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Some Attempted Strategies towards the Control of Avian Coccidiosis: A Review

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Abstract

his paper focuses on anticoccidial drugs and resistance, poultry management, alternatives for anticoccidial drugs including dietary modulation, natural additives and herbs comprising of botanicals to coccidia. The paper also viewed at the treatment programme for coccidiosis control as well as its potential implications in meat tissue to man.

Keywords: Anticoccidial drugs; Avian Coccidiosis; Coccidiostats

Introduction

Anticoccidial feed additives have been used for more than 50 years to remedy or treat coccidiosis in poultry [1] and the aim of the paper was to review some attempted strategies employed towards the control of avian coccidiosis. Coocidiosis causes annual losses of US $ 2.4 billion to the poultry industry worldwide [2] in both the layer and broiler industries. Conventional disease control strategies depend on vaccination and proplylactic use of anticoccidial drugs. However, resistance against anticoccidial compounds is widely spread and coccidiostats as feed additives was banned in Europe by the year 2012 [Regulation [EC] No 1831/2003 of the European parliament and of the council of 22 September, 2003 on additives for use in animal nutrition]

Anticoccidial Drugs

These are synthesized drugs, which include variant groups of completely different chemical classes:

1. Amprolium is good against *E. tenella* but is not very effective against *E.acervulina* and *E. maxima.*
2. Nicarbazin is a broad-spectrum anticoccidial, it is used in colder seasons or climatic areas and the drugs should not be used in birds older than 20 days because the possibility of strong growth depression. - Robendine is safe broad-spectrum anticoccidial but it must be used with caution because of it's potential fast resistance build up.
3. Halofuginone and Lerbek effects on *E. tenella* are coccidiostatic activity and no coccidiocidal effect, but good for control of *E. acevurlina.*
4. Clinacox [Dicluzuril]. This has a broad-spectrum activity against all Eimeria species. The potential of *Eimeria* species, especially *Eimeria tenella* and *Eimeria maxima* to develop resistance to the drug is low. It is also used for "clean-up" program after the use of ionophore [3].

Sulfonamide Products

The drug exerted a major impact on the worldwide production of poultry meat [4]. Veterinarians and Animal scientist regularly use sulfonamides for therapeutic and prophylactic. Sulfadimethoxine, and sulfaquinoxaline are mainly used for prevention or treatment of poultry coccidiosis, and are generally co-administered in feed. The treatment of hens with sulfonamides-supplemented feed may result in sulfonamides residues being present in market eggs if these drugs have been improperly administered or if the withdrawal time for the treated hens has not been observed. To assure the food safety for consumers, the European Union has set a maximum residue limit for sulfonamides in foods of animal origin such as meat, milk, and eggs [5]. Misuse of these veterinary drugs in laying hens is of great concerns because the drug residues are turning up in eggs, which is an indispensable food for the consumers because it is highly nutritious, cheap and readily available.

A strong residue monitoring of sulfonamides in eggs is thus an important specific activity to guarantee the food safety. Removing the waste of organic solvents is also a serious problem on the world scale. From the view point of the effect of organic solvents to environments and analysts, analytical methods for the monitoring should avoid the use of organic solvents [6, 7].The feeding of 2,500 parts per million [ppm] sulfaquinoxaline causes a severe anemia in chickens with hemorrhages on the legs, breast muscle, and in abdominal organs [8]. Toxicity is more likely to be observed when medication is given in the water during hot weather. Feeding 300-ppm sulfaquinoxaline to growing chickens for 8 weeks reduced the weight gain of female birds but adverse, effects were not observed when sulfaquinoxaline was administered to growing chickens at 300-ppm in various feeding schedules. Continuous feeding of 125-ppm sulfaquinoxaline was highly efficacious in preventing naturally acquired caecal and intestinal coccidiosis. The total efficacy benefits of sulfaquinoxaline in comparison with other sulfonamides were associated to the fact that it is more readily absorbed than other sulfonamides when given in the feed.

Ionophore Products

Ionophores are the major group of poultry feed additives the polyether antibiotics commonly called Ionophores. Six compounds have become available [Monensin, Laslocid, Salinomycin , Narasin , Maduramycin and Semduramycin], the mechanism of action of all ionophores is very similar since they mediate the transport of mono and divalent cations throw the membrane of the parasite, resulting in disturbance of its osmotic balance. Ionphores can be divided into three groups according to the precise of action and chemical structure; monovalent [Monensin, Narasin and Salinomycin], monovalent glycoside [Maduramycin and Semduramycin] and divalent [Laslocid]. Laslocid and Maduramycin are more effective against E. tenella than Monensin, Narasin and Salinomycin [3].

