MEDICINAL PLANTS AS NATURAL ALTERNATIVE TO COCCIDIAL SYNTHETIC DRUGS IN BROILER CHICKEN PRODUCTION

Ljiljana Kostadinović1,*, Sanja Popović2, Dragana Ljubojević Pelić3, Ivana Čabarkapa2, Olivera Đuragić2, Jovanka Lević2

1Planet Fresh, Podgorički put bb, 81402 Nikšić, Montenegro
2Institute of Food Technology, University of Novi Sad, Bulevar cara Lazara 1, 21000 Novi Sad, Serbia
3Scientific Institute of Veterinary Medicine “Novi Sad”, Rumenački put 20, 21000 Novi Sad, Serbia

*Corresponding author:
E-mail address: ljiljana.m.medjedovic@gmail.com; info@planet-fresh.com

ABSTRACT: Coccidiosis is well known as an expensive, parasitic disease for the poultry industry worldwide. The disease causes real economic losses by causing poor growth and feed efficiency in broilers even leading to high mortality. Consequently, large amounts of money are being spent on vaccination and the inclusion of anticoccidial drugs into diets. In recent years, the development of resistance to coccidiostats, elevated costs of systematic vaccination and increasing consumer demand for natural food products has fuelled the development of natural, plant-based alternatives for coccidial control in poultry farming. The anticoccidial properties of numerous natural products such as Ageratum conyzoides extract, Polygonum bistorta, Agele marmelos, Artemisia sieberi, Artemisia absinthium, Azadirachta indica, Artemisia annua and Aloa vera based supplements have been reported. This article summarises the experimental knowledge relating to the efficacy, possible modes of action and different aspects of application of medicinal plant supplements as feed additives for the treatment of poultry diseases, especially coccidiosis.

Key words: coccidiosis, disease, poultry, medicinal plants

INTRODUCTION

The prevention of diseases and enhancement of growth, feed intake and feed efficiency are critical factors in modern animal production today (Vare, 2002; Kostadinović and Lević, 2018). Nowadays farm poultry production systems face new challenges with the concept of “clean, green and ethical” (CGE) animal production being promoted (Bickell et al., 2010; Puvača et al., 2019). This concept promotes limited use of drugs, chemicals, and hormones with emphasis on reducing the impact of food production on the environment and poultry welfare. The prophylactic use of antibiotics in poultry nutrition to improve growth, feed consumption, feed utilization and decrease mortality from clinical diseases is well documented (Iovine and Blaser, 2004). The use of antibiotics is strictly regulated by the U.S. Food and Drug Administration (FDA), while in Europe it is regulated by the European Agency for the Evaluation of Medicinal Products (EMEA). Recommendations from the FDA, the World Health Organisation (WHO) and
the EMEA for veterinary medicine state that, whenever it is possible, synthetic drugs should be replaced with plant-based preparations in order to reduce the presence of synthetic drugs and their metabolites (residues) in final animal products. One of the potential alternatives to synthetic drugs is the use of medicinal plant supplements or their essential oils because some have potent properties and complex bioactivity (Si et al., 2006; Puvača et al., 2013; Aćimović et al., 2019). Substitution of synthetic drugs with plant-based supplements could ensure healthy food for the human population, reduce the reliance on synthetic drugs and thus reduce the development of pathogen resistance. Bioactive plants and their compounds may assist in some aspects of the proposed concept, as they are often less expensive, well received by consumers and are generally considered to be environmentally safe (Blache et al., 2008; Kostadinović et al., 2015).

The use of medicinal plants supplements and their extracts as feed additives has increased during the last decade due to their antibacterial (Lević et al., 2011; Oliveira et al., 2013), anti-oxidation (Botsoglou et al., 2002; 2004; Kostadinović et al., 2010a; 2010b; Kostadinović et al., 2011) and hypocholesterolemic activity (Srinivasan, 2004). In addition, certain components have been related to various stimulatory effects on the digestive system (Jamroz et al., 2006; Puvača et al., 2013) and digestive enzyme production (Hernandez et al., 2004). Furthermore, medicinal plants components have been shown to manifest anti-viral (Bishop, 1995), anti-mycotic (Mari et al., 2003), antioxygenic (Juglal et al., 2002), anti-parasitic (Pessoa et al., 2002) and insecticidal (Karpouhtsis et al., 1998) properties. These features are possibly related to the function of these compounds in plants (Mahmoud and Croteau, 2002). Recent publications demonstrate renewed research interest in the use of medicinal plant supplements as feed supplements for poultry diseases (Kostadinović et al., 2010c). Medicinal herbs such as oregano, garlic, thyme, rosemary, and sage are currently the most frequently used phytobiotics in poultry nutrition (Puvača, 2008; Kostadinović et al., 2010c; Stanačev et al., 2010; 2011; Kostadinović et al, 2011; Puvača et al., 2016). Additionally, many plant supplements have been shown to improve growth and performance (Kostadinović et al., 2008b; Kostadinović et al., 2008a; Lević et al., 2009). This review summarises the latest research in the application of medicinal herbs in the prevention and treatment of coccidiosis.

