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The Potential Use of Essential Oil Nanoemulsion as a Novel Alternative to Antibiotics in Poultry Production-A Review

Review Article

A.P. Baskara[1], B. Ariyadi[2], N.D. Dono[1], R. Martien[3] and Z. Zuprizal[1*]

[1] Department of Animal Nutrition and Feed Science, Faculty of Animal Science, Gadjah Mada University, Yogyakarta, Indonesia
[2] Department of Animal Production, Faculty of Animal Science, Gadjah Mada University, Yogyakarta, Indonesia
[3] Department of Pharmaceutics, Faculty of Pharmacy, Gadjah Mada University, Yogyakarta, Indonesia

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*Correspondence E-mail: zuprizal@ugm.ac.id

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ABSTRACT

Antibiotics are commonly used due to their antimicrobial activity and widely used for promoting growth, preventing diseases or therapy in poultry. The misuse of antibiotics in livestock production induces resistant bacteria into the environment. Therefore, the need to develop alternatives to antibiotics become increasingly important, that protect and improve global public health. The phytobiotics especially essential oils are known to have antimicrobial activity, thus potentially as an alternative candidate to antibiotics. The volatile bioactive components contained in the essential oils, makes it possess that antimicrobial activity, yet the volatile bioactive components also become a limiting factor in essential oils application. Nanoemulsions carrier systems can be a solution to overcome that limiting factor. Nanoemulsion is increasingly being utilized for improving the bioavailability of certain types of volatile components which most of them are lipophilic substances. In this review, we are going to discuss the non-antibiotic alternative of plant essential oils, including current research in poultry nutrition, and the potential application of essential oils using nanoemulsion as an alternative candidate to antibiotics in poultry production.

KEY WORDS antibiotic, essential oil, nanoemulsion, poultry.

INTRODUCTION

In commercial poultry production, antimicrobial agents such as antibiotic, are widely used to prevent and treat diseases (Landoni and Albarellos, 2015). Various antibiotics such as penicillin have already discovered and applied for more than 70 years ago. Antibiotics become critically important for preventing, controlling, and treatment of several diseases in both humans and animals (Cheng *et al.* 2014). In animal nutrition, some antibiotics had been used in feeds as feed additives for increasing the animal growth, enhancing the feed efficiency and improving the quality of the animal products (Yang *et al.* 2009; Cheng *et al.* 2014).

Furthermore, antibiotics being used to increase the effectiveness of the production process and ensure the development and intensification in livestock farming industries. The misuse of antibiotic can lead the risks concerning the development of antibiotic-resistant, thus allegedly caused the spread of resistant bacteria and the resistant factors between animals and humans (Stanton, 2013). Therefore, in order to reduce the spread of resistant bacteria, improvement of health benefits and societal demands on consumer health and environmental protection, studies of non-antibiotic alternatives in poultry nutrition have become very interesting to researchers (Pan and Yu, 2014; Criste *et al.* 2017; Saracila *et al.* 2018).

The need for a non-antibiotic alternative has increased the research interest in the scope of animal nutrition lately. According to Cheng *et al.* (2014), the non-antibiotics alternative should respect some conditions as follows: not toxic to animals, completely excreted out of the body or no residues, no lead to resistance, stable for the bioavailability, easy to degrade and not pollute the environment, has good palatability, maintain the beneficial microbiota of the animals, suppress the growth of potentially pathogenic bacteria, enhance the immunomodulatory system, increase feed efficiency and animal growth, and have no side effects. The study of alternatives to antibiotic is conducted not only to keep the animal health and productivity but also keep public health and environment condition at a good level. Several types of alternatives to the antibiotic are essential oils, nanoparticles, phytoncides, phytogenic feed additives, bacteriophages, bacteriocins, immunomodulator, organic acids, enzymes, prebiotics and probiotics (Mehdi *et al.* 2018). One potential example as an alternative to replace antibiotics in poultry production is phytobiotic (Windisch *et al.* 2008).

