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Phytobiotics in Poultry Industry as Growth Promoters, Antimicrobials and Immunomodulators – A Review

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ABSTRACT

Due to the hazardous use of antimicrobials in poultry production sector, development of drug resistance have become a worldwide problem. Therefore, using biotic or natural products, such as phytobiotics (phytogenics or botanicals) have received a great attention as antibiotic substitutes. The use of phytobiotics or their constituents have been considered as a relatively new class of natural herbs that gained popularity and acceptability among poultry farmers. The incorporation of several types of phytobiotic additives in poultry feed have proved their ability to enhance the productive performance of broilers as well as layers. Moreover, phytbiotics presented great efficacy in counteracting intestinal pathogenic microorganism while maintaining the population of normal inhabitant beneficial microflora. Immunostimulatory effect on both humoral and cellular immunity as well as antioxidant properties were recorded as characters of phytobiotics. Therefore, this review article aimed to give a spotlight on the uses of different types of phytobiotics as poultry dietary additives to improve the productive parameters, reduce the pathogenic intestinal bacteria, and potentiate the immune response, especially after vaccination processes.

Keywords: Antimicrobial, Immunity, Performance, Plants, Poultry

INTRODUCTION

From several decades till now, poultry industry has been recognized as an important subsector of agricultural and veterinary fields due to increasing demand for meat and eggs as low cost protein sources. Continues feeding by sub-therapeutic levels of antimicrobials as growth promoter agents or antimicrobial compounds have had a negative impact on the balance of normal inhabitants of gut microflora, accumulation of antibiotic tissues residues as well as developing new strains of drug-resistant pathogenic bacteria (Castanon, 2007). Therefore, in 2006, the European Union Commission banned using of antibiotics in animal feeds as a growth promoter in different countries (Europe Union Commission, 2005).

Phytobiotics are also termed as phytogenics or botanicals. They are defined as natural, less toxic, and residue free plant-derived compounds that have been used as feed additives for livestock production (Wang et al., 2008). Phytobiotics are composed of natural bioactive components or substances of plant origin including terpenoids, alkaloids, glycosides and phenolics (Shad et al., 2014). Phytobiotics could be classified as herbs from flowering, non-woody and non-persistent plants, botanicals or spices from non-leaf parts like seeds, fruits, bark or root, essential oils or extracts and oleoresins (Bote, 2004).

Numerous studies have been conducted to demonstrate the effect of phytobiotics as growth promoter feed additives like prebiotics and probiotics to enhance overall performance parameters as well as health conditions of poultry (Yasodha et al., 2019; Özbudak, 2019). Phytobiotics have been also used as antimicrobial, antiparasitic, anticoccidial as well as immunostimulant agents in poultry field (Manafi, 2015; Gilani et al., 2018; Hafeez et al., 2020). Phytogenic substances were extremely studied in different species of monogastrics (Gheisar and Kim, 2018), rabbits (Alagawany et al., 2018; Al-Sagheer et al., 2019) and fish (Naiel et al., 2019).

So, the purpose of current article review was to spotlight on phytogenic compounds that used in poultry field and their effects on the productive performance, antimicrobial activities and immuno-stimulatory properties.

Production parameters

Improved growth parameters were detected in birds fed on different kinds of herbs, polysaccharides or essential oils components (Yasodha et al., 2019). The enhancement of the growth performance parameters after supplementation of phytobiotics may be depends on the synergistic mechanism among their active molecular complex (Hussein et al., 2020a). Phytobiotics could maintain or improve normal intestinal architecture, increase the villus length and consequently increase the surface of intestinal absorption (Tabatabaei, 2016). It has been demonstrated that phytobiotics are able to stimulate saliva production, secretion of digestible enzymes and bile production resulting in improving the performance and digestibility (Alloui et al., 2014). Moreover, phytobiotics enhance the digestion and digestion and utilization of protein in the intestine (El-Gendi, 1996), decrease the gut pathogens (Kubkomawa et al., 2013) and increase *Lactobacillus* spp. count (Windisch et al., 2008). It has been observed that supplementation with herbal feed additives can alter the histological structure of the intestine and indicated elevation of the intestinal villi by deepening of its crypts (Murali et al., 2012), increasing the dendritic cells absorption capacity in the intestinal lumen, stimulation of toll-like receptors and activation of epithelial to release the mucosal cytokines. Alcicek et al. (2004) assumed that feeding of broilers on phytobiotics stimulated the secretion of high amount of intestinal mucus and consequently reducing the pathogens adhesion and establishment of gut microbial eubiosis.