Polyether Ionophors

They are produced by fermentation of *Streptomyces* or *Actinomadura* and they are the most widely used agents, such as salinomycin, monensin, lasalocid and narasin. They act through a general mechanism of changing ion transport and disrupting osmotic balance in the parasite.

Mode of Action of Anticoccidial Drugs

The biochemical effects of anticoccidials are numerous, but each class of chemical compound is unique in the type of action exerted on the parasite and its development stage. Different modes of action have been observed and this can be divided into different broad categories, according to Chapman [1997] [9] and McDougald [2003].

Drugs that Affect Cofactor Synthesis

Several drugs affect biochemical pathways that are dependent upon an important cofactor. For instance, amprolium competitively inhibits the uptake of thiamine by the parasite.

Drugs that Affect Mitochondrial Function

These drugs inhibit energy metabolism in the cytochrome system of the *Eimeria*. For instance, quinolones and clopidol inhibit electron transport in the parasite mitochondrion, but by different pathways.

Drugs that Affect Membrane Function

Ionophores in common have the ability to form lipophylic complexes with alkaline metal cations [Na^+, K^+, and Ca^{++}] and transport these cations through the cell membrane and then affect a range of processes that depend upon ion transport, such as influx of sodium ions thus, causing severe osmotic damage. These drugs act against the extracellular stages of the life cycle of the *Eimeria.*

Resistance to Anticoccidial Drugs

In 1963, the World Health Organization [WHO] defined resistance as "ability of a parasite strain to multiply or to survive in the presence of concentrations of a drug that normally destroy parasites of the same species or prevents their multiplication". Resistance may be relative [increasing doses of the drug being tolerated by the host] or complete [maximum doses being tolerated by the host] [10]. Anticoccidial drugs added to the feed are a good preventive measure and are well adapted to large-scale use, but continuous use of these drugs leads inevitably to the emergence of *Eimeria* strains that are resistant to all anticoccidial drugs, including ionophores [1]. Resistance can develop quickly, as in the case of quinolones and clopidol, or it may take several years for the Coccidia to become tolerant, as in the case of polyether ionophores [11].

Origin of Resistance Anticoccidial Drugs

There are three key factors contributing to drug resistance in commercial poultry production [12]:

- The intense and the continuous use of anticoccidial drugs in the poultry industry providing the basis for changing gene frequency through genetic selection.
- Coccidia are ubiquitous in poultry facilities and the large reproductive potential forms a large reservoir of genetic variation, which leads to the development of drug resistance.
- The life cycle of *Eimeria* is complex and involves a period of asexual and sexual stages. The nuclei of the asexual stage of *Eimeria* contain haploid complement chromosomes. Most drugs are active against this haploid stage, resulting in the removal of the most sensitive ones. This enables the more resistant ones to increase and thus rapidly becoming the dominant phenotype that spreads through the parasite population.

Poultry House Management

The high standard of flock hygiene, sanitation and poultry farm management helps in achieving optimal benefit from the use of anticoccidial drugs in preventing coccidiosis [9]. However, the sanitary practice alone is inadequate for complete removal of coccidial oocysts. This is because of the following:

- There have been too many failures in sanitary programs
- Oocysts are extremely resistant to common disinfectants
- House sterilization is never complete
- An oocyst-sterile environment for floor-maintained birds could prevent early establishment of immunity and thus allow late outbreaks [11].

Alternative for Anticoccidial Drugs

The constant and extensive use of the anticoccidial drugs for prevention and control of coccidiosis in poultry has been a major factor in the success of the industry. This beneficial use of anticoccidial drugs is associated with a widespread drug resistance of Coccidia in the United States, South America and Europe [11]. The first step of defense against development of resistance is the use of shuttle or dual programs [two or more drugs employed within a single flock] and frequent rotation of drugs [rotation of different compounds between flocks] [11]. The awareness by the consumers to avoid chemotherapeutics, the high development costs and low profits have not encouraged the pharmaceutical industry to develop new anticoccidial products [9]. Thus, alternatives progressively and currently been sought.