Phytobiotic is defined by Mehdi *et al.* (2018) as plant-derived extracts or products which are given to promote animal growth and performance. Plants are a source of various kinds of bioactive substances, such as antimicrobial substance, that plays an important role against external stressor. The two major properties belonging to phytobiotics are antimicrobial activity and immunomodulatory activity which are essential for the health and well-being of the poultry (Yang *et al.* 2009). The use of phytobiotic in poultry production is known not only to maintain the growth and immune system but also reduce the stress effects. Several studies have reported that phytobiotics or phytogenic compounds have potential as an alternative to antibiotics (Ghasemi *et al.* 2014), increase the performance (Ghasemi *et al.* 2014; Li *et al.* 2015), decrease poultry pathogen colonization (Upadhyay *et al.* 2017) and reduce pathogen transmission in poultry products (Upadhyaya *et al.* 2015; Nair and Johny, 2017). Phytobiotic can promote growth by maintaining the normal digestive function, poultry microbiota (Mountzouris *et al.* 2011) and preventing the subclinical infections, causing an improvement on nutrient uptake (Huyghebaert *et al.* 2011). Phytobiotics are complex mixtures of organic and some bioactive compounds that have different modes of antimicrobial activity, therefore making them effective to prevent the development of resistant bacteria (Suresh *et al.* 2018).

Most of phytobiotics such as polypeptides, polyphenols, alkaloids, terpenoids, lectins, and polyacetylenes are secondary metabolites and known to be antimicrobial agents (Nabavi *et al.* 2015), allegedly have no nutritional value and produced during the normal metabolism of plants (Hashemi and Davoodi, 2011). Various plant-derived products, especially essential oils have been known for their antimicrobial activity (Jayasena and Jo, 2013) which makes them potentially suitable as antibiotics replacer (Chaves *et al.* 2008). The volatile bioactive components contained in essential oils give them biological activity such as antimicrobial activity (Mahmoud and Croteau, 2002). However, those volatile components also become a limiting factor in essential oils application due to its volatile properties and poor bioavailability.

One of the potential solutions to overcome the limiting factor of essential oils application is nanoemulsion. Nanoemulsions carrier systems are widely being used in the pharmaceutical and food industries by encapsulating, protecting, and delivering poorly water-soluble bioactive components (McClements, 2012). Several types of poorly water-soluble or lipophilic substances can be encapsulated within nanoemulsions to increase the bioavailability, which leads to increase in the bioactivity (Acosta, 2009). In this review is going to discuss the non-antibiotic alternatives of plant essential oils, including current research in poultry nutrition, and the potential application of essential oils using nanoemulsion as a novel candidate of an alternative to antibiotics in poultry production.

Antibiotic in poultry production

Antibiotic is natural, semi-synthetic and synthetic compounds, commonly applied orally, parenterally or topically in both human and animal for prevention and treatment diseases, and several purposes including growth promoter in livestock and being widely used due to their antimicrobial activity (Phillips *et al.* 2004; Allen *et al.* 2013; Diaz-Sanchez *et al.* 2015). The discovery of antibiotic is a great leap in human history and changes the medicated way in many respects (Davies and Davies, 2010). Since the 1950 s, antimicrobial agents have been commonly used in the livestock and poultry production process (Mathew *et al.* 2007). In livestock production, antibiotics are used for some purposes such as growth promotion, prophylaxis or therapy (Chattopadhyay, 2014). Antibiotic growth promoters (AGP) is defined as a low subtherapeutic dosage of any antibiotics to decrease or inhibit bacterial growth and administered in livestock (Ronquillo and Hernandez, 2017). *Clostridium* spp., salmonellosis and mycoplasmosis have been made a significant economic loss by causing several diseases, such as colibacillosis and enteritis, to the poultry production (Mathew *et al.* 2007) and antibiotics are an effective solution to that problem (Singer and Hofacre, 2006). According to Van Boeckel *et al.* (2015), the highest consumption of antimicrobial in livestock production is swine (172 mg/PCU) followed by poultry (148 mg/PCU) and cattle (45 mg/PCU). Antimicrobial agents are used for growth promotion as a consequence of livestock intensification to fulfill the increasing of food demand and efficiency by preventing the diseases, increasing growth and feed efficiency. Thus, those practices are very important for livestock businesses and large-scale intensive agricultural operations that makes routinely use of AGP increasing day by day (Phillips *et al.* 2004; Van Boeckel *et al.* 2015).