Supplementing broiler feed or water with essential oil mixtures of thymol and cinnamaldehyde (Tiihonen et al., 2010), thymol and star anise (Kim et al., 2016), clove and cinnamaldehyde (Chalghoumi et al., 2013), coriander (Ghazanfari et al., 2015; Hady et al., 2016), oregano (Hashemipour et al., 2014), a mixture of oregano, anise, and citrus peel (Abdelnaser et al., 2019), carvacrol (Jamroz et al., 2006), a blend of carvacrol, cinnamaldehyde and capsicum oleoresin (Bravo and Ionescu, 2008) and ginger extract (Olaifa et al., 2019) had been detected for improving all performance parameters including; feed intake, feed conversion rate and body weight. Moreover, supplementation of broilers diet with garlic (Elagib et al., 2013), a mixture of garlic, mushroom and propolis (Daneshmand et al., 2012), turmeric powder (Ahmadi, 2010), guggul resin (Iranparast et al., 2014), dried ground leaves of stevia (Atteh et al., 2008) and black cumin seeds (Khalaji et al., 2011) presented the enhancement of broilers performance. Studies on the effects of herbal compounds on the production of broilers Japanese quail's revealed improvement of all performances (Manafi et al., 2016).

The laying hens represented improvement in egg production, eggshell strength and thickness as well as internal egg quality after treatment with mixture of plant extracts and essential oils (Bölükbaşi et al., 2008; Radwan et al., 2008; Kaya et al., 2013).

Antimicrobial effect

It has been demonstrated that phytochemical compounds of phytobiotics have a strong antimicrobial activity against Gram-positive and Gram-negative bacteria either *in vivo* (Al-Kassie, 2010; Daka, 2013) or *in vitro* environment (Al-Mariri and Safi, 2014). Some phytochemical compounds as alkaloid inhibit DNA synthesis (Karou et al., 2005) and form saponin complexes with the cell membrane (sterols) which leading to cells damage and collapse (Morrissey and Osbourn, 1999). The antimicrobial effect of essential oils could be refer their ability to penetrate through the bacterial membrane (Helander et al., 1998), their chemical structure (Farag et al., 1989) and their aromaticity (Bowles and Miller, 1993).

Modulation of the gut microflora by phytogenic compounds plays an important role in maintaining host health (Tollba et al., 2012). Several studies revealed that phytogenic compounds or their extracts reduce the population of intestinal pathogenic organisms and their metabolites, but increase the number of intestinal normal and helpful microflora which relief the intestinal challenge and immune stress and consequently increase intestinal performance (Liu et al., 2014). It has been speculated that organic acids of some phytobiotic feed additives may lower the intestinal pH that leaded to inhibiting the pathogenicity of local pathogens and lowering the level of their toxic products (Manafi et al., 2016).

Antibacterial effect

Essential oils could reduce the growth of common intestinal poultry pathogens. Inoculation of thyme and cinnamon in the broiler ration reduces the total bacterial as well as coliform count in the intestinal tract (Karangiya et al., 2016). An *in vitro* study revealed that flowers of Calendula presented growth inhibitory effects on *Escherichia coli* (*E. coli*) (Arora et al., 2013). However, some reports indicated the inhibitory effects of dietary phytobiotics or plant extracts on *E. coli* activity *in vivo* (Abd El-Ghany and Ismail, 2014; Diaz-Sanchez et al., 2015; Elmenawey et al., 2019). Diet containing thyme essential oil helped for increasing in *Lactobacillus* and decreasing in *E. coli* counts in the intestine of Japanese

quail (Khaksar et al., 2012). Essential oils of oregano revealed antimicrobial properties on broiler carcasses through reduction of the total bacterial count especially *Salmonella* spp. (Aksit et al., 2006). Short chain fatty acids of phytobiotics revealed growth promoting effect on the intestinal beneficial microbiota as well as controlling the growth of *Salmonella enteritidis* (*S. enteritids*) (Hansen et al., 1997). Quail's diet containing phytobiotic feed additives had significant (P≤0.05) increase in the number of *Lactobacilli*, decrease in *E. coli* population and inhibit the growth of *Salmonella* in the intestinal tract (Dorman and Deans, 2000).

