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RESEARCH ARTICLE

MEDICINAL PLANTS AS POTENTIAL BIORESOURCE OF ANTICOCCIDIAL DRUGS

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ABSTRACT

Coccidiosis is a lethal managemental disease of poultry. It causes high mortality in affected flocks and results in the annual loss of millions of US dollars by the poultry industry. To control coccidiosis, yearly expenditures on anticoccidial drugs total approximately $650,000. For poultry producers, this is probably the largest expenditure for medication. In India and other developing countries where a large percentage of the population is unemployed, cheap food production is necessary. If the control of the coccidian parasite could be made more economical, these savings could be passed on to the consumer. In Europe, where the economics are different, people are becoming more aware of the potential dangers of using antimicrobials in producing animal protein. A solution to all these problems could be the use of plant products that function by mechanisms other than those of chemotherapeutics, with the additional advantage of a natural origin. The present article provides a background on coccidiosis and reviews the advantage of using medicinal plants as source of anticoccidial drugs.

INTRODUCTION

Commercial poultry farming is expanding day by day and contributing in the provision of affordable and high quality proteins (Ahmad *et al*., 2010; Ghafoor *et al*., 2010). However, this sector is still confronted with many enteric diseases like coccidiosis which are hindering its progress (Saima *et al*., 2010; Hafez, 2011). Coccidiosis is an intestinal disease of chickens caused by various species of protozoan parasites within the genus Eimeria (Williams, 1998; Morris and Gasser, 2006). Seven species of Eimeria (*E. acervulina, E. brunetti, E. maxima, E. mitis, E. necatrix, E. praecox* and *E. tenella*) are recognized, causative agents of coccidiosis in chickens, and these species differ in their pathogenicity (Williams, 1998; McDougald, 2003; Shirley *et al*., 2005). The most common species are *Eimeria tenella*, which causes the cecal or bloody type of coccidiosis, *E. acervulina* and *E. maxima*, which cause chronic intestinal coccidiosis. Normally, most birds pass small numbers of oocysts in their droppings without apparent ill effects. Coccidiosis becomes important as a disease when animals live, or are reared, under conditions that permit the build-up of infective oocysts in the environment. The intensive rearing of domestic chickens may provide these conditions. Young chickens pick up the infection from contaminated premises (soil, houses, utensils, etc.). These may have been contaminated previously by other young infected birds or by adult birds that have recovered from the condition. Wet areas around water fountains are a source of infection. Oocysts remain viable in litter for about a month (Williams, 1995). In this way they can contaminate a farm from time to time. Many anticoccidial drugs have been developed and introduced in the poultry industry all over the world. Since the discovery of sulfanilamide for curing coccidiosis in chickens, various anticoccidial feed additives, predominantly polyether ionophorous antibiotics, have been developed and used. Importantly, genetic resistance in Eimeria against anticoccidial drugs is widespread and has developed to all compounds currently in use (Chapman, 1997). So there is urgent need to find new alternatives for controlling this parasite.

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Economic burden of Coccidiosis

Coccidiosis is recognized as the parasitic disease with the greatest economic impact on poultry industries worldwide (Allen and Fetterer, 2002) due to production losses and costs for treatment or prevention (Shirley *et al*., 2005). The control of coccidiosis in replacement birds, which includes broiler breeders and egg producing stock, is a continuing problem. Most anticoccidial drugs cannot be given to birds in egg production yet most adult birds live in an infected environment (Long *et al.,* 1979). Coccidiosis is responsible for 6–10% of all broiler mortalities, and the global economic losses occur as a result of reduction in growth rate and feed conversion efficiency, (Weber, 1997; Banfield *et al.,* 1999). The annual cost of anticoccidial drugs worldwide is estimated at about US $800 million (Williams, 1998).