Dietary Modulation of Coccidia

The study of the interactions between diet composition and Coccidia is of great interest. Before the availability of effective anticoccidial drugs, recommendations for coccidial control included the formulation of diets that were considered capable of reducing the severity of infection such as diets containing skimmed milk, buttermilk, or whey [13]. But due to the development of the efficient, low-cost anticoccidial drugs caused lesser interest in dietary modulation. However, with the appearance of resistance to coccidiostats, the consumers' concern, and the expected regulations to ban the coccidiostats in the future, the possible role of nutrition has recently attracted interest [14].

Vitamins and minerals

Many vitamins change the immune status and the resistance of the host against Eimeria infections. Many works reported that vitamin A deficiency depresses T-lymphocyte response to mutagens [15] and reduces specific antibody production to protein antigens. Recently, [16] reported that vitamin A deficiency in chickens caused alteration in the IEL subpopulation, reduced the local cell-mediated immunity, and lowered the ability of birds to resist *E. acervulina* infection. Vitamin E and selenium generally improve resistance to coccidiosis, improve weight gain [El-Boushy, 1988], and reduce mortality due to E. tenella infection [17].

Vitamin C is known to possess immunity-enhancing effects in chickens and positive effect on birds' performance during coccidial challenge has been observed [18], but it had no effect on the lesion scores due to *E. tenella* or *E. acervulina* infection [19] found that feeding a diet with extra vitamins A, C, D_3, K, and selenium had no beneficial effects on the performance of chickens with subclinical infection caused by *E. maxima*, and *E. tenella*. Additional, the authors reported that performance in the birds supplemented with vitamins was even poorer than in birds fed the control diet. These results are inconsistent with previous work of [17] who fed 0.025 or 0.50 mg Se/kg of diet, noted a reduced mortality, an increase in body weight, and improved resistance against E. tenella.

Products Rich in N-3 Fatty Acid

The n-3 fatty acids are polyunsaturated fatty acids, the major fatty acids being eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA], found abundantly in fish oil, and alpha-linolenic acid [ALA], being a major component of flaxseed oil. Allen et al. [20-22], they reported that fish-liver oil exerts favorable control on the course of coccidiosis. They also worked on a series of experiments using fish oil, flaxseed oil and flaxseed in diets fed to male chickens from day 1 of age through 3 weeks of age and challenged with *E. tenella* at 2 weeks of age. The researchers reported a significant reduction in caecal lesion scores and in the histological examination, a significant reduction in the degree of parasitaization and retarded development of the *E. tenella* parasite was observed. The suggested mode of action is that the n-3 fatty acids infiltrate the tissues of the parasite, which in turn become more susceptible to oxidative attack by phagocytic cells.

Additionally, n-3 fatty acids have been shown to enhance the immune response in birds infected with E. tenella. However, little if any response was seen in the birds' performance, which is of most importance in poultry production. The n-3 fatty acids were proven ineffective against moderate or severe infection with E. maxima, and did not counteract reduced body-weight gain and lesion scores. The reason for the differences in response between these two Eimeria species to dietary n-3 fatty acids is not yet known [23].

Betaine Supplementation

Betaine supplementation has been shown to have positive effects on the water balance of broiler chicks stressed by high ambient temperature or coccidiosis [24], and to protect the cells from osmotic stress, allowing them to continue regular metabolic activities under conditions that would normally inactivate the cell [25]. [26] reported that betaine, in combination with the ionophore and salinomycin had a significant positive effect on the performance of chickens infected with *E. acervulina*, *E. maxima,* and *E. tenella*, the effect being greater than that mediated by betaine or salinomycin alone. Moreover, the combination resulted in a slight decrease in development and invasion of the epithelium by *E. acervulina*, while there was an increase in the invasion of *E. tenella.*

However, the diet supplemented with betaine alone decreased the invasion of E. acervulina and E. tenella as indicated by the number of sporozoites present in the intestinal epithelium after the challenge. Klasing *et al.* [2002] later clarified this effect when they found that chickens fed betaine had more lymphocytes in the epithelium and in the lamina propria during *E. acervulina* infection than those fed the diet without betaine. This effect of betaine could result in more effective clearance of sporozoites that explain the decreased numbers in the epithelium as reported by [26], while [27] found that betaine as a single feed supplement significantly improved chickens' body weight and tended to reduce the feed conversion ratio during coccidiosis infection. When betaine was used in the combination with the ionophore narasine, betaine showed no effects on birds' performance when *Eimeria tenella* was the major pathogenic species. The exact action of betaine is not fully understood. [26] suggested that betaine might increase performance in chickens infected by coccidiosis by inhibition of coccidial invasion and indirectly by supporting intestinal structure and function that could enhance the ability of the infected chickens to with stand coccidial infection.

