunsaturated fatty acids and initiate a process as a chain reaction known as lipid peroxidation. In living systems, lipid peroxidation changes the enzymatic activity and structure of amino acids thus causes damage to DNA and toxic to the cell (Lima and Abdalla, 2001). Normally, the generation and elimination of ROS remains in dynamic equilibrium, but, if the production of ROS becomes elevated beyond the protection capacity of natural antioxidant defense system, the established equilibrium could be disturbed. This impaired equilibrium in support of oxidants is called oxidative stress and it is involved in the pathogenesis of various infections, including parasitic diseases (Costantini and Moller, 2009; Bansal and Bilaspuri, 2011). Therefore, compounds having the antioxidant properties and meeting the demands of antioxidant defense system or directly interfere with free radicals can restore the balance of oxidants/ antioxidants, leading to improvement of birds in coccidiosis.

The use of antioxidants as anticoccidial remedies, therefore, holds promise as an alternate in the control of coccidiosis. Now days, use of antioxidant rich plant extracts has gained special importance because of the restriction in use of synthetic compounds against coccidial infections due to emergence of resistance and their drug residues (Ahn *et al*., 2002: Abbas *et al*., 2011a; 2012a). Naidoo *et al*. (2008) also described the antioxidant rich plant extracts as potential candidates in controlling coccidiosis in poultry. Therefore, the use of natural antioxidants may alleviate the difficulties related to synthetic drugs, as they are not only natural products but may comprise new molecules to which resistance has not yet developed. The use of natural antioxidants may also satisfy the growing interests of poultry consumers, on condition that they prove to be both effective and safe. A number of natural compounds such as saponins, tannins and flavonoides have been reported in literature for their combined antioxidant and anticoccidial effects. This review paper summarizes the importance of oxidative stress during coccidiosis infection and the role of various antioxidants in reducing the harmful effects of oxidation with ultimate objective of controlling coccidiosis.

Oxidative stress during coccidiosis: In various physiological and pathological conditions, the systemic amounts of free radicals and reactive oxygen species are higher than normal (Vladimirov, 2004). Free radical oxidative species are known to be produced during the host's cellular immune response to invasion by *Eimeria* species (Allen *et al*., 1997), which plays important role in defending against parasitic infections. However, their high concentrations may become intolerable to cell causing tissue damage and cytotoxicity and partially contributing to the pathology of infection. In some parasitic infections, changes in the content of some low-molecular antioxidants (Vitamins A, C and E) occur in the host cell (Evans and Halliwell, 2001). Antioxidants related to metal enzymes are also changed (Koinarski *et al*., 2005). Another free radical oxidative species, nitric oxide promotes vasodilation and hemorrhages in coccidian infections and could be toxic to both parasite as well as to host cells harboring the coccidian parasite (Ovington and Smith, 1992). Georgieva *et al.* (2011a, b) described that *E. acervulina* oocysts motivate the lipid peroxidation, increase oxidative damage and imbalance in the antioxidant status in the infected birds by disturbing the oxidative balance. Therefore, to alleviate or reduce the oxidative stress natural (e.g. Vitamin E, Se) and synthetic (e.g. butylated hydroxytoluene) antioxidants as feed supplements are commonly used in the poultry industry. Antioxidant compounds are also well known to have a cellular protective action against oxidative stress and reduce the severity of *E. tenella* infections by altering the degree of intestinal lipid peroxidation (Allen *et al*., 1998).

Natural sources of antioxidants: Most of the antioxidants occur as dietary constituents and the most commonly investigated natural dietary antioxidant is Vitamin E (α-tocopheryl acetate), which generally deposits in broiler meat as α-tocopherol and delays lipid peroxidation in muscles and improves its meat quality. Many fruits like berries, cherries, olives, grapes, apples, pears, and vegetables like cacao beans, tomatoes, spinach and garlic are rich source of antioxidants (Moure *et al.*, 2001; Bampidis *et al.*, 2005; Botsoglou *et al.,* 2010). Red wine, green and black tea, coffee and chocolate are other potential sources of natural antioxidants (Bampidis *et al.*, 2005). Moreover, Masuda *et al*. (1999) and Christaki *et al*. (2010) reported that seashore plants and algae (micro and macro) have strong antioxidant capacity.