Life cycle of coccidian parasites

The most depicted of the monoxenous coccidian lifecycles is that of the geneus *Eimeria* in poultry, however others such as that of the genus *Isospora* share similar features (Fayer, 1980, Levine, 1973). An infection is established upon the ingestion of sporulated oocysts from

contaminated feed or water by a vertebrate host and once inside the vertebrate stomach, the oocyst wall is broken down by mechanical and chemical action releasing the sporocytes which contain infective sporozoites (Lee *et al*., 2000, Levine, 1973). Excystation results in the opening of the anterior cap of sporocysts to release infective sporozoites. Interactions of the apical complex with the plasma membrane of epithelial cells allow sporozoites to penetrate the host cell (Grimwood and Smith, 1996). Within the cells, the sporozoites transform into merozoites which multiply asexually for 2-7 generations, the exact number being species dependent (Lee *et al*., 2000). With each asexual generation, the host cell is destroyed to release merozoites that infect new cells (Levine, 1973). Following the final asexual division, the merozoites enter new epithelial cells and transform into gamonts, with the majority developing into macrogamtes (i.e female gametes), while a few undergo further division and develop flagella to become microgametes (i.e male gametes) (Fayer, 1980). The resultant diploid zygote produced upon fertilisation lays down a heavy resistant oocyst wall around itself and enters the intestinal lumen (Fayer, 1980). Sporulation occurs within the young oocyst to produce sporocysts, within which the infective sporozoites develop and contaminate the environment to begin a new cycle (Lee *et al*., 2000, Levine, 1973).

Anticoccidial activity of medicinal plants

The herbs especially *Azadirahta indica, Hobrrhena antidysentrica, Berberis aristata, Embelia ribes, Acorus calamus* and *Artemisia annua* have strong anticocidial activity. Zycox, a herbal product of India containing *Hobrrhena antidysentrica, Berberis aristata, Embelia ribes* and *Acorus calamus* is used as a prophylactic measure against coccidiosis. Zycox at 0.3% in feed offers a convenient, effective and economically indigenous alternative for prophylactic medication against coccidial infection in chicken. It causes least interference to the natural development of immunity and is safe and not likely to induce resistance. Tipu *et al.* (2002) compared the anticoccidial efficacy of salinomycin sodium and neem fruit in boilers. They concluded that the addition of 0.3% ground neem fruit in boiler feed has tremendous efficiency in combating coccidiosis as compared to salinomycin sodium. They reported that neem fruit has compound margosate, responsible for the breakdown of Eimeria life cycle. Similarly, Allen *et al.* (1997) investigated the effect of feeding dried *Artemisia annua* leaves and its components to birds infected with *Eimeria acervulina*, *E. tennela* and *E. maxima.* When fed at a dose rate of 1% for 5 weeks prior to infection, significant protection was noted for both *E. tenella* and *E. acervulina*. Artemisia contains artemisinin which protected weight gains and reduced oocyst yields for both *E. tenella* and *E. acervulina*. The benefit of using natural products is that problem of health hazards due to drug residues in meat can be overcome. Further the use of medicinal plant and mushroom extracts can bless us with drugs having better efficacy for combating coccidiosis.

A systematic overview of literature

Dalloul *et al.* (2002) investigated the effects of vitamin A (Vit-A) deficiency on the host intestinal immune response and disease susceptibility to coccidiosis in broiler chickens following oral infection with *Eimeria acervulina* (*EA*). The A-DEF birds showed depressed ConA-induced lymphoproliferation response and produced lower serum interferon-γ than CONT birds. These data show that Vit-A deficiency compromised local immune defenses of challenged birds, as reflected in lymphocyte profiles, oocyst shedding, and interferon-γ levels in A-DEF birds. Allen (2003) conducted an experiment to examine the effects of dietary supplementation with 0.1% and 0.5% ground root preparations of *Echinacea purpurea* (EP; common name: purple cone flower) on the development of immunity following live vaccination and subsequent challenge with multiple coccidia species in an experimental model using a commercial live vaccine preparation. In this experiment, combined live vaccination and feed supplementation with 0.1% or 0.5% EP during the first 2 weeks of life provided significant weight gain advantage compared to live vaccination alone. This advantage persisted through 2 weeks of EP withdrawal and subsequent challenge infection. EP supplementation also significantly lowered total lesion scores but did not significantly modify the effects of vaccination and challenge on plasma carotenoids or $NO2^-$+$NO3^-$. Guo *et al.* (2004) investigated the effects of polysaccharide extracts from two mushrooms, *Lentinus edodes* (LenE) and *Tremella fuciformis* (TreE), and an herb, *Astragalus membranaceus* (AstE), on cellular and humoral immune responses of *Eimeria tenella*-infected chickens. The results suggested that supplementation with mushroom and herb extracts results in enhancement of both cellular and humoral immune responses in *E. tenella*-infected chickens. Mwale *et al.* (2005) studied the extent of the usage of *Aloe vera* and *Aloe spicata* in the health management of chickens. The results showed that birds treated with medicated water showed signs of good health. Arab *et al.* (2006) aimed to investigate the occurrence of artemisinin in *A. sieberi* (AS) and to test the anticoccidial effects of plant extract in broiler chickens. The anticoccidial effects of artemisinin were shown by significant decrease in output of number of oocysts per gram of faeces in chickens challenged with different species of Eimeria. Tipu *et al.* (2006) studied the antibacterial, antioxidant, anticarcinogenic, antifungal, analgesic, insecticidal, anticoccidial and growth promoter activity of *Azadiracht indica, Zizyphus vulgaris, Ocimum gratissimum* and *Atlanta monophylla.*