Whole Wheat

The use of whole grains in broiler feeds is a frequent practice in Europe [28]. Many works indicated that offering broilers a whole cereal grains and balanced pellets greatly reduced the severity of infection with *Eimeria* as judged based on the reduction in output of oocysts [29-34] investigated the effects of whole wheat inclusion in broiler feeds with or without access to grit, and they observed no significant differences in faecal oocyst yields, lesion scores, or performance in birds infected with *E. tenella* or *E. maxima.* They concluded that the decrease in output of oocysts as caused by inclusion of whole cereals in the diet, and observed in the previous experiments, was not due to the increase in the viscosity of the digesta or the crushing of oocysts by an active gizzard and that whole wheat addition to the diet of broiler chickens provides no control of coccidiosis.

Exogenous enzymes

The use of exogenous enzymes in food processing started as early as 1900 and the majority of the enzymes have been derived from fermentation by microorganisms [35]. When broilers fed diet rich in wheat, barley, oat, or rye, the presence of non-starch polysaccharides [arabinoxylans and β-glucans] can give rise to high viscosity in the small intestine thereby decreasing the contact of endogenous digestive enzymes and its substrates. This results in a decrease in absorption and broilers' performance, and increase in the size of the GIT, pancreas, and the liver [36,37] reported an improvement in broilers' performance, a reduction in the size of digestive organs and the GIT size, and an increase in the total volatile fatty acids in the caecum, when a wheat-based diet was supplemented with the 200 mg exogenous enzymes xylanase or β-glucanase per kg feed. Addition of exogenous xylanase has been found to improve the performance and to reduce ileal digesta viscosity in *Eimeria*-infected birds [38]. It was concluded that intestinal viscosity and the size of the gizzard might affect the severity of the *Eimeria* infection. However, others did not observe effects of increased intestinal digesta viscosity on the severity of the *Eimeria* infection, when a large increase in viscosity was being induced by the inclusion of carboxymethyl cellulose in the feed [19, 34].

Electromagnetic Fields

Electromagnetic fields [EMF] have been in use as therapeutic modalities for at least 40 years. It is well known that selected electromagnetic fields [EMF] can have beneficial effects on bones, joints, and neurological disorders, as well as wound healing [39]. Anti-inflammatory aspects of EMF exposure have been reported to be due to the activation of A_2A adenosine receptors in human neutrophils [40]. Generally, inflammation is characterized by massive infiltration of T lymphocytes, neutrophils and macrophages into the damaged tissue [41].

In earlier studies, it has been reported that EMF mediate positive effects on wound healing, controlling the proliferation of inflammatory lymphocytes, and therefore demonstrating beneficial effects on inflammatory disease [42]. Many authors [42- 44] have discussed the effects initiated by various EMF signals and stated that EMF causes stress at the cellular level and that this leads to production of cytokines and consequently a biological response, including an immune response. Recently, [45] reported that exposure of broiler chickens to EMF antagonized the effects of coccidial infection in birds infected with a mixture of sporulated oocysts containing *E. acervulina, E. maxima,* and *E. tenella*. It was found that the severity of the intestinal lesions mediated by *E. acervulina* and *E. maxima* were reduced in the EMF-treated birds.

Natural Additive and Herbs

A number of natural herbs have been tested as anticoccidial dietary additives. Artemisinin isolated from Artemisia *annua,* is a naturally occurring endoperoxide with antimalarial properties. It has been found effective in reducing oocyst output from both *E. acervulina* and *E. tenella* infections when fed at levels of 8.5 and 17 ppm in starter diets [22]. The mode of action is thought to involve oxidative stress. Extracts from 15 Asian herbs were tested for anticoccidial activity against *E. tenella* and the test criteria were survival rate, bloody diarrhoea symptoms, lesion scores, oocyst output, and technical performance. Practical applications of these findings, such as the use of the products in starter rations or combinations of them with current anticoccidials or vaccines, appear possible and need to be investigated [1]. Therefore far, chemoprophylaxis and anticoccidial feed additives have controlled the disease but the situation has been complicated by the emergence of drug resistance [46] and their potentially toxic effects on the animal health [47].