Medicinal plants and their extracts, herbs and spices are mostly rich in polyphenolic contents, have been used since many years in conventional medicine. In recent times a large number of research studies are more concerned with their antioxidant properties mainly due to their polyphenolic compounds (Robards *et al.,* 1999; Botsoglou *et al.,* 2002; Florou-Paneri *et al.,* 2006).

Types of natural antioxidants: There are thousands of substances in nature having antioxidant properties and capable of neutralizing reactive oxygen species. The biological/natural antioxidants are generally classified in two broad divisions, depending upon their solubility; either they are water soluble i.e. hydrophilic (ascorbic acid or vitamin C, glutathione, lipoic acid, uric acid) or fat soluble or hydrophobic (α-tocopherol or vitamin E, carotenoids, coenzyme Q). Water soluble antioxidants react with free radicals present in the blood plasma and cell cytosol, while lipid soluble antioxidants inhibit the lipid peroxidation to protect cell membranes (Surai, 2007). Some of the antioxidants used to treat coccidiosis are discussed in following sections.

Vitamin E: Vitamin E (D-α tocopherol) is a fat soluble natural antioxidant that prevents the production of reactive oxygen species and donates the electrons to free radicals to form tocopherol radicals in cell membranes and turns them to their reduced stage (Traber and Stevens, 2011), maintaining the integrity of cell membranes and making them stable (Packer *et al*., 2001). Poultry birds are unable to synthesize vitamin E within the body and its concentration is usually reduced below the normal under stress conditions. Commercially, vitamin E is generally added as DL-α tocopherol acetate (VE-AC) to poultry feeds at levels from 17 to 48 mg/kg (Erf *et al*., 1998). The proposed mechanism of action of vitamin E involves hydrolysis and rapid absorption of DL-alpha tocopherol through the epithelial cells of intestine in unesterified form. Then it is merged to the cell membranes where it promotes integrity of cellular membranes acting as antioxidants, protecting against oxidative stress produced by free radicals (Tappel, 1972). Effects of dietary supplementation of alpha tocopherol on avian coccidiosis have been investigated. Colnago *et al*. (1984) studied that dietary supplements of alpha tocopherol at levels of 100 IU/kg resulted in increased weight gains and decreased lesion scores after *E. tenella* challenge infection of immunized chickens. In a recent experimental study, Jafari *et al.* (2012) concluded that *E. tenella* infection promotes lipid peroxidation in broiler chickens and the dietary VE-AC at 316 mg/kg can improve the oxidant/antioxidant system in infected birds, but use of high doses can unbalance the antioxidant function in the cells, damaging the immunomodulatory system of chickens.

Vitamin A: Generally Vitamin A refers to group of retinoids. These are fat soluble and involved in immune function, vision, reproduction and cellular communication. It also helps in cell growth and differentiation, playing an efficient role in the normal formation and maintenance of the vital organs. The role of vitamin A as an antioxidant is not clear but it possibly have some antioxidant characteristics because the carotenoids such as beta-carotene (precursor of Vitamin A) have been reported to act as pro-oxidants (Volpe, 2000).

Vitamin A affects the humoral as well as cell-mediated immune responses. This vitamin plays a significant role in the differentiation of epithelial cells, thus maintaining the integrity of mucosal surfaces (Chew and Park, 2004). Vitamin A deficiency causes increase susceptibility to enteric infections in poultry like coccidiosis, hinder the local immune responses to produce their effects within the gut lymphoid tissues of broiler birds (Chew, 1995; Dalloul *et al*., 2003). This effect is best characterized by obvious reduction in intraepithelial lymphocyte subpopulations, mostly in T lymphocytes and CD4 cells. Change in the intraepithelial lymphocyte sub population levels caused by vitamin A deficiency suppresses the bird ability to resist *E. acervulina* infection, resulting in increased oocyst shedding. Moreover, vitamin A deficiency also affects the systemic immune system by reducing the ability of splenic T lymphocytes to respond *in vitro* mitogen stimulation and also results in lower IFN-γ secretion (Dalloul *et al*., 2002). So, dietary vitamin A levels can affect gut immunity in broiler chickens causing immunosuppression at those specific sites resulting in increased susceptibility to *Eimeria* species. However, more research is needed to understand the role of vitamin A and its precursors as an antioxidant in poultry nutrition.