Antibiotic supplementation in the diet significantly affects the performance and host immunity at the early period of poultry raising process (Kumar *et al.* 2018). Gut integrity and function that are affected by pathogen infection will pose a threat to the immune system (Neish, 2002). The use of antibiotics can increase the poultry productivity. Recent research in poultry nutrition showed that antibiotics at low subtherapeutic doses can be used to promote growth (Chattopadhyay, 2014) and maintain the birds health by reducing the total bacterial load and pathogenic suppression, modulating the immune system and thinning of the mucosal layer (Lee *et al.* 2012). In addition, antibiotics mostly affect productivity by controlling microbiota and gastrointestinal infections in the poultry intestine (Singh *et al.* 2013). The antibiotics activity also decreases the bile salt hydrolase activity which is an enzyme produced by bacteria in the intestine and gives a negative effect on host fat digestion and utilization (Lin, 2014). Growth-promoting effects of antibiotics can emerge by increasing nutrient absorption by the host and manipulating the beneficial bacteria community in favor of non-antagonistic functions (Butaye *et al.* 2003; Phillips *et al.* 2004). The use of AGP can never be separated from the modulation of intestinal bacterial populations and growth promotion (Lin, 2014). The antimicrobial activities of antibiotic can be classified into two mechanisms based on the cellular component or system they affect. The bacteriostatic that inhibit the growth of the organism, and the bactericidal that kill the organism (Kohanski *et al.* 2010), but only a few of the antibiotics that have been well investigated in livestock (Butaye *et al.* 2003).

Almost all of the antibiotics used in the livestock production process, which are up to 90% of consumed doses, excreted out of the body to the environment in the form of parent compounds and their metabolites (Carvalho and Santos, 2016). Furthermore, the misuse of antibiotics in livestock production as therapeutic, prophylactic purposes or growth promoters, induces pathogenic and commensal microorganisms to become resistant to antibiotic substances (Wegener, 2003). The resistance to an antibiotic can intrinsically occur by random chromosome mutations, and transmitted vertically when cells divide, or extrinsic occurs by transferring the resistance genes to other bacteria which known as horizontal gene transfer (HGT) mechanisms (Diarra and Malouin, 2014; Toutain *et al.* 2016). The emergence of antibiotic resistance in the past few decades has been considered as a critical public health problem (Khameneh *et al.* 2016; Rios *et al.* 2016; Frieri *et al.* 2017; Marquardt and Li, 2018). Antibiotic resistance is a natural mechanism to protect organisms that produce antibiotics from their own products, and another competitive attack in nature. The overuse of antibiotics will increase the risk of resistance to develop among pathogens and commensals bacteria (Phillips *et al.* 2004). Hence, the spread of antibiotic-resistant bacteria results in reduced effectiveness of antibiotics to treat diseases and create serious public health problems (Wegener, 2003).

Removing antibiotics from poultry nutrition has caused an increase in cases of certain poultry diseases, such as necrotic enteritis and dysbacteriosis which lead to a decrease in animal performance (Huyghebaert *et al.* 2011). It is very important to develop other alternatives with different targets to avoid several types of resistance mechanisms that bacteria already have on antibiotics (Suresh *et al.* 2018). The problem of antibiotic resistance must be solved by multifactorial and interdisciplinary research so as to provide a guarantee for discovering an alternative to antibiotics because it cannot be overcome by one intervention. A multipurpose approach is needed to solve the antibiotic resistance (Allen *et al.* 2013). Therefore, the need to develop alternatives to antibiotics is becoming increasingly important, with the aim of maintaining and improving public health globally (Goossens *et al.* 2005).

Essential oils in poultry production

The phytobiotic bioactive substances have some bioactivities such as increase amylase and protease activity, affect the production and activity of digestive enzymes (Jang *et al.* 2007), improve the poultry growth performance by promoting the proliferation and growth of absorptive cells in the gut so that deeper crypt and higher villus are obtained (Jamroz *et al.* 2006). Phytobiotics are generally known as one of the potential alternative feed additives to AGP in the poultry production process (Windisch *et al.* 2008). The advantages of phytobiotics or other plant-derived products compared to antibiotics or inorganic chemicals compounds are safer, no residue, not for medical or veterinary purposes and have a favorable effect on livestock production (Hashemi *et al.* 2008). Herbs, spices, essential oils, and oleoresins are the classification of several kinds of common phytobiotic compounds based on origin and processing (Windisch *et al.* 2008).