The results showed that *Azadiracht indica, Zizyphus vulgaris, Ocimum gratissimum* and *Atlanta monophylla* have the strong antibacterial activity, whereas ocimum plant has strong antioxidant, anticarcinogenic, antifungal, analgesic and antipyretic properties. Leaves of *Azadirachta indica* can be used for feeding and reducing the parasitic load of animals. The fruit of *Azadirachta indica* also has the anticoccidial activity for poultry. Durrani *et al*. (2007) evaluated the effect of aqueous extract of wild mint (*Mentha longifolia*) on the overall performance of broiler chicks at NWFP Agricultural University, Peshawar in July 2005. Three levels of fresh wild mint infusion at the rate of 50, 40 and 30 mL L-1 of fresh drinking water were provided to chicks in groups A, B and C, respectively and group D was kept as control, each group was replicated four times with 10 chicks per replicate, reared for 35 days, in an open sided house in cages of the same size. No vaccination was practiced. Data were recorded daily for feed intake, water intake and for weight gain on weekly basis. Feed conversion efficiency, dressing percentage, percent mortality, weight of different body organs (breast, thigh and leg), giblets (liver, heart and gizzard), intestine and economics for each group was calculated at the end of experimental period. It was found that group B receiving 40 mL L-1 of wild mint infusion in drinking water had a significant ($p<0.05$) effect on mean body weight gain, feed intake, water intake, feed conversion efficiency, dressing percentage and weight of different body organs (breast, thigh and leg). Significant ($p<0.05$) differences were also found in mortality, highest mortality was observed in group D (10%) as compared with groups A, B and C, however there was no significant effect on giblets (liver, heart, gizzard), intestine and weight of abdominal fat. Mean feed cost and gross return was significantly ($p<0.05$) effected for group B. Feed cost was lower and gross return was significantly ($p<0.05$) higher for group B than other treated groups and control. Brisibe *et al*. (2008) studied the influence of adding dried *Artemisia annua* L. leaves as a botanical coccidistat in coccidia-infested broilers. The results suggested that the addition of *A. annua* leaves to poultry feed serves as a potentially rich source of medication and nourishment for the birds.

Khan *et al.* (2008) studied the efficacy of some herbal and homeopathic preparations against coccidiosis on the basis of weight gain, feed conversion ratio, oocyst count and mortality rate. Chicks were treated with *Polygonum bistorta* Linn. (Anjbar), *Agele marmelos* (Bael), Merc sol. (*Mercurius solubilis*) and Darvisul liquid. *A. marmelos* (Bael fruit) and Darvisul liquid showed better results in terms of weight gain, feed consumption, oocyst count as compared

