Paper received: 18.07.2019. Journal of Agronomy, Technology and Engineering Management
Paper accepted: 05.10.2019. ISSN: 2620-1755 Kostadinović et al., 2019. Vol. 2(5): 325-334

Review paper

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

Ljiljana Kostadinović[1,*], Sanja Popović[2], Dragana Ljubojević Pelić[3], Ivana Čabarkapa[2], Olivera Đuragić[2], Jovanka Lević[2]

[1]Planet Fresh, Podgorički put bb, 81402 Nikšić, Montenegro
[2]Institute of Food Technology, University of Novi Sad, Bulevar cara Lazara 1, 21000 Novi Sad, Serbia
[3]Scientific 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 (Varel, 2002; Kostadinvić 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 phytoadditives in poultry nutrition (Puvača, 2008; Kostadinović et al., 2010c; Stanaćev 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

Species	Site	Oocyst size (µm)		Pathogenicity
		Average length	Average width	
E. tenella	Caecum	22.80	19.65	High
E. acervulina	Duodenal loop	18.95	15.00	Low
E. necatrix	Mid gut	17.95	14.80	High
E. maxima	Mid gut	32.00	23.15	Low to moderate
E. mitis	Anterior gut	15.20	14.50	Low
E. praecox	Anterior gut	22.25	17.75	No
E. brunetti	Lower intestine	25.50	21.15	Moderate

(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 anti-coccidial 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).

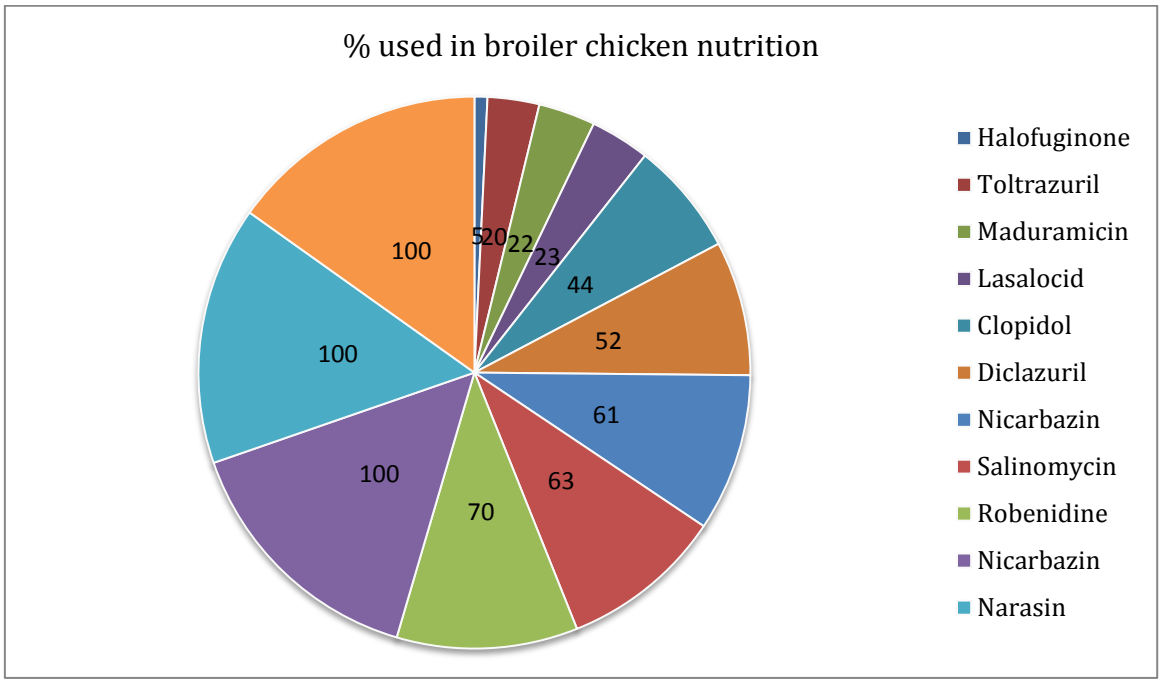

Figure 1. Anticoccidial drugs in broiler production

MEDICINAL PLANT SUPPLEMENTS AS COCCIDIOSTATS IN BROILER CHICKENS

A number of natural feed additives have shown anticoccidial activity and the plants *Azadirahta 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