**COCCIDIOSIS AND COCCIDIOSTATS**

Coccidiosis is an infective disease of many species of mammals and birds caused by protozoa which causes diarrhea, retarded growth, slower feed conversion, and increased mortality. It is caused by parasites of the genus *Eimeria*, *Isospora* and *Cryptospora* with a complex life cycle, affecting mainly the intestinal tract of flow, especially in chickens. Poultry coccidiosis is the most studied, as this parasite causes the most damage in chicken production due to the fact that chickens are reared in large numbers and high densities (Peek, 2010). Tyzzer et al. (1932) was the founder of contemporary coccidiology who worked the life cycle of coccidia in different hosts and parasite morphology. He described nine species of *Eimeria* in poultry however, now only seven are considered to be economically important. In intensive poultry production the most important are *E. acervulina*, *E. tenella*, *E. maxima*, *E. brunetti*, *E. mitis*, *E. necatrix*, and *E. pracox*. All kinds of *Eimeria* spp. cause intestinal coccidiosis although operate in different parts of the intestinal tract. Young individuals fall ill frequently, while older birds tend to be carriers. Generally, coccidia is highly host organ and tissue-specific.
Table 1 summarises the morphology characteristics of *Eimeria* spp. in chickens. Coccidiosis is one of the most serious diseases in chicken production as economic losses is possible even before the manifestation of clinical signs of the disease and require the administration of various drugs through feed and water. In other poultry breeds such as geese, ducks, turkeys, pheasants, etc. coccidiosis occurs rarely and mainly in young animals. Coccidiosis is traditionally treated by chemotherapy but the appearance of drug-resistant types of coccidia indicates the importance of developing alternative strategies.

Table 1. Morphology and pathogenicity of chicken coccidia species

<table>
<thead>
<tr>
<th>Species</th>
<th>Site</th>
<th>Oocyst size (µm)</th>
<th>Pathogenicity</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>E. tenella</em></td>
<td>Caecum</td>
<td>22.80</td>
<td>High</td>
</tr>
<tr>
<td><em>E. acervulina</em></td>
<td>Duodenal loop</td>
<td>18.95</td>
<td>Low</td>
</tr>
<tr>
<td><em>E. necatrix</em></td>
<td>Mid gut</td>
<td>17.95</td>
<td>High</td>
</tr>
<tr>
<td><em>E. maxima</em></td>
<td>Mid gut</td>
<td>32.00</td>
<td>Low to moderate</td>
</tr>
<tr>
<td><em>E. mitis</em></td>
<td>Anterior gut</td>
<td>15.20</td>
<td>Low</td>
</tr>
<tr>
<td><em>E. praecox</em></td>
<td>Anterior gut</td>
<td>22.25</td>
<td>No</td>
</tr>
<tr>
<td><em>E. brunetti</em></td>
<td>Lower intestine</td>
<td>25.50</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

(Levine, 1985; Williams, 1999)

Management has always been important to controlling coccidiosis in poultry, however, it is very difficult to keep chickens coccidia free as oocytes are omnipresent and spread widely in the poultry house. Management focuses on decreasing coccidial numbers to keep infection at a minimum until immunity is established in young birds since species specific immunity develops rapidly. Hygiene, anticoccidial drugs and vaccines all play major roles in commercial operations. Figure 1 shows the percentage share of drugs and their combinations that are commonly used in the prevention of coccidiosis in broiler farms. The most commonly applied is narasin, monensin, and nicarbazin. Widely used are salinomycin and robenidine, while the least used are diclazuril, lasalocid, maduramicin, clopidol, toltrazuril and halofuginone (Elliot, 2003). The continuous use and misuse of anticoccidial drugs have led to the emergence of drug-resistant species (Ruff and Danforth, 1996), and their residues in poultry products are undesirable for consumer health (McDougald and Seibert, 1998). Most anticoccidial drugs have a withdrawal period of seven days before marketing (McDougald, 2003). Legislation that banned the use of medication until slaughter was introduced due to the concern that residues from drugs may contaminate poultry and be toxic to human health (Vermeulen et al., 2001). However, if the drug is removed then the bird is susceptible to infection because there may be no protective immunity acquired while the chicken is on anticoccidial drugs; any infective oocytes in the litter may thus cause severe infection (Reid, 1990). Subsequently, there is a need to discover safe alternatives for the control of avian coccidiosis. In this context, a number of medicinal plants supplements and herbal products have been found to be effective for a wide range of parasites such as protozoa, arthropods, and helminths (He and Zhang, 1989; Matsuda et al., 1991; Dutta et al., 1990; Quan, 1990).
Figure 1. Anticoccidial drugs in broiler production