with *P. bistorta* Linn. (Anjbar) and Merc sol. Lee *et al*. (2008) studied the effect of dietary supplementation with a lyophilized powder made from plums (P) on host protective immune responses against avian coccidiosis. Dietary supplementation of P increased body weight, reduced fecal oocyst shedding, and increased the levels of mRNAs for interferon-γ and interleukin-15 in the P 1.0 group at 10 days post-infection compared with the P 0 group. Furthermore, chickens fed either the P 0.5 or P 1.0 diets exhibited significantly greater spleen cell proliferation compared with the non-plum P 0 group. Naidoo *et al*. (2008) studied the use of plant products that function by mechanisms other than those of chemotherapeutics, with the additional advantage of a natural origin. Four plant extracts with antioxidant activity were screened for their anticoccidial activity in vivo with toltrazuril as the positive control. *Combretum woodii* (160 mg/kg) proved to be extremely toxic to the birds, while treatment with *Tulbaghia violacea* (35 mg/kg), *Vitis vinifera* (75 mg/kg) and *Artemisia afra* (150 mg/kg) resulted in feed conversion ratios similar to toltrazuril, and higher than the untreated control. *T. violacea* also significantly decreased the oocyst production in the birds. Chandrakesan *et al.* (2009) tested the anticoccidial efficacy of a herbal complex consisting of *Solanum nigram* (35%), *Aloe vera* (15%)*, Moringa indica* (35%) and *Mentha arvensis* (15%) against *Eimeria tenella* infection in broilers. Thirty day old broiler chicks were divided into 5 experimental groups, each group having 6 chicks, and were maintained on an anticoccidial free diet. Groups A, B, C and D were challenged with 30,000 sporulated oocysts of *E. tenella* at day 28 of age, while group E served as the uninfected unmedicated control. After 3 days of challenge infection, the birds belonging to groups A and B were treated with herbal complex at the dose rate of 5 and 10% for 7 days continuously. Group C was fed with Salinomycin mixed feed for the same period. In the treatment groups, the birds that received 10% (group B) herbal complex showed better body mass gain between the 4th and 5th weeks (344.34 ± 59.81gm), superior feed conversion ratio (1.77 ± 0.43) and moderate caecal length (11.5 ± 1.19 cm). However, there was no significant difference in the oocyst output between all the treated and control groups. The body mass gain, FCR and caecal length of the uninfected unmedicated group were 461.86 ± 87.03, 1.70 ± 0.46 and 16.9 ± 1.2 cm respectively. Mortality of birds was recorded in groups A and D only.

Abbas *et al.* (2010) studied the comparative efficacy of turmeric (*Curcuma longa* L.) crude powder and salinomycin sodium on the occurrence of coccidiosis and growth performance of broilers. The results suggested that in groups treated with ration supplemented with 3% turmeric powder and salinomycin sodium, the peak excretion of oocysts was delayed about 1 or 2 days relative to the control infected group. Anosa and Okoro (2010) studied the anticoccidial activity of the methanolic extract of *Musa paradisiaca* root in chickens. The results of this study demonstrated that the extract has anticoccidial activity in a dose-dependent manner and at a dosage of 1,000 mg/kg body weight, it shows similar efficacy with amprolium in the treatment of chicken coccidiosis. Naphade *et al*. (2010) studied the efficacy of homoeopathic medicine (*Mercurius corrosivus*) against experimental caecal coccidiosis in broiler chicks. The infection was raised by giving the dose of 50,000 sporulated oocyst of *E. tenella*. Gross pathological changes observed in an infected untreated control group were paleness of the mucosal membrane, ballooning of the caeca with clotted and non clotted blood. However, less severe changes were observed in the groups treated with amprolium and *Mercurius corrosivus*. They also studied on the histopathology of intestinal caeca in different groups of birds (treated and untreated). In the infected untreated control group the intestinal mucosa was hypertrophied containing schizonts and gametocytic stages of coccidial pathogen. There was desquamation of intestinal mucosa and denudation of intestinal villi cells, where as the other groups showed less severe histopathological changes. They finally concluded that the drug was found to be effective as a curative remedy against experimental caecal coccidiosis. Nidaullah *et al.* (2010) studied the role of aqueous extract from Garlic (*Allium sativum*)*,* Ginger *(Zingiber officinale),* Neem *(Azadirachta indica)* and Berberry *(Berberis lycium)* fed in-mix for their effect upon growth performance, immunostimulation and coccidiosis in broilers. The results suggested that aqueous mixed extract of medicinal plants is better for immunomodulatory response against ND, IB, and IBD and to reduce coccidial oocysts burden, without affecting growth of the broilers. Otoikhian and Oyefia (2010) studied the possible use of *Chromolaena odorata* (Awolowo weed, Nigeria) as a curative herb for coccidiosis in ducks. Keets were inoculated via oral injection of contaminated faecal sample. Treatment with baycox 2.5% had a recovery period of 5 days after treatment, which came 2 days later than *Chromoleana odorata* treatment, which implies that treatment of coccidiosis in ducks can be achieved earlier than when it is treated with (baycox 2.5%) coccidiostat. However, there is need to determine the dosage level since excessive usage may result to toxification in birds. Pablos *et al.* (2010) studied maslinic acid (2-α, 3-β-dihydroxiolean-12-en-28-oic acid), found in the leaves and fruit of the olive tree (*Olea europaea* L.), as a new natural coccidiostatic product against *Eimeria tenella.* A considerable increase in weight was found in the chicks treated with maslinic acid compared with those in the control group. Histopathological studies of the caecum at 120 h post-infection showed that the infection rate decreased significantly in chicks treated with maslinic acid.