The efficacy of a mixture of seven essential oils that inhibited the growth of *Clostridium perfringens* (*C. perfringens*) *in vitro* has been reported by Si et al. (2009). In the field studies of Mitsch et al. (2004), Siragusa et al. (2008), McReynolds et al. (2009), Abudabos et al. (2018), El-Sheikh et al. (2018) and Hussein et al. (2020b), different phytobiotic feed additives caused reduction of intestinal colonization and proliferation of *C. perfringens*, lesion score and mortalities as well as improvement in performance of broilers and their carcass quality.

The reduction in *C. perfringens* virulence after supplementation with essential oil compounds may be related to the stimulation of some digestible enzymes like trypsin which inactivates α toxin of type A and β toxin of type C strains of *C. perfringens*, stabilization of natural resident gut microflora like *Lactobacillus* spp. and consequently inhibition of the organism pathogenicity (Cho et al., 2014).

Moreover, essential oils of lemon, green tea and turmeric blend proved great efficacy in reducing the count of *S. enteritidis* and *Campylobacter jejuni* on the surface of chicken's carcass (Murali et al., 2012). The Eucalyptus volatile oils have been found to have the ability to relief broilers complicated respiratory distress caused by Mycoplasma gallisepticum (Abd El-Ghany, 2008).

Antifungal and detoxifying effect

Phytogenic compound have antifungal properties. Akgul and Kivanc (1988) reported about the inhibitory effects of some spices and oregano components on some foodborne fungi. Essential oil of marjoram reduced the *in vitro* growth of *Aspergillus flavus*, *A. niger*, *A. ochraceus* and *A. parasiticus* up to 89% (Deans and Waterman, 1993). The oil of lemon and orange can reduce the formation of *A. flavus* (Hasan et al., 2005). It has been demonstrated that *Allium sativum* has a great (60-80%) *in vitro* antifungal activity against *Aspergillus* and *Penicillium* spp. (Afzal et al., 2010). Onion, garlic and ginger revealed antifungal activity against *A. flavus*, *A. niger* and *Cladosporium herbaru*, *Cinnamomum verum* and *Piper nigrum* which was studied with successful results by Tagoe et al. (2011). Phytobiotics *like Ocimum gratissimum, Cymbopogon citratus, Xylopia aethiopica, Monodora myristica*, *Syzygium aromaticum* proved their ability to inhibit the formation of non sorbic acid which is a precursor in the pathway of aflatoxin synthesis (Awuah, 1996). Neem extract represented inhibitory effects on biosynthesis of aflatoxins (B and G) (Bhatnagar et al., 1990). Also, neem leaf extract and its oil have been found to inhibit the growth and morphology of *Penicillium* spp. and consequently prevent the production of ochratoxin A (Bhatnagar et al., 1990).

Anticoccidial effect

The anticoccidial activity of some herbal plants have been documented (Willis et al., 2013). Phytogenic compounds have been found to reduce the severity of *Eimeria* spp. infection in broilers by alleviation of droppings score, intestinal lesions score and also reducing oocyst shedding (Zyan et al., 2017). Numerous phytobiotics as Atemesia annua (Allen et al., 1997), *Astragulus membranaceus* and *Sophora flavescens* (Youn and Noh, 2001), green tea (Jang et al., 2007), *Ageratum conyzoid* (Nweze and Obiwulu, 2009), *Musa paradisiaca* (Anosa and Okoro, 2010), olive tree (De Pablos et al., 2010), oregano essential oil (Tsinas et al., 2011), *Carica papaya* leaf extract (Nghonjuyi et al., 2015) and coconut oil (Hafeez et al., 2020) have indicated an excellent anticoccidial activity against different types of *Eimeria* spp. in birds.

Some essential oils presented similar drug efficacy in prevention and control of coccidiosis in broilers. The oregano oil and other mixtures of oils were similar to ionophores lasalocid (Giannenas et al., 2003) and monensin (Oviedo-Rondón et al., 2006), while a mixture of carvacrol, camphor, cineole and thymol was similar to salinomycin (Bozkurt et al., 2014) in terms of reduction of shedding and lesions of different *Eimeria* spp. in broilers.

Combined experimental infection of *C. perfringens* and *E. maxima* has been ameliorated after dietary treatment of three breeds of broilers with Capsicum, Curcuma longa oleoresins (Kim et al., 2015) and Allium hookeri root (Lee et al., 2018).