Zinc: Antioxidants or trace elements usually mixed in feed which help to maintain proper antioxidant balance in many infections (Evans and Halliwell, 2001). The role of zinc (Zn) as an antioxidant is well established (Bray and Bettger, 1990). In cell membrane lipids, primary targets of reactive oxygen species are the polyunsaturated fatty acids, that causes lipid peroxidation (Abuja and Albertini, 2001). It is well known fact that the reduction of the trace elements/antioxidants such as Zn leads to a decrease in the activity of antioxidant enzymes (Bou *et al*., 2005). Zinc supplementation has been shown to improve the activity of antioxidant enzymes, notably catalase and superoxide dismutase (Newsome and Swartz, 1988). By this means, Zn inhibits the free radical chain reaction protecting the cell from damage (Hidalgo *et al*., 1989). The mechanism of action of Zn as an antioxidant establishes two types of effects i.e acute and chronic effects (Powell, 2000). In chronic effects, prolonged exposure of an organism to Zn results in stimulation of some other substances such as metallothionein, the ultimate antioxidant. Acute effects further exhibit two types of action: Protein sulphydryl groups protection or reduction of OH ion formation from H_2O_2 through the antagonism of redox-active transition metals, such as copper and iron (Gabrashanska *et al*., 2008). The researchers observed the deviations of antioxidant enzyme levels following *Eimeria* infection causing oxidative damage. In a recent experimental study, Georgieva *et al.* (2011a) investigated the effect of Zn-Cu mixed salt [$CuZn(OH)_3Cl$] in *E. acervulina* infected chickens and proved the ameliorating role of this Zn based salt against *E. acervulina* induced oxidative stress suggesting the antioxidant role of Zn by improving the activity of antioxidant enzymes in infected birds.

Selenium: Selenium (Se) is an essential trace mineral that is incorporated into proteins to make selenoproteins, which are essential antioxidant enzymes. Selenium also plays a significant role in the body defense system due to its requirement by the Se-dependent Glutathion Peroxidases (GSHPx), an antioxidant enzyme which prevents the cellular damage and protects the cell from free radicals. The understanding of antioxidant system functions concerning the GSHPx enzymes are the basis for new advancement in the Se based diets in poultry (Surai, 2002). In some other studies, an impaired blood antioxidant status was observed in broiler chickens infected with *E. tenella.* Increased concentrations of malonyl dialdehyde, decreased amounts of superoxide dismutase and Se-glutathione peroxidase, increased erythrocyte catalase activities (Georgieva *et al.,* 2006) and reduced levels of some vitamins and Se were also reported during coccidiosis in chickens (Gabrashanska *et al*., 2009). The protective function of Se supplementation in diets against lipid peroxidation in several parasitic infections has been well recognized (Rama and Verma, 1998; Surai, 2002). Inorganic Se in the form of selenite, selenate, selenide, and organic forms, Se enriched yeast and Se enriched algae, may be used as dietary supplements. Conventionally, the Se supplement in animal feed has been in inorganic form. Recently, however, organic sources of Se have been explored as an alternative to inorganic supplementation. The amount of Se available for assimilation by the tissue is dependent on the source, and it has been shown that organic Se is deposited into the animal tissue more efficiently than inorganic Se (Choct *et al*., 2004). Recently, Georgieva *et al.* (2011b) have confirmed that dietary supplementation of Se at low doses may promote the antioxidant dependent protective mechanism in the broiler chickens infected with *E. acervulina*. So, diet supplemented with inorganic Se could be more valuable for the host in improving antioxidant capacity of *E. acervulina* infected birds as well as their body performance is also enhanced.

Botanical antioxidants: Botanical antioxidants are likely to play an increasing role in the control of the disease since they are well accepted by consumers (Brenes and Roura, 2010). The value of plant extracts for controlling *Eimeria* infections has been investigated due to the association of coccidial infection with the lipid peroxidation of the intestinal mucosa (Naidoo *et al*., 2008). World health organization (WHO) reported that 80% of world population still depends upon herbal medicines for their prevention and cure especially in developing countries (Gurib-Fakim, 2006). Plant products are free from residues, and their mechanism of action and function is different from other synthetic drugs, involving new therapeutic molecules which are beneficial and against which resistance has not been developed. Among the natural antioxidants, those that are lipid soluble seem to be more effective because they can penetrate into the cell and affect the intracellular stages of the coccidian parasite. Plants have been reported to be the excellent source of antioxidants (Abbas *et al*., 2012 a & b; Mahmood *et al*., 2012; Zubair *et al*., 2012; Atawodi *et al*., 2013). Some plant based antioxidants are discussed here in detail.