Furthermore, drug or antibiotic residues in poultry products may be potentially hazardous to consumers. Another approach for coccidiosis control is the vaccination of birds with live *Eimeria* oocysts, but, in cases of poor management, these vaccines can trigger severe reactions that may affect the performance of flocks, mainly in broilers because of their rearing period [48]. As a result of this drawback of live vaccines, attenuated vaccines [with reduced pathogenicity] have been developed, but these are expensive to produce.

Botanicals and Coccidiosis

Cost effective alternative strategies are being tried for more effective and safer control of avian coccidiosis [49]. The use of botanicals has played a strong role in the control of avian coccidiosis, as they are not only natural products but may include new therapeutic molecules to which immunity has not yet developed. The use of botanicals as anticoccidial reduces, therefore, holds possible as an alternative in the control of coccidiosis.

Aloe Species

Aloes are believed to have several medicinal properties and are used to treat various ailments. There are more than 360 known Aloe species, but the most recommended type of Aloe in controlling coccidiosis is Aloe *excelsa* [50] revealed that the anticoccidial effects of *A. excelsa* were comparable with sulphachlopyrazine sodium monohydrate in terms of improved live weight gains and reduction in oocyst output in infected broiler chickens. Other species of *Aloe* plant such as *Aloe vera* have also been reported to have anticoccidial activities.

Aloe vera treatments show toxic effects on the intestinal tract by benefiting microflora and reducing bowel putrefaction as well as reducing inflammation [51]. An in vitro study was undertaken to determine the effect of three concentrations [15%, 30%, and 45%] of *A. Vera* and *A. spicata* on the inhibition of the sporulation of avian coccidia oocysts [52]. The two extracts showed a concentration-dependant anticoccidial effect; however, *A. spicata* inhibited sporulation to a greater extent than *A. vera.* In another study [37] dietary supplementation of *A. Vera* resulted in significantly lower gut lesion scores and reduced faecal oocyst shedding of *E. maxima* in broiler chickens. These authors [37] suggested that reduced faecal oocyst shedding, a protective role against *Eimeria* infection, in *Aloe*-based chicken diets could be associated more with cell-mediated responses than antibody responses.

Artemisia Species

The most common species is *Artemisia annua* which has been reported for its antiparasitic activities. *A. annua* is a common type of wormwood botanical anticoccidials: Abbas *et al.* [2004] and [53] conducted the first experimental trial to evaluate the anticoccidial activity of *A. annua* extracts against *E. tenella* in chickens. *A. annua* extracts showed the anticoccidial activity in terms of improved weight gain, improved feed conversion ratio and reduced lesion scores in infected chickens. Later, [23] reported a significant anticoccidial effect of *A. annua* against *E. tenella*, measured as reduced lesion scores, when fed to broiler chickens for three weeks as dried leaves at a dietary concentration of 5% [equivalent to 17 ppm pure artemisinin].

The pure form of artemisinin, fed for a period of 4 weeks at levels of 2, 8.5 and 17 ppm, significantly decreased oocyst output from single and dual species infection with *E. tenella* and *E. acervulina*. Moreover, artemisinin isolated from *A. sieberi* was also found to be effective against *E. tenella* and *E. acervulina* but not against *E. maxima* [54]. So far, a limited amount of work has been carried out to determine the anticoccidial effect of Artemisia spp. in layer chickens. [55] Studied the effect of feeding 20% dried pulverized *A. annua* leaves against *E. tenella* both in broiler and layer chickens. The anticoccidial effects of diets containing *A. annua* leaves were almost equal to the commercial anticoccidials both in broiler and layer chickens. The proposed mechanism of action of artemisinin involves cleavage of endoperoxide bridges by iron producing free radicals [hypervalent iron-oxo species, epoxides, aldehydes, and dicarbonyle compounds] which damage biological macromolecules causing oxidative stress in the cells of the parasite [56].