Immunomodulatory effect

In poultry production, reduction of infection as well as improvement of production by stimulation of the immune system after using phytogenic substances were

investigated previously (Zaki et al., 2016). The immunomodulatory mechanism of phytogenic active substances in poultry have been studied (Hashemi and Davoodi, 2012). Polysaccharide are very important immunoactive components of phytobiotics (Xue and Meng, 1996). Phytogenic compounds also induce their immunomodulatory effects through increasing immune cells proliferation, arising cytokines expression and elevation of antibody titers (Lee et al., 2010; Park et al., 2011; Pourhossein et al., 2015). The immunogenicity of phytobiotics could be manifested as increasing macrophages, lymphocytes and natural killer cells activities as well as stimulation of interferon production (Hashemi and Davoodi, 2010; Kumar et al., 2014). Plants contain flavonoids, vitamin C and carotenoids are able to enhance the immune system (Craig, 1999). Some herbs and species like garlic, echinacea and liquoric have immunostimulatory properties due to their composition of vitamin C, carotenoids and flavonoids as well as their abilities to stimulate macrophages, lymphocytes and natural killer cells activities and interferon production (Frankic et al., 2009). Detecting *in vitro* immuno-stimulatory effect of dandelion, mustard and safflower either on lymphocytes and macrophages of chickens was performed by Lee et al. 2007. The results indicated inhibition of tumor cell growth, antioxidant effects, stimulation of lymphocyte proliferation and nitric oxide production by macrophages. The immunostimulant effect of some essential oils extracts of phytobiotics may be due to the presence of certain compounds that may bind to Immunoglobulin G (Ig G) receptors which leaded to stimulation of immune response (Ahmed et al., 2013). In the study of Placha et al. (2014), inoculation of thymol in the broiler diet increased the trans-epithelial electrical resistance of duodenal mucosa.

It has been found that mushroom and plant polysaccharides have immunomodulatory effects in chickens infested with *Eimeria tenella* (Guo et al., 2004).

Potential antiviral activity of plant seeds was recorded (Yaseen, 2003). Different types of herbs mix, spices, plant extracts and essential oils presented enhancement of immune response of birds (Huang et al., 2007; Pourali et al., 2010; Kavyani et al., 2012; Abou-Elkhair et al., 2014; Awaad et al., 2016).

A significant ($P<0.05$) elevation of antibody Enzyme-linked immunosorbent assay (ELISA) titer after vaccination with Newcastle Disease Virus (NDV) vaccine (Chowdhury et al., 2018) was recorded after feeding on clove bud and cinnamon plant, while peppermint essential oil helped in significant ($P<0.05$) rising in Haemagglutination Inhibition (HI) antibody titer against Avian Influenza (AI) virus vaccines (H9N2) in broiler chicks (Sultan et al., 2017). In addition, significant ($P<0.05$) increase in HI titers against NDV vaccine and sheep red blood cells were observed in broiler chicks treated with Aloe vera gel (1%) in the drinking water for six weeks (Darabighane et al., 2017)

Laying hens presented significant ($P>0.05$) increase in ELISA titer after vaccination with ND, Infectious Bronchitis (IB) and Infectious Bursal Disease (IBD) vaccines (Özek et al., 2011). Landy et al. (2011) observed that inoculation of broiler ration with neem powder for six weeks resulting in an elevation of HI antibody titer against AI vaccine, but not against ND vaccine. Barbour et al. (2008) evaluated the effect of using Eucalyptus and peppermint essential oils during vaccination of ND and IBD. The results indicated improved health conditions of the birds associated with elevation of ELISA titers against the used virus vaccines. Moreover, an increase in IgG and IgM ELISA titers has been observed in chickens fed on oregano essential oils for three weeks period (Malayoglu et al., 2010). Recently, Abdelnaser et al. (2019) indicated that treatment with essential oils of oregano, anise, and citrus peel at level of 125 gm/ton induced positive effects on the immune response of *C. perfringens* challenged broilers after vaccination against ND, IB, AI and IBD viruses as well as increasing in relative spleen weight.

CONCLUSION

Using of phytobiotics in poultry diet as a feed additive and considering them as an antimicrobial substitute has been became a very essential and critical issue currently. Phytobiotic compounds could replace antibiotic growth promoters to improve the productive performance of chickens, act as antibacterial, antifungal and antiparasitic agents as well as it has been considered as potential immunostimulants especially after routine vaccination programs of chickens. This review spotlight on the significant using of phytobiotics in poultry field and industry as natural antibiotic alternatives to avoid the emerged problem of antibiotic resistance,

Competing interests

The author have not declared any conflict of interest.

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