a) Plants rich in saponins: Saponins are surfactants found in variety of plants reducing the superficial tension of fluids and allowing better absorption of nutrients by the intestinal epithelium and used as feed additives in poultry nutrition. A major source of natural saponins is *Yucca schidigera* plant that prevents the growth of protozoan parasite by interacting with the cell membrane cholesterol contents, which can modify the cell membrane structure and function, thus resulting in parasite death (Wang *et al*., 1998). The natural ability of saponins to form pores in cell membranes has paid attention to their common use in physiological and biological research (Plock *et al*., 2001). Alfaro *et al*. (2007) have experimentally proved that the supplementation of *Y. schidigera* extract containing saponins in vaccinated birds attenuated the reaction to the vaccine and resulted in higher villus:crypt ratios and suggested a beneficial effect of saponin supplementation on intestinal cell turnover.

b) Plants rich in flavonoids: Flavonoids consist of the largest group of plant phenolics among the eight thousand naturally occurring phenolic compounds (Ruberto *et al*., 2007). The beneficial effects derived from phenolic compounds have been attributed to their antioxidant activity. Studies have shown that flavonoids have the capacity to act as powerful antioxidants by scavenging free radicals and terminating oxidative reactions (Gonzalez-Paramas *et al*., 2004; Yilmaz and Toledo, 2004; Ruberto *et al*., 2007). Flavonoids having multiple hydroxyl groups also act as pro-oxidants (Heim *et al*., 2002; Miguel, 2010). The proposed mechanism of action of flavonoids is conversion of hydroxyl group into pro-oxidant when oxidized by ROS present in inner cell membrane and able to oxidize lipids, proteins and DNA, thus may lead to late necrosis or apoptosis of damaged cells by eliminating potential mutants (Bakkali *et al*., 2008). Many researchers conducted the study on medicinal plants and forages having polyphenolic compounds as an alternative strategy to treat coccidiosis. In a study on anticoccidial effect of grape seed proanthocyanidine extract (natural polyphenolic antioxidant) against *E. tenella* infection, the significant reduction in mortality and improved bird performance was observed (Wang *et al*., 2008). Proanthocyanidins are multifunction and powerful antioxidants having free radical scavenging activity (Cos *et al*., 2003). Furthermore, proanthocyanidins are potent inhibitor of the pro-inflammatory cytokine and chemokine responses induced by lipopolysaccharides (Bodet *et al*., 2006). Xanthohumol (XN), a prenylated flavonoid, obtained from the hops plant, has been reported to have anticoccidial activity against different *Eimeria* species in chickens (Allen, 2007). Xanthohumol resulted in significant reduction in lesion scores in birds challenged with *E. acervulina*. Moreover, chickens infected with *E. acervulina* and *E. maxima* fed 20 ppm XN, shed numerically fewer oocysts than untreated control groups. *E. tenella* shizonts showed a definite inhibitory effect from 20 ppm XN. Reduction in invasion appeared to be associated with physical disruption of the anterior portion of the shizonts and thus XN treatment proved detrimental to further parasite development within the host. *Camellia sinensis* is a natural flavonoid rich plant which is identified to have anticoccidial effects due to their antioxidant properties (Jang *et al*., 2007; Chen *et al*., 2008). Another plant *Ageratum conyzoides*, containing flavonoids, showed a significant reduction in the oxidative stress caused by *E. tenella* when fed in diet at rate of 500-1000 mg/kg body weight (Nweze and Obiwulu, 2009).

c) Plants rich in tannins: Tannins are potential biological antioxidants. They can be classified into two major groups on the basis of their structure: the hydrolysable and the condensed tannins (Khanbabee and van Ree, 2001). Condensed tannins are polyphenolic compounds commonly found in the seed coats of many plants and in the foliage of several legumes and grass cultivars and commonly used as feed additives (Terrill *et al*., 1992). The possible mechanisms of antioxidant activity of tannins are free radical scavenging activity, chelation of transition metals and inhibition of prooxidative enzymes. Molan *et al*. (2009) investigated the effect of Pine bark extract which is a unique mixture of tannins (85%) and flavonoids (8%) on sporulation of three *Eimeria* species and concluded that Pine bark extract has anticocidial effect by showing significant reduction in sporulation of *E. tenella, E. maxima* and *E. acervulina* under laboratory conditions. According to Koleckar *et al*. (2008) daily intake of large amounts of tannins are not advisable due to their adverse effects, however small doses of tannin rich food can be health beneficial.