Plant	Major essential oil components	Total volatiles, %	Source
Pimpinella anisum	trans-anetole	92.9	Sharifi et al. (2008)
Origanum vulgare	p-cymene	5.80	D'Antuono et al. (2000)
Azadirachta indica	b-caryophyllene	12.73	Pandey et al. (2012)
Berberis lycium	ligustilide	24.58	Khare (2004) Shabbir et al. (2012)
Sophora flavescens	2-ethyl-1-hexanol geranyl	3.25	Li et al. (2012)
Artemisia annua	camphor	44.00	Juteau et al. (2002)
Artemisia absinthium	chrysanthenyl acetate	29.45	Blagojević et al. (2006)

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 monoterpene) (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 Azadirahta* (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* extract 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.

ACKNOWLEDGEMENTS

This paper is a part of project III 46012 which is financed by the Ministry of Education, Science and Technological Development of the Republic of Serbia.

REFERENCES

AĆIMOVIĆ, M., SIKORA, V., BRDAR-JOKANOVIĆ, M., KIPROVSKI, B., POPOVIĆ, V., KOREN, A. and PUVAČA, N. (2019). *Dracocephalum moldovica*: cultivation, chemical composition and biological activity. *Journal of Agronomy, Technology and Engineering Management,* **2(1):** 153-167.

AKHTAR, M. and RIFAAT, S. (1987). Anticoccidial screening of *Melia azedarach* Linn. (Bakain) in naturally infected chickens. *Pakistan Journal of Agricultural Sciences,* **24**: 95-99.

ALLEN, P.C., LYDON, J. and DANFORTH, H.D. (1997). Effects of components of *Artemisia annua* on coccidian infections in chickens. *Poultry Science,* **76**: 1156-1163.

ARAB, H.A., RAHBARI, S., RASSOULI, A., MOSLEMI, M. and KHOSRAVIRAD, H. (2006). Determination of artemisinin in *Artemisia sieberi* and anticoccidial effects of the plant extract in broiler chickens. *Tropical Animal Health and Production,* **38**: 497-503.

BICKELL, S.L., DURMIC, Z., BLACHE, D., VERCOE, P.E. and MARTIN, G.B. (2010). Rethinking the management of health and reproduction in small ruminants. Updates on ruminant production and medicine. Proceedings of 26th World Buiatrics Congress, Santiago, Chile, pp. 317-325.

BISHOP, C.D. (1995). Antiviral activity of the essential oil of *Melaleuca alternifolia* (Maiden and Betche) Cheel (tea tree) against tobacco mosaic virus. *Journal of Essential Oil Research,* **7**: 641-644.

BISWAS, K., CHATTOPADHYAY, I., BAERJEE, R.K. and BANDYOPADHYAY, U. (2002). Biological activities and medicinal properties of neem (*Azadirachta indica*). *Current Science,* **82**: 1336-1345.

BLACHE, D., MARTIN, G.B. and MALONEY, S.K. (2008). Towards ethically improved animal experimentation in the study of animal reproduction. *Reproduction of Domestic Animals*, **2**: 8-14.

BLAGOJEVIĆ, P., RADULOVIĆ, N., PALIĆ, R. and STOJANOVIĆ, G. (2006). Chemical composition of the essential oils of Serbian Wild-Growing Artemisia absinthium and *Artemisia vulgaris*. *Journal of Agricultural Food Chemistry,* **54**: 4780-4789.