Essential oil is defined as natural, volatile and aromatic substances, oily liquids which can be extracted from several parts of the plants (Bakkali *et al.* 2008). In addition, essential oils are known as plants secondary metabolites which highly contain a lot of isoprenoid compounds (Brewer, 2011).

Studies have been reported about the antimicrobial activities of several essential oils (Burt, 2004), that make plant origin essential oils potentially to be induced in poultry nutrition. Essential oils can promote the intestinal functions by stimulating the bile secretion, digestive enzymes, and mucus (Platel and Srinivasan, 2004). Essential oils are potentially used in poultry nutrition mainly because of their antimicrobial and antioxidant activity. Those activities can modulate the gastrointestinal ecosystem, stimulate the digestion process and extend to animal metabolism (Lee *et al.* 2004). Furthermore, by modulating the gastrointestinal ecosystem or having antimicrobial activities, essential oil affects the digestibility of starch, protein (Hernández *et al.* 2004) and fat (Lee *et al.* 2004). The phytobiotics especially essential oils have been known to have a positive effect on the performance and feed intake of poultry by improving flavor and palatability of feed (Grashorn, 2010).

Several plant origin essential oils have been known to prevent the emergence of enteric diseases and pathogens in poultry (Micciche *et al.* 2019). Dietary inclusion of plant origin trans-cinnamaldehyde and eugenol are effectively reduced the pathogenic bacteria (*Salmonella enteritidis*) in 20-d-old broiler chickens (Kollanoor-Johny *et al.* 2012). Moreover, Mitsch *et al.* (2004) reported that dietary inclusion a mixture of several essential oils such as curcumin, carvacrol, piperin, thymol, and eugenol has a positive effect at reducing the colonization and proliferation of *Clostridium perfringens* in the chicken gastrointestinal tract. According to Windisch *et al.* (2008), essential oils have potential activity against *C. perfringens* and *E. coli*. Herbs origin essential oils can be used to decrease *E. coli* (Jang *et al.* 2007) and *Campylobacter* spp. (Kelly *et al.* 2017) that inhabits the digesta of broiler chickens. Comparing to the inclusion of antibiotic-containing ciprofloxacin, *Oreganum aetheroleum* essential oil can help the chicken against *E. coli* infections by enhancing the cell-mediated and humoral immune responses, thus becoming more effective for the treatment of *E. coli* infection in the broiler chicken (El-Ghany and Ismail, 2013). Oregano and thyme essential oil effectively counter a wide range of pathogenic bacteria such as *Salmonella* strains that inhabited in the gastrointestinal tract of the chicken (Koščová *et al.* 2006). Some essential oils such as thyme, oregano, rosemary, clove, and cinnamon are used to protect the intestinal wall from damage due to the effects of coccidial multiplication and hence can be used as growth promoters (Hashemi *et al.* 2008). In addition, a positive effect on the activity of trypsin and amylase enzyme has been shown by providing essential oils to chickens (Jamroz *et al.* 2005). One gram per kilogram of thyme essential oil supplementation gives a significant increment in body weight (BW) gain of broiler chickens. Different result is achieved when 10 g/kg of the thyme herb was included in the diet. This observation noted that thyme essential oil has a better result compared to the herb (Cross *et al.* 2007). Compared to the control group, the mixture of essential oils consist of oregano, anise, and clove shows significantly increment by approximately 16% for the BW gain and after 5 weeks of trial and the inclusion of 200 mg/kg from the mixture of the essential oil gave the best result (Ertas *et al.* 2005). Feed conversion significantly increased the chicken growth with essential oils blend supplementation in feed consisted of anise, citrus, sage, oregano, and bay leaf due to the high nutrient's availability by modulating in the intestinal ecosystem (Cabuk *et al.* 2006). According to Peng *et al.* (2016), the inclusion of 300 and 600 mg/kg oregano essential oil (*Origanum genus*) in broiler chicken feed increased the birds average daily gain (ADG) which is to be due to an increase in both villus height and crypt depth of the jejunum. Recent studies (Khattak *et al.* 2014; Pirgozliev *et al.* 2015; Peng *et al.* 2016) reported that several essential oils have good potential as an alternative to AGP for improving the poultry productivity. Essential oils are also possible to play a preventive and curative of necrotic enteritis diseases in poultry production (Jerzsele *et al.* 2012).