Azadirachta Indica [Neem] Plant

Azadirachta indica [neem] plant is commonly available in Asian and African countries and is well known in the therapy of a number of infectious diseases including coccidiosis. Neem fruit, at a concentration of 150 g/50 kg feed, has been found to have anticoccidial effects against *E. tenella* infection by reducing oocyst excretion and mortality in broiler chickens [57]. In addition to the anticoccidial effect of neem fruit, some reports have shown the anticoccidial activity of an aqueous extract of neem leaves against E. tenella alone [58] as well as in a mixed infection [Biu *et al.,* 2006], which was comparable to the commercial anticoccidials amprolium and baycox.

The exact mechanism of action of neem against coccidian parasites is unknown, but a report by the National Research Council [1992] [59] suggested that aqueous neem leaf extract, when taken orally, produces an increase in red cells, white blood cells and lymphocyte counts thus enhancing the cellular immune response, increasing antibody production and so most pathogens can be removed before they cause the symptoms associated with disease. Further study is needed to determine the maximum safe levels of neem supplementation because the higher doses, due to its bitterness, may show adverse effects on feed intake which will change the performance parameters of birds.

Beta Vulgaris

The beneficial effects of incorporating sugar beet [Beta vulgaris] solids in animal feeds on livestock growth and overall performance have been known for a long time. One of the active ingredients is betaine which protects cells against osmotic stress by stabilizing cell membranes through the maintenance of osmotic pressure in the cells.

Curcuma Longa

Curcuma longa L. [Zingiberaceae], commonly known as turmeric, is a medicinal plant widely used and cultivated in the tropical regions. In developing countries like Pakistan, poultry farmers provide turmeric powder as a feed additive for the control of coccidiosis in broilers [60]. The active compound of turmeric is the phenolic compound curcumin, which has been shown to have antioxidative, anti-inflammatory and immunomodulatory properties [56]. In an experimental study, the anticoccidial effect of dietary supplementation of 1% curcumin was observed in chickens after infection of *E. maxima* and *E. tenella species.* Improved weight gain, reduced lesion scores and oocyst counts were shown only against *E. maxima*. A significant reduction of plasma $NO2^-$ and $NO3^-$ was found only in *E. maxima*-infected and curcumin-treated birds, and hence provides a possible explanation for the difference in anticoccidial activity found for both *Eimeria species* [56]. Later [60] reported that dietary supplementation with 3% *C. longa* powder was effective against a mild infection of *E. tenella.*

The proposed mechanism of action of *C. longa* [curcumin] involves the induction of oxidative stress against coccidia. Further researches are required to determine the possible anticoccidial activity of different concentrations of whole *C. longa* and its active ingredient curcumin against different *Eimeria species* in poultry.

Echinacea Purpure

Echinacea and its different preparations contain a variety of active substances such as flavonoids, polysaccharides, glycoproteins, alkamides, cinnamic acids, essential oils and phenolic compounds [61; 62] which are effective in treatment of various ailments and are proven to be beneficial in promoting immunity [Bauer, 1999]. This plant is known to have anti-inflammatory, antioxidant and immunomodulating properties that may be linked to its anticoccidial effects [62]. In an experimental trial [56…], ground root preparations of *E. purpurea* [0.1% -0.5%] were offered to broilers for two weeks which ameliorated weight gain reduction and birds had fewer coccidial lesions after a mixed challenge infection with E. *acervulina, E. maxima, E. tenella* and *E. necatrix.* The exact mechanism of action is still unknown, but because of its antioxidant properties *Echinacea* therapy may induce a state of oxidative stress against *Eimeria species*.

Origanum Vulgare

The essential oils of *Origanum vulgare* are well known for their antiprotozoal activity [63, 64] carried out a study to examine the effect of dietary supplementation of *O. oregano* [*O*. vulgare] essential oil on performance of broiler chickens experimentally infected with *E. tenella.* It was concluded that *O. oregano* essential oils, mainly carvacrol and thymol, had anticoccidial effects against *E. tenella*. Some studies suggest that vaccination against coccidiosis, in combination with *O. oregano* containing compounds, may be an alternative control method for intestinal health in chickens [Waldenstedt, 2000a]. In addition, some works suggested the use of dried oregano leaves as a natural herbal growth promoter for early maturing of birds [65]. The dietary supplementation of *O. oregano* containing plants like *O. vulgare,* thus, seems equally effective for maintaining the performance and reducing pathogenic parameters in infected birds.