BOTSOGLOU, N.A., CHRISTAKI, E., FLOROU-PANERI, P., GIANNENAS, I., PAPAGEORGIOU, G. and SPAIS, A.B. (2004). The effect of a mixture of herbal essential oils or alpha-tocopheryl acetate on performance parameters and oxidation of body lipid in broilers. *South African Journal of Animal Science,* **34**: 52-61.

BOTSOGLOU, N.A., FLOROU-PANERI, P., CHRISTAKI, E., FLETOURIS, D.J. and SPAIS, A.B. (2002). Effect of dietary oregano essential oil on performance of chickens and on iron-induced lipid oxidation of breast, thigh and abdominal fat tissues. *British Poultry Science,* **43**: 223-230.

D'ANTUONO, L.F., GALLETTI, G.C. and BOCCHINI, P. (2000). Variability of essential oil content and composition of *Origanum vulgare* populations from a north Mediterranean area (Liguria Region, Northern Italy). *Annals of Botany,* **86**: 471-478.

DRAGAN, L., TITILINCU, A., DAN, I., DUNCA, I., DRAGAN, M. and MIRCEAN, V. (2010). Effect of *Artemisia annua* and *Pimpinella anisum* on *Eimeria tenella* (Phylum Apicomplexa) low infection in chickens. *Scientica Parasitologica,* **11**: 77-82.

DUTTA, G.P., MOHAN, A. and TRIPATHI, R. (1990). Study of the ametocytocidal/sporontocidal action of qinghaosu (artemisinin) by electron microscopy. *Journal of Parasitology*, **76**: 849-852.

ELLIOT, C. (2003). A review of coccidiostat residues in poultry. Food Safety Promotion Board, Queen´s University, Belfast.

FERREIRA, J.F.S. (2009). Artemisia species in small ruminant production: their potential antioxidant and anthelmintic effects. Proceedings of Medicinal Botanicals Program, Mountain State University, pp. 156 200.

GIANNENAS, A.I., FLOROU-PANERI, P., PAPAZAHARIADOU, M., CHRISTAKI, E., BOTSOGLOU, N.A. and SPAIS, A.B. (2003). Dietary oregano essential oil supplementation on performance of broilers challenged with *Emerita tenella*. *Archive of Animal Nutrition,* **57**: 99-106.

HE, J. and ZHANG, L. (1989). Effects of sweet wormwood (*Artemisia annua*) essence on Trypanosoma evansi. *Traditional Chinese Veterinary Medicine*, **2**: 5-6.

HERNÁNDEZ, F., MADRID, J., GARCIA, V., ORENGO, J. and MEGIAS, M.D. (2004). Influence of two plants extracts on broiler performance, digestibility, and digestive organ size. *Poultry Science,* **83**: 169-174.

IOVINE, N.M. and BLASER, M.J. (2004). Antibiotics in animal feed and spread of resistant Campylobacter from Poultry to humans. *Emerging Infectious Diseases,* **10**: 1158-1189.

JAMROZ, D., WERTELECKI, T., HOUSZKA, M. and KAMEL, C. (2006). Influence of diet type on the inclusion of plant origin active substances on morphological and histochemical characteristics of the stomach and jejunum walls in chicken. *Journal of Animal Physiology and Animal Nutrition*, **90**: 255-268.

JUGLAL, S., GOVINDEN, R. and ODHAV, B. (2002). Spice oils for the control of co-occurring mycotoxinproducing fungi. *Journal of Food Protection*, **65**: 683-687.

JUTEAU, F., MASOTTI, V., BESSIERE, J.M., DHERBOMEZ, M. and VIANO, J. (2002). Antibacterial and antioxidant activities of *Artemisia annua* essential oil. *Fitoterapia,* **73**: 532-536.

KARPOUHTSIS, I., PARDALI, E., FEGGOU, E., KOKKINI, S., SCOURAS, Z.G. and MAVRAGANITSIPIDOU, P. (1998). Insecticidal and genotoxic activities of oregano essential oils. *Journal of Agricultural Food Chemistry,* **46**: 1111-1115.