The decrease of the pathogenic bacteria affects positively to increase the nutrient availability for animal utilization due to decrease the nutrient competition and prevent several intestinal diseases (Yitbarek, 2015). The hydrophobicity of essential oils or their components become an important characteristic that makes essential oils able to penetrate the lipid-containing bacterial cell membrane and provide the antimicrobial activity (Smith-Palmer *et al.* 2004). In addition, the exposure of essential oil increases the membrane permeability, leading to cell lysis due to leakage of the cell contents (Carson *et al.* 2002). Essential oil constituents have high hydrophobicity properties because of their short carbon chain extension, allowing for tight interactions with lipid cell membranes. The interaction of volatile terpene groups with lipid-containing bacterial cell membrane provides inhibitory activity on cell function and its lipophilic properties which lead to the death of pathogenic bacteria. That inhibitory activity can affect and disrupt the fluidity of cell membrane and mitochondrial membranes (Calo *et al.* 2015). Moreover, crossing the cell membrane and bind to specific proteins also can be done by the oil components as another inhibitory activity (Pedro *et al.* 2013). The antimicrobial activity of essential oil is attributable to more than one specific mechanism because of plant-derived compounds mostly contain several chemical groups (Carson *et al.* 2002; Burt, 2004; Smith-Palmer *et al.* 2004). As an illustration, essential oils are generally contained up to more than 100 single constituents (Bilia *et al.* 2014; Calo *et al.* 2015). In general, the chemical contents of essential oil are terpene compounds (mono-, sesqui- and diterpenes), alcohols, acids, esters, epoxides, aldehydes, ketones, amines and sulfide which can be divided into terpene compounds and aroma compounds (Bakkali *et al.* 2008). Hence, using essential oils as an antimicrobial agent is hypothesized to reduce the potential for bacteria to develop resistance and spread it out (Smith-Palmer *et al.* 2004).

The limiting factor of essential oils as an alternative to antibiotic is due to most of the constituents have high volatility, thermolabile, photolabile, and less stable (Yitbarek, 2015). The characteristic of essential oil is easy to oxidize when directly exposed to heat, air, light, and humidity because of the high volatility of their constituents (Bilia *et al.* 2014).

In addition, essential oils have become very susceptible to oxidation by light or heat due to their main constituents are unsaturated carbon chains. The oxidation of essential oils produces terpenes that have been known to have high allergenic activity, and other plant metabolites especially oxidized sesquiterpenes with lacone rings and terpenoids (Vigan, 2010).

Therefore, the characteristics of essential oil such as high volatility, unstable substances, and poorly water-soluble limit their possible routes of administration. The consequences of the low solubility of essential oils in biological fluids inhibit their absorption and lead to the very low bioavailability (Pedro *et al.* 2013; Natrajan *et al.* 2015). Thus, a solution with a new approach is needed to overcome the limiting factor for the application of essential oils to improve their bioavailability.

Potential uses of nanoemulsion

In recent years, the research focus of drug formulations development has been conducted to create a drug delivery system that is able to delay and maintain drug release after administration (Maderuelo *et al.* 2011). That kind of formulation is known as a modified drug delivery system and widely investigated because it provides several advantages compared to conventional systems. Colloidal systems have played an important role in the field of pharmaceutical research among other controlled drug release systems. Colloidal particles can reach average sizes ranging in nanometric scales, also known as nanoparticles (Kamble *et al.* 2010).