d) Aromatic plants: Aromatic plants (herbs or spices) have been used as feed preservatives since ancient times to enhance the flavor and aroma of food. The origin of these plants is Mediterranean part of the world (Christaki *et al*., 2012). The commonly known aromatic plants are rosemary, thymus, peppermint, oregano, garlic, sage, basil and anise (Ocak *et al*., 2008; Kadri *et al*., 2011). They mostly contain bioactive compounds such as polyphenols, quinines, flavonols, alkaloids, polypeptides or their oxygen substituted derivatives (Perumalla and Hettiarachchy 2011; Negi, 2012). The phenolic compounds of aromatic plants and their essential oils are excellent sources of natural antioxidants, e.g., eugenol, thymol, carvacrol (Franz *et al*., 2010). Polyphenols generally occur as glycosides, although the bioactivity is attributed to aglycon structures and mainly to catechol in aglycons (Sakakibara *et al*., 2003). It is considered that the antioxidant activity of these compounds is due to their high redox properties. Bioactive components in the aromatic plants as an antioxidant possess the ability to protect the body from damage caused by free radicals induced oxidative stress by binding single oxygen and inducing cytochrome or other enzymes in the cell cytoplsm (Madsen and Bertelsen, 1995; Couladis *et al*., 2003). Giannenas *et al*. (2005) described that a combination of α-tocopherol acetate (Vitamin E) and dehydrated oregano supplementation in broiler feed exhibited antioxidant activity higher than that exhibited by α-tocopherol acetate supplementation alone.

Aromatic plants of the family *Labiatae* and especially oregano exhibit coccidiostatic action against *E. tenella*, when the essential oil or ground leaves, flowers and stems of the plant are incorporated into chicken diets (Giannenas *et al*., 2003, 2004). Another aromatic plant belonging to the *Labiatae* family, Olympus tea (*Sideritis scardica*), exerted a coccidiostatic effect in broiler chickens challenged with sporulated oocysts of *E. tenella*, although this effect was considerably lower than that exhibited by the commercially used anticoccidial lasalocid (Florou-Paneri *et al*., 2004). Similar results were reported by Christaki *et al.* (2004) in which a mixture of herbal extracts from the plants *Agrimonia eupatoria, Echinacea angustifolia, Ribes nigrum* and *Cinchona succirubra* were fed to chickens experimentally challenged with *E. tenella*. Arczewska-Wlosek and Swiatkiewicz (2012) investigated that treatment with a herbal extract mixture containing *Allium sativum*, *Salvia officinalis*, *Echinacea purpurea*, *Thymus vulgaris* and *Origanum vulgare* partly alleviates the negative impact of *Eimeria* experimental infections (*E. acervulina*, *E. tenella*, *E. maxima* and *E. necatrix*) in broiler chickens. Likewise, the supplementation of poultry feed with mixture of essential oils blend from clove, thyme, peppermint and lemon has been proved to be effective in reducing the coccidian oocysts excretion in chicks (Evans *et al.*, 2001). In a recent research work (Orengo *et al*., 2012), authors concluded that the supplementation with cinnamaldehyde might reduce the pathogenic effects of *E. acervullina* infection particularly in terms of reducing the intensity of intestinal lesions.

These studies are considered important to find new substitutes to chemical anticoccidials. Aromatic plants, their extracts and essential oils have a variety of functional bioactive compounds which act as antioxidants; however there is need to standardize their extraction and composition properly to generate meaningful data for further studies.

Conclusion: Due to widespread development of resistance to anticoccidial drugs, there is shift to reduce the use of these chemical compounds. Efforts have been made to develop new strategies for control of avian coccidiosis. These efforts include a search for new agents with anticoccidial activity such as naturally occurring compounds that are considered most effective and safe. The control of oxidative damage caused by ROS and free radicals produced within the cell is major field of study now days. Latest research on natural antioxidants including herbal antioxidants have proved their health benefits against oxidative stress which is involved in the pathology of several diseases in living organisms including coccidiosis in poultry. They can be considered as best substitutes to chemical anticoccidials. However further experimental studies are required to explore the efficacy of herbal antioxidants and their modes of action.

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