KHAN, M.A., YOUNAS, M., KHAN, I., ABBAS, R.Z. and ALI, M. (2008). Comparative efficacy of some herbal and homeopathic preparations against coccidiosis in broilers. *International Journal of Agriculture and Biology*, **10**: 358-60.

KHARE, C.P. (2004). Encyclopedia of Indian Medicinal Pants. Springer-Verlag Heidelberg.

KOSTADINOVIĆ, LJ., DOZET, G., LEVIĆ, J., PAVKOV, S. and GALONJA, T. (2010b). Uticaj esencijalnog ulja origana na karakteristike brojlera posle eksperimentalne infekcije kokcidijama. Proceedings of 51st Symposium on oil production, pp. 265-271.

KOSTADINOVIĆ, LJ., DOZET, G., PAVKOV, S. and LEVIĆ, J. (2008a) Uticaj lekovitog bilja na proizvodne rezultate tova brojlera. Abstract proceeding book of 9th Symposium on Botanical supplements, Kosmaj, pp. 64.

KOSTADINOVIĆ, J. and LEVIĆ, J. (2018). Effects of phytoadditives in poultry and pigs diseases. *Journal of Agronomy, Technology and Engineering Management,* **1(1):** 1-7.

KOSTADINOVIĆ, LJ., DOZET, G., PAVKOV, S. and LEVIĆ, J. (2008b). Primena lekovitog bilja kao promotora rasta u hrani za brojlere. Thematic Proceedings of III International Scientific Meating „Multifunctional Agriculture and Rural Development", pp. 292-297.

KOSTADINOVIĆ, LJ., LEVIĆ, J., GALONJA-COGHILL, T. and RUŽIČIĆ, L. (2012). Anticoccidia effects of the *Artemisia absinthium* L. extracts in broiler chickens. *Archiva Zootechnica*, **15**: 69-77.

KOSTADINOVIĆ, LJ., LEVIĆ, J., PAVKOV, S. and KALUĐEROVIĆ, D. (2010a). Effect of oregano essential oil on antioxidative system of broilers blood and liver. Proceedings of the 14 International Feed Symposium, Novi Sad, Serbia, pp. 282-287.

KOSTADINOVIĆ, LJ., LEVIĆ, J., PAVKOV, S., DOZET, G. and GALONJA-COGHILL, T. (2010c). Effect of Mentha piperita on antioxidative status in broiler chickens. *Contemporary Agriculture*, **59**: 145-150.

KOSTADINOVIĆ, LJ., PAVLOVSKI, Z. and PAVKOV, S. (2001). Effect of amprolium on the lipid peroxidation and the activity of superoxide dismutase in broilers blood and liver. *Archiv für Geflügelkunde*, **65**: 118-122.

KOSTADINOVIĆ, LJ., PUVAČA, N., POPOVIĆ, S. and LEVIĆ, J. (2015). Botanical supplements as anti-coccidial alternatives in poultry nutrition. *World's Poultry Science Journal,* **71**: 27-36.

KOSTADINOVIĆ, LJ., VEKIĆ, LJ., GALONJA-COGHILL, T., LEVIĆ, J. and PAVKOV, S. (2011). Effect of Mentha piperita on antioxidative status, growth performances and quality of poultry meat. Proceedings of the 9th International Scientific Conference „Serbia Facing the Challenges of Globalisation and Sustainable Development", Belgrade, pp. 295-301.

KOUL, A., GHARA, A.R. and GANGAR, S.C. (2006). Chemomodulatory effects of Azadirachta indica on the hepatic status of skin tumor bearing mice. *Journal of Colloid and Interface Science*, **20**: 169-77.

LEVIĆ, J., ČABARKAPA, I., TODOROVIĆ, G., PAVKOV, S., COGHILL-GALONJA, T. and KOSTADINOVIĆ, LJ. (2011). In vitro evaluation of antibacterial activity of essential oils from family Lamiaceae. *Romanian Biotechnological Letters*, **16**: 6034-6041.