The nanoparticle can be made to be a nanocarrier and commonly being used to protect the essential oil from oxidation or evaporation. Nanocarriers can help essential oils against the possibility of degradation even improve the stability, function, and has a positive effect to increase the shelf life of the products also controlling the release of the bioactive molecules (Liang *et al.* 2012). Nanocarriers also facilitate their activity by providing various diffusion properties that make them passing through the biological membranes due to the nanoscale dimension of particles. Many formulations that use this technology are working effectively in the form of nanoscale emulsions or nanoemulsion (Pedro *et al.* 2013).

Conventional emulsions containing very small particles with an average radius of about 10 to 100 nm or also called mini emulsions can be considered as nanoemulsion (Mason *et al.* 2006). Nanoemulsion is also known as an isotropic mixture, a combination of oil and surfactant which spontaneously forms fine emulsions of oil in water due to mild agitation, as well as when administration to other aqueous media, such as gastrointestinal fluid (Wang *et al.* 2009). When diluted, the nanoemulsion will produce small droplets between 20 and 200 nm in size. These nano-sized droplets can result in an increase in the dissolution rates and bioavailability of poorly water-soluble substances. Nanoemulsion has more stable formulation characteristics compared to conventional emulsions and is easier to improve on a large scale (Chakraborty *et al.* 2009). Nanoemulsions play as a colloidal delivery system for poorly water-soluble or lipophilic bioactive substances in the food industry, pharmaceutical, agrochemical, and cosmetics industry (McClements, 2012; Ghosh *et al.* 2013). The encapsulation of essential oils into nanoemulsion is classified as a novel technology and can offer a solution that allows to overcome the limiting factors of their usage. The encapsulation of essential oils into nanoemulsion can enhance the distribution and solubility of the encapsulated essential oils (Calo *et al.* 2015), improve the microbial stability (Jayasena and Jo, 2013), also protect essential oils against possible thermal or photodegradation which lead to increase the stability (Pedro *et al.* 2013). Nanoemulsion has the capability to decrease the volatility, improve the stability, alter the solubility, and maintain the therapeutic efficacy of the encapsulated essential oils (Bilia *et al.* 2014). There are two types of methods that can be distinguished in the nanoemulsion formulation. The first is a high-energy emulsification method, namely the input of high mechanical energy input, such as high shear stirring, high-pressure homogenizers or ultrasounds, to produce nanoemulsion. The second method is self-emulsification or low-energy method which uses chemical energy from the mixture as its forming mechanism by using the phase transitions during the emulsification process as a result of a change in the spontaneous curvature of the surfactant (Solè *et al.* 2010). Oil-in-water (O/W) nanoemulsion is formed when oil droplets are dispersed in the water phase, while water droplets that dispersed in the oil phase forms water-in-oil (W/O) nanoemulsion (McClements and Rao, 2011).

Table 1 Researches of nanoemulsions essential oils and their antimicrobial activity

Oil	Targeted	Reference
Eugenol (clove) oil	*Fusarium oxysporum* f. sp. *vasinfectum*	(Abd-Elsalam and Khokhlov, 2015)
Clove oil	*Bacillus subtilis*, *Staphyloccocus aureus*, *Proteus vulgaris*, *Pseudomonas aeruginosa* and *Klebseilla pneumonia*	(Anwer *et al*. 2014)
Cinnamon oil	*Bacillus cereus*	(Ghosh *et al*. 2013)
Oregano, thyme, lemongrass or mandarin oils	*Escherichia coli* and *Listeria innocua*	(Guerra-Rosas *et al.* 2017)
Cinnamon bark oil	*Salmonella enteritidis*, *Escherichia coli* O157:H7, and *Listeria monocytogenes*	(Hilbig *et al*. 2016)
Cleome viscosa oil	*Staphylococcus aureus*, *Streptococcus pyogenes*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*	(Krishnamoorthy *et al*. 2018)
Citral oil	*Staphylococcus aureus* ATCC 27690, *Escherichia coli* ATCC 23815, *Pseudomonas aeruginosa* ATCC 15442, *Enterococcus faecalis* ATCC 29212, *Salmonella typhimurium* ATCC 14028, and *Listeria monocytogenes* ATCC 19113	(Lu *et al.* 2018)
Thymus daenensis oil	*Escherichia coli*	(Moghimi *et al.* 2016)
Oregano oil	*S. aureus* ATCC 25923 *and E. coli* ATCC 25922	(Moraes-Lovison *et al.* 2017)
Lemongrass, clove, tea tree, thyme, geranium, marjoram, palmarosa, rosewood, sage or mint oil	*Escherichia coli*	(Salvia-Trujillo *et al.* 2015)
Eucalyptus oil	*Staphylococcus aureus*	(Sugumar *et al*. 2014)
Eucalyptus oil	*Listeria monocytogenes*	(Sugumar *et al*. 2015)
Anise oil	*Listeria monocytogenes* and *Escherichia coli* O157:H7	(Topuz *et al*. 2016)
D-limonene (citrus oil)	*Staphylococcus aureus* ATCC6538, *Bacillus subtilis* ATCC 6633, *Escherichia coli* ATCC 8739, and *S. cerevisiae* ATCC 9763	(Zhang *et al.* 2014)
Blended cloves/cinnamon oil	*Escherichia coli*, *Bacillus subtilis*, *Salmonella typhimurium*, and *Staphylococcus aureus*	(Zhang *et al*. 2017)