MEDICINAL PLANT SUPPLEMENTS AS COCCI DiOSTATS IN BROILER CHICKENS

A number of natural feed additives have shown anticoccidial activity and the plants *Azadirachta indica*, *Hobrrhena antidysentrica*, *Barberis aristata*, *Embelia ribes*, *Acorus calamus*, *Artemisia annua*, and *Artemisia absinthium* have been shown to possess strong anti-coccidial activity. Most medicinal plants supplements do not have residual effects, and if they have an approved application in human medicine, they can be added to animal feed for the control of different animal diseases. Plants and their active ingredients that exhibit the most pronounced anti-coccidial effects are shown in Table 2.

Table 2. Examples of medicinal plants supplements with anti-coccidial activity

<table>
<thead>
<tr>
<th>Plant</th>
<th>Major essential oil components</th>
<th>Total volatiles, %</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pimpinella anisum</em></td>
<td>trans-anetole</td>
<td>92.9</td>
<td>Sharifi et al. (2008)</td>
</tr>
<tr>
<td><em>Origanum vulgare</em></td>
<td>p-cymene</td>
<td>5.80</td>
<td>D’Antuono et al. (2000)</td>
</tr>
<tr>
<td><em>Azadirachta indica</em></td>
<td>b-caryophyllene</td>
<td>12.73</td>
<td>Pandey et al. (2012)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Shabbir et al. (2012)</td>
</tr>
<tr>
<td><em>Sophora flavescens</em></td>
<td>2-ethyl-1-hexanol, geranyl</td>
<td>3.25</td>
<td>Li et al. (2012)</td>
</tr>
<tr>
<td><em>Artemisia annua</em></td>
<td>camphor</td>
<td>44.00</td>
<td>Juteau et al. (2002)</td>
</tr>
<tr>
<td><em>Artemisia absinthium</em></td>
<td>chrysanthenyl acetate</td>
<td>29.45</td>
<td>Blagojević et al. (2006)</td>
</tr>
</tbody>
</table>

Neem (*Azadirachta indica*) is a traditional medicinal plant (Biswas et al., 2002) which contains limonoids, protolimonoids, tetranortriterpenoids, pentanortriterpenoids, hexanortriterpenoids nonterpenoid, some of which are thought to have an influence on
eimeria life cycle switching (Koul et al., 2006). Tippu et al. (2002) compared the anticoccidial efficacy of salinomycin sodium and neem fruit in boilers. It was concluded that the addition of 0.3% ground neem fruit in the boiler diet showed efficiency in the repression of coccidiosis as compared to salinomycin sodium. Similarly, Allen et al. (1997) investigated the influence of Artemesia annua on poultry infected with Eimeria acervulina, E. tenella or E. maxima. Four experiments were conducted to investigate the anti-coccidial activities of Artemisia annua leaves when added to broiler chicken diets. In the first investigation, broilers were fed a mixture containing 5% dried leaves of A. annua. A statistically significant reduction in the number of oocytes E. tenella but not E. acervulina or E. maxima was observed. In the second investigation, chickens were fed a diet containing 1% dry A. annua leaves for five weeks. This leaf amount provided a reduction in oocyte numbers of E. acervulina and E. tenella. When the broiler chickens were fed a diet containing 17 ppm of pure artemisinin for three weeks there was a decrease in the number of oocytes of E. tenella but not E. acervulina. Other components such as A. annua - camphor, and 1.8 - cineole in an amount of 119 ppm were shown to increase chicken body weight and decrease the number of lesions caused by E. tenella.