LEVIĆ, J., ČOLOVIĆ, R., SREDANOVIĆ, S., PAVKOV, S. and KOSTADINOVIĆ, LJ. (2009). Effect of diet supplementation with ground herbs on performance of broiler chickens. 3rd International Feed Safety

Conference „Methods and Challenges“, Book of Abstracts, RIKILT-Institute of Food Safety, Wageningen, pp. 119.

LEVINE, N.D. (1985). Veterinary Protozoology. Iowa State University Press, Ames.

LI, A., HAN, L. and HAN, C.C. (2012). Antioxidant and neuroprotective activities of essential oil，isolated from Chinese herb pairs of Angelica sinensis and Sophora flavescens. *Journal of Applied Pharmaceutical Science,* **2**: 1-4.

MAHMOUD, S.S. and CROTEAU, R.B. (2002). Strategies for transgenic manipulation of monoterpene biosynthesis in plants. *Trends in Plant Sciences*, **7**: 366-373.

MARI, M., BERTOLINI, P. and PRATELLA, G.C. (2003). Non-conventional methods for the control of post-harvest pear diseases. *Journal of Applied Microbiology*, **94**: 761-766.

MATSUDA, K., YAMADA, K., KIMURA, M. and HAMADA, M. (1991). Nematicidal activity of matrine and its derivatives against pine wood nematodes. *Journal of Agricultural Food Chemistry,* **39**: 189-191.

MCDOUGALD, L.R. (2003). Coccidiosis. Diseases of Poultry. Imes, Iowa, pp. 974-1159.

McDOUGALD, L.R. and SEIBERT, B.P. (1998). Residual activity of anticoccidial drugs in chickens after withdrawal of medicated feeds. Veterinary Parasitology 74: 91-9.

MILLER, L.H. and SU, X. (2011). Artemisinin: discovery from the Chinese herbal garden. Cell 146: 855-858.

OLIVEIRA, A.A., SEGOVIA, J., SOUSA, V., MATA, E., GONÇALVES, M., BEZERRA, R., JUNIOR, P. and KANZAKI, L. (2013). Antimicrobial activity of amazonian botanical supplements. Springer Plus 2: 371-377.

PANDEY, I.P., AHMED, S.F., CHHIMWAL, S. and PANDEY, S. (2012). Chemical composition and wound healing activity of volatile oil of leaves of *Azadirachta indica* A. juss. *Advances in Pure and Applied Chemistry*, **1**: 2167-0854.

PEEK, H.W. (2010). Resistance to anticoccidial drugs: alternative strategies to control coccidiosis in broilers. PhD thesis, Utrecht University, pp. 1-244.

PESSOA, L.M., MORAIS, S.M., BEVILAQUA, C.M.L. and LUCIANO, J.H.S. (2002). Anthelmintic activity of essential oil of *Ocimum gratissimum* Linn. and eugenol against Haemonchus contortus. *Veterinary Parasitology,* **109**: 59-63.

PUVAČA, N. (2008). Effect of phytoadditive (*Allium sativum* L.) in fattening chicks nutrition. Proceedings of the 32nd International Conference of Agriculture, Novi Sad, pp. 116-121.

PUVAČA, N., KOSTADINOVIĆ, LJ., POPOVIĆ, S., LEVIĆ J., LJUBOJEVIĆ, D., TUFARELLI, V., JOVANOVIĆ, R., TASIĆ, T., IKONIĆ, P. and LUKAČ, D. (2016). Proximate composition, cholesterol concentration and lipid oxidation of meat from chickens fed dietary spice addition (*Allium sativum, Piper nigrum, Capsicum annuum*). *Animal Production Science,* **56(11)**: 1920-1927.

PUVAČA, N., LJUBOJEVIĆ PELIĆ, D., ČABARKAPA, I., POPOVIĆ, S., TOMIČIĆ, Z., NIKOLOVA, N. and LEVIĆ, J. (2019) Quality of broiler chickens carcass fed dietary addition of garlic, black pepper and hot red pepper. *Journal of Agronomy, Technology and Engineering Management,* **2(1):** 218-227.