Saccharum Officinarum

Sugar cane [*Saccharum officinarum*] extract [SCE], a well known natural immunostimulant, is reported to have protective effects against E. tenella infection in chickens [66]. Some studies [67] showed a significant increase in the number of IgM- and IgG plaque-forming cell responses of peripheral blood leukocytes [PBL], intestinal leukocytes, splenocytes, in addition to significantly higher phagocytic activity of PBL and antibody responses in chickens that had been orally administered with either sugar cane extract [SCE] or the polyphenol-rich fraction [PRF]. Most recently, [68] reported the immunotherapeutic effects of sugar cane extract against mixed *Eimeria species* in broiler chickens. The results of these researches suggested that sugar cane extract has an immunostimulating effect in chickens and their administration may augment protective immunity against coccidiosis.

Triticum Aestivum

The *supplementation* of whole *Triticum aestivum* [wheat] grains in broiler feeds is common practice in Europe [28] because dietary fibre anti- oxidants may actually quench the soluble radicals that are continuously formed in the intestinal tract [69]. Many reports [56] have noted the protective effects of whole cereal grains against coccidiosis in broiler chickens measured as a reduction of oocyst output. However,[32] and [34] demonstrated the effects of whole wheat inclusion in broiler feeds with or without access to grit, and observed no significant differences in oocyst counts of mixed *Eimeria species*. They concluded that the reduction in output of oocysts by supplementation with whole cereals in the diet was not a result of the crushing of oocysts by an active gizzard or the increase in the viscosity of the digesta. Furthermore, they concluded that the whole wheat supplementation provided no control of coccidiosis in broiler chickens.

Yucca Schidigera

Plant extracts with high saponin content are a good source of natural antimicrobial compounds. *Yucca schidigera* is a major source of natural saponins that cause the inhibition of protozoan development by interacting with the cholesterol present on the parasite cell membrane, thus resulting in parasite death [70]. Several studies have shown a beneficial and synergistic effect between the coccidiosis vaccine and the *Y. schidigera* extract in improving weight gains, feed conversion ratio and maintaining the integrity of the intestinal villi in chickens [71]. These improvements in the performance parameters of birds may be the result of the potential of saponins [extracted from the *Y. schidigera*] to improve the absorption of nutrients by the intestinal mucosal surface [72]. These saponins are steroidal glycosides with strong surfactant activity, reducing the superficial tension of fluids and allowing better absorption of nutrients by the intestinal epithelium.

Treatment Programme for Coccidiosis Control

Shuttle or Dual Program

The use of one product in the starter and another in the grower feed is called a shuttle program in the US and a dual program in other countries. The shuttle program usually is intended to manage coccidiosis control. Intensive use of the polyether ionophore drugs for many years produced strains of coccidia in the field that have reduced sensitivity to the ionophores. It is a common practice to use another drug such as nicarbazin or halofuginone in the starter or grower feed to bolster the anticoccidial control and take some pressure off the ionophore. The use of shuttle programs is thought to reduce buildup of drug resistance. In 1988, approximately 80% of the US producers used some type of shuttle program [73], in which two compounds usually a synthetic agent[such as Incarbazin] and Ionophore [such as Salinomycin] are employed successively in single flock. During 1999 in the US, shuttles involving synthetic drugs followed by Ionophores were employed by approximately 25% of broiler complexes [74].

Future Hazards of Anticoccidial Residues in Broilers Meat Tissues to Man

Anticoccidial drugs play an important role in animal production, especially in intensive broiler production. They are used for disease prevention and therapy, as well as for their growth-stimulating effect. These drugs add to the recovery of animals from protozoal endoparasites, increase breeding productivity and decrease economic losses caused by coccidiosis. However, mass and long-term administration of these substances has brought problems connected to the occurrence of unfavorable residues in animal products for human consumption.

The residues of anticoccidial drugs represent a potential risk to human health. Proper administration of these substances will ensure minimal content in animal products that will minimize health risks. To protect the health of consumers against the entry of residues of anticoccidial drugs into the food chain, it is necessary to monitor drug residues in animals for food production and for valid veterinary hygienic legislation to pay appropriate attention to this group of drugs [75]. Some anticoccdial drugs such as ionophores are not used in human medicine due to their potent cardiovascular effects. Ensure that recommended withdrawal periods are observed, it has been suggested that residues of ionophores in food could cause adverse health effects in humans as a result of their cardiovascular toxicity. Since poultry litter is extensively applied to land as manure ionophores and their degradation products may readily enter the soil and water environment.