Manafi (2011) carried out an experiment using 200, day old unsexed broiler chicks to study the efficacy of herbal anticoccidial agent in broiler chickens. Chicks belongs to group I received control diet, group II herbal anticoccidial agent (500g/ton), group III coccidia oocysts and group IV received both herbal anticoccidial agent(500g/ton) and coccidia oocysts. The doses of 50,000 sporulated oocysts were adjusted in 1.0 ml of suspension. 1.0 ml of suspension was inoculated by oral route to the experimental birds on 21st day of age in the groups III and IV. The group (III) showed dullness, anorexia, huddling together, blood mixed droppings and ruffled feathers. The bloody droppings appeared upto 7th day of post infection (dpi). The group IV showed a marked recovery after 7th dpi, when compared to coccidia control group. The severities of clinical signs were less throught the period of post infection. It was also observed in the present study that the herbal anticoccidial agent treated birds (group IV) showed significant reduction in oocysts output when compared to birds infected with coccidia alone (groupIII). Ogbe and Affiku (2012) evaluated the effects of polyherbal aqueous extracts from *Moringa oleifera*, Gum Arabic and wild *Ganoderma lucidum* as safe and natural alternative to reduce over-dependence on the use of antibiotic (growth promoters) on the basis of growth performance and haematological parameters of broiler chickens. the results of this study showed that *Moringa oleifera* leaves, gum arabic and wild *Ganoderma lucidum* contained appreciable amount of crude protein, dietary fibre, fatty acids and minerals, which are nutritional requirements of broiler chickens. Moreover their results also showed that the polyherbal extracts had no adverse effects on haematological parameters of broilers.

The haematological values were all within the normal range. Oyagbemi and Adejinmi (2012) studied the anticoccidial efficacy of the herbal mixture of *Vernonia amygdalina* (VA 10%) and *Azadirachta indica* (AI 10%) against naturally infected broiler coccidiosis. A total of 100 four week old broilers naturally infected with coccidiosis were divided into five treatment groups based on the number of coccidian oocyst they contained. Group I which contained 20,700 oocyst counts served as a negative control. Group II contained 20,000 oocyst counts served as a positive control and was treated with a synthetic drug, amprolium, at recommended dose of 0.6 g/L for seven days. Groups III and IV with 20,200 and 20,500 oocyst counts were treated with 10% of *V. amygdalina* and 10% *A. indica*, respectively. Group V contained 20,400 oocyst count and was treated with the mixture of 10% each of *V. amygdalina* and *A. indica.* Groups II, III, IV and V were treated continuously for seven days. Oocysts EPG decreased steadily in all the treated groups with a marked reduction in groups II and V. The packed cell volume (PCV), red blood cell (RBC) and white blood cell (WBC) count were determined

using standard haematological methods. PVC, haemoglobin (Hb) and RBC count of the treated birds were significantly ($p< 0.05$) higher than those of the infected untreated groups. Hematological parameters and histological features showed a significant increase in WBC, RBC and lymphocytic infiltration; indicative of cell mediated immune response. Lower heterophil/lymphocytic ratio of the groups III, IV and V after treatment suggested immunomudulatory effect of the herbs (*V. amygdalina* and *A. indica*). Hence, the plants are capable of boosting the immunity of birds with either clinical or sub-clinical coccidia infection following subsequent exposure.

Conclution

In the face of development of drug resistance almost all over the world and drug residues in food, there is an urgent need to take a shift towards alternative ways for the effective and long term control of avian coccidiosis. Using alternatives, mentioned in this review, provide a novel approach for controlling wide spread drug resistant *Eimeria* strains in intensive poultry production systems. Most of the alternates enhance the immunity of the birds and thus could play a vital role to minimize or eliminate the burden of anticoccidial chemotherapeutic agents in poultry production. Integration of the alternates proposed above for the treatment and control of avian coccidioisis may be one of the viable options. However, there is need of large scale experimental trials to establish the efficacy of alternative agents because most of these studies lack the sufficient replication, proper experimental designing and appropriate controls.

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