PUVAČA, N., STANAĆEV, V., GLAMOČIĆ, D., LEVIĆ, J., PERIĆ, L., STANAĆEV, V. and MILIĆ, D. (2013). Beneficial effects of phytoadditives in broiler nutrition. *World's Poultry Science Journal,* **69**: 27-34.

QUAN, J. (1990). Therapy of swine toxoplasmosis with Artemisia annua. *Chinese Journal of Traditional Veterinary Science,* **4**: 4.

REID, W.M. (1990). History of avian medicine in the United States. X. Control of coccidiosis. *Avian Diseases,* **34**: 509-525.

RUFF, M.D. and DANFORTH, H.D. (1996). Resistance of coccidian to medications. Proceedings of 20th World's Poultry Congress, pp. 427-430.

SHABBIR, A., SHAHZAD, M., ARFAT, Y., ALI, L., AZIZ, R.S., MURTAZA, G., WAQAR, S. and ALAMGEER, A. (2012). Berberis lycium Royle: A review of its traditional uses, phytochemistry and pharmacology. *African Journal of Pharmacy and Pharmacology,* **6**: 2346-2353.

SHARIFI, R., KIANI, H., FARZANEH, M. and AHMADZADEH, M. (2008). Chemical composition of essential oils of Iranian Pimpinella anisum L. and Foeniculum vulgare miller and their antifungal activity against postharvest pathogens. *Journal of Essential Oil Bearing Plant,* **11**: 514-522.

SI, W., GONG, J., TSAO, R., ZHOU, T., YU, H., POPPE, C., JOHNSON, R. and DU, Z. (2006). Antimicrobial activity of essential oils and structurally related synthetic food additives towards selected pathogenic and beneficial gut bacteria. *Journal of Applied Microbiology,* **100**: 296-305.

SRINIVASAN, K. (2004). Spices as influencers of body metabolism: an overview of three decades of research. *Food Research International,* **38**: 77-86.

STANAĆEV, V., GLAMOČIĆ, D., MILOŠEVIĆ, N., PUVAČA, N., STANAĆEV, V. and PLAVŠA, N. (2011). Effect of garlic (*Allium sativum* L.) in fattening chicks nutrition. *African Journal of Agricultural Research,* **6**: 943-948.

STANAĆEV, V., MILOŠEVIĆ, N., PLAVŠA, N., BJEDOV, S., STANAĆEV, V., PUVAČA, N. and ARAPOVIĆ, Ž. (2010). Phyto additives (*Allium sativum* L.) in the diet of fattening chickens. Proceedings of the 14th International Symposium of Feed Technology, Novi Sad, pp. 295-302.

TIPPU, M.A., PASHA, T.N. and ALI, Z. (2002). Comparative efficacy of salinomycin sodium and Neem fruit (*Azadiracht indica*) as feed additive anticoccidials in broilers. *International Journal of Poultry Science*, **1**: 91-93.

TYZZER, E.E., THEILER, H. and JONES, E.E. (1932). Coccidiosis in gallinaceous birds II. A comparative study of species of Eimeria of the chicken. *American Journal of Hygiene,* **15**: 319-393.

VAREL, V.H. (2002). Livestock manure odor abatement with plant-derived oils and nitrogen conservation with urease inhibitors: a review. *Journal of Animal Science,* **80**: 1-7.

VERMEULEN, A.N., SCHAAP, D.C. and SCHETTERS, P.M. (2001). Control of coccidiosis in chickens by vaccination. *Veterinary Parasitology*, **100**: 13-20.

WILLIAMS, R.B. (1999). A compartmentalized model for the estimation of the cost of coccidiosis to the world's chicken production industry. *International Journal for Parasitology,* **29**: 1209-1229.

YOUN, H.J. and NOH, J.W. (2001). Screening of the anticoccidial effects of herb extracts against Emerita tenella. *Veterinary Parasitology,* **96**: 257-263.