Some studies have been published regarding the environmental fate of ionophores and thus it is difficult to assess their potential impact. Biodegradation studies have indicated that monensin is degradable under aerobic conditions with or without manure and in manure piles within 33 days. Degradation in manure piles under anaerobic conditions was less extensive. It should be assumed that the microbiological activity of soil will be affected, at least initially following application of ionophore containing manure and this may affect nutrient release.

Direct effects on plants are not expected except that an inhibitory effect on apple pollen has been reported for monensin. Ionophores may cause irritation and allergic reaction in humans and protective clothing and dust masks should be used whenever there is a risk of exposure. Alarming human health hazards, the emergence of resistant strains of bacteria in birds and passage of these or other resistant factors via food chain from birds to human beings. Use of antibiotics at sub-therapeutic levels in broiler feeds may lead to the development of resistant strains of bacteria in the bird. While consuming the meat containing residues of antibiotics over protracted period may lead to emergence of resistant gut flora and pathogens in human beings such as E. Coli and Salmonella spp. Production of harmful effects from direct toxicity or from the allergic reactions [hypersensitivity reactions] in persons already sensitized to them.

Certain drugs and or their metabolites possess carcinogenic potential e.g.sulphamethazine residues containing meat preserved with sodium nitrate may develop a triazine complex that has a considerable carcinogenic potential. Prolonged ingestion of tetracycline present in the broiler meat has detrimental effects on teeth and bones in growing children. Some tetracyclines, most therapeutic antibiotics are relatively heat stable and resist both pasteurization and cooking process [76]. Adverse effects on the cartilage development in children may result if the broiler meat contains quinolone residues. Drug residues may destroy the useful micro flora of gastrointestinal tract, especially in children and hence lead to enteritis [diarrhoea, dysentery] like problems. Super infections that refer to as fresh invasion or re40 infection added to an already existing infection. Candidiasis caused by Candida albicans is a classical example of the unhealthy consequence of the use of antibiotics. Residues of chloramphenicol are known to cause bone marrow depression and problems like anaemia in consumers [76].

In addition, there are many safe veterinary drugs and none withdrawal period like, amprolium [77]. Factors that leading to the occurrence of antibiotics residues in animal products are; failure to observe drug withdrawal period, extended usage or excessive dosages of antibiotics, non-existence of restrictive legislation or their inadequate enforcement, poor records of treatment, failure to identify treated animals, lack of advice on withdrawal periods, off-label use of antibiotics, availability of antibiotics to lay persons as over the counter drugs in the developing countries, the addition of antibiotics as milk preservatives during hauling from the centre of production[villages] to the centers of consumption [cities or factories] and lack of consumer awareness about the magnitude and human health hazards associated with antibiotic residues in the food of animal origin [76].

Anticoccidial Testing in Birds

Three types of tests are generally used to study anticoccidial drugs in broiler birds. These are; Battery tests: Done 7–14 days, tests with birds in wire cages, Standard grow-out test: Done 6–8 weeks tests on birds in floor pens and Full-scale tests which is done in commercial facilities. Each type has a different objective and value to the investigator for example; the battery test is used most effectively to measure the efficacy of an anticoccidial drug against a variety of field isolates of Coccidia. This is an efficient and relatively inexpensive testing procedure. The floor- pen test is an intermediate testing procedure with a primary goal of providing statistically useful performance data under controlled conditions. Individually, the predictive value of each test is limited. One cannot, for example, confidently extrapolate performance data in a seven-day battery test to market weight, nor can one predict from a few commercial trials the efficacy of an anticoccidial agent in preventing the lesions of major species of Coccidia. As a whole, when properly conducted, the tests complement one another by providing a comprehensive picture of the efficacy, safety and economic value of an anticoccidial agen.

Conclusion

Treatment and control of the disease are beset with several problems prominent of which is the poor understanding of the immune response. Another factor is the increasing incidence of drug resistance in field strains of *Eimeria*. Furthermore, due to health awareness there is increasing concern regarding drug residues in poultry products and growing pressure from Government and consumer on the production of drug-free poultry products [78].

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