When chickens were fed for four weeks with a diet containing 2, 8.5 and 17 ppm of artemisinin, a significant reduction in the number of oocytes of E. acervulina and E. tenella in the case of mixed infections were observed. These findings led to the conclusion that pure artemisinin is the most effective against all species of Eimeria when used as an additive in the diet. Chemically artemisinin is a sesquiterpene lactone containing an unusual peroxide bridge and represents a basic active component isolated from plants traditionally known in Chinese medicine - Artemisia annua, Asteraceae (sweet wormwood). It is believed that the peroxide is most responsible for the artemisinin interaction. It is known that several other compounds contain such peroxide bridges and one of them is Askaridol (bicyclic monoterpen) (Miller and Su, 2011). The genus Artemisia of the family Compositae (Asteraceae) includes over 300 species that have spread around the world. In the last ten years or so several studies have been conducted with Artemisia species whereby it was found that crude extracts of some of them containing artemisinin, exhibit anti-parasitic, or anti-coccidial effects and high antioxidant capacity (Ferreira, 2009). Kostadinović et al. (2012) investigated the anti-coccidial activity of artemisinin obtained by the extraction of white wormwood (Artemisia absinthium L.). The study was conducted in vivo on 150 broiler chickens of Arbor Acres heavy line hybrids of both sexes infected with E. tenella oocytes (20000 oocytes/per bird). Infected chickens were treated with the extract of Artemisia absinthium mixed in the chicken’s diet at levels of either 1, 2 or 3 mg/kg per day. It was found that the extract obtained from A. absinthium reduced the number of oocytes of Eimeria tenella in the feces of infected broilers when mixed in broiler feed in an amount of 3 mg/kg per day. The results showed that Artemisia absinthium L. added to broiler feed in an amount of 3% expressed anti-coccidial activity and therefore can be used as an alternative to standard coccidiostats drugs which may cause resistance of the microorganisms that cause coccidiosis or lead to the appearance of residues in the meat of broilers (Kostadinović et al., 2012). An in vivo study testing the anti-coccidial activities of artemisinin isolated from the plant Artemisia sieberi on Ross 308 broilers showed that the extract reduced the number of E. tenella and E. acervulina oocytes, but not E. maxima (Arab et al., 2006). The anticoccidial activity of the plants Artemisia annua and Pimpinella anisum on E. tenella oocytes were examined by Dragan et al. (2010). Artemisia annua caused a significant reduction (90.7%) in the number of oocytes in the
faeces of broilers infected with *E. tenella* compared with the infected control group fed a 
standard diet. *P. anisum* reduced the number of *Eimeria oocytes* in the faeces to a smaller 
extent (58.83%). At the end of the experiment (32 days after infection) chicks which 
were supplemented with *Artemisia annua* had the best feed efficiency and increased 
daily weight gain in comparison to the other experimental groups. Khan et al. (2008) 
compared the effect of selected medicinal plant supplements (*Polygonum bistorta* and 
*Agele marmelos*) with homeopathic preparations (*Mercurius solubilis* and Darvisul 
liquid) on the suppression of coccidiosis in chickens. They concluded that the herb 
extracts examined expressed anti-coccidial activity and increased feed conversion ratio, 
daily gain, and reduced chicken mortality rate. These results are consistent with other 
researchers studying the anti-coccidial activity of other plants such as *Melia azedarach* 
(Akhtar and Rifaat, 1987) and *Indica Azadirachta* (Tippu et al., 2002). The effect of 
oregano oil (*Origanum vulgare*) was investigated on the performances of broilers after 
experimental infection of coccidia *Eimeria tenella* (5×104 oocytes/chicken) compared 
with salinomycin. It was concluded that the essential oil of oregano caused a significant 
reduction of *E. tenella* but these effects were still lower in the coccidiostats salinomycin 
(Kostadinović et al., 2010c). Giannenas et al. (2003) examined the anticoccidial effect of 
the essential oils of oregano and found that the essential oil of oregano added to the feed 
of broilers at an inclusion rate of 300 mg/kg affected the suppression of coccidiosis 
caused by *E. tenella*. Youn and Noh (2001) reported the most pronounced anti-coccidial 
effect against *Eimeria tenella* from fifteen plants studied was from *Sophora flavescens* 
extrag which was even stronger than *Artemisia annua*.

CONCLUSIONS

Recently medicinal plant supplements have received much attention for their use in 
animal nutrition. From this review, it can be concluded that medicinal plant 
supplements can be used in animal diets as plant-based alternatives for coccidia control 
in poultry farming and these would also enhance animal wellbeing. Collaborative efforts 
among scientists and farmers must particularly be directed towards establishing and 
developing innovative feeding systems using feed additives obtained from natural 
products, such as essential oils, medicinal plants, and extracts obtained from herbs 
which have a beneficial effect in coccidian control in poultry production. These additives 
have not yet shown resistance development in coccidial pathogens, making them 
appropriate for application in chicken diets. Moreover, the removal of drug residues in 
poultry products is also important for consumer health.

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