Essential oils nanoemulsion has been studied in the food industry. Studies with sunflower oil nanoemulsion have been carried out by showing antibacterial activity against foodborne bacteria such as *Listeria monocytogenes*, *Salmonella typhi* and *Staphylococcus aureus*, as well as has high fungicidal and a sporicidal activity against *Rhizopus nigricans*, *Aspergillus niger*, *Penicillium* spp., *Bacillus cereus*, and *Bacillus circulans*. In addition, antimicrobial activity in food products such as raw chicken, apple juice, milk and mixed vegetable are significantly reduce the population of native bacteria and fungi that could be obtained from sunflower oil nanoemulsion using *in situ* evaluations (Joe *et al.* 2012).

Another study reported about self-nanoemulsifying drug delivery system (SNEDDS) of zedoary turmeric oil which is an essential oil extracted from the dry rhizome of *Curcuma zedoaria* for oral delivery. The bioactive components of zedoary turmeric oil showed good stability in the optimized formulation when stored at room temperature for at least one year. In addition, oral administration of zedoary turmeric oil SNEDDS in rats showed an increment of dissolution rate and bioavailability when compared to the unformulated zedoary turmeric oil (Zhao *et al*. 2010). Sood *et al*. (2014) reported that intranasal delivery for brain targeting using curcumin nanoemulsion does not show any toxicity and safe.

Nanoemulsions is significantly producing higher dissolution rate compared to drug solution during *in vitro* diffusion studies. In addition, higher flux and permeation across sheep nasal mucosa can be achieved using mucoadhesive nanoemulsion. Ginger essential oil (GEO) can be used to extend the durability of chicken breast fillet (Noori *et al.* 2018). Further studies are needed to explore potential effects for enhanced antimicrobial efficacy and broader applications (Upadhyay *et al.* 2019). Other associations of nanoemulsions essential oils and their antimicrobial activity are shown in Table 1.

Any antimicrobial treatment in the poultry industry should be the most practical and economical method to adopt by the farmers (Venkitanarayanan *et al.* 2013). Nanoemulsions can be an alternative application in the delivery of poorly water-soluble substances into the beverage of livestock animals (Vandamme and Anton, 2010). Because of unhealthy birds tend to decrease the feed intake but will often continue to drink, therefore drinking water is the preferred mode of antimicrobial inclusion (Landoni and Albarellos, 2015). Medication through drinking water has several advantages in relation to therapeutic and metaphylactic treatment, compared to other methods, such as low cost, easy to apply, direct and fast therapeutic care for all birds in the flock, and in addition easy to change the medication and/or dose (Vermeulen *et al*. 2002).

CONCLUSION

It can be concluded that essential oil has potential as a novel alternative to the antibiotic in poultry production. Essential oils have the potential due to their antimicrobial activity with the aim of reducing pathogenic pressure, have an important role in increasing the activity of digestive enzymes and absorption capacity and maintain gut health. Essential oils have beneficial effects in modulating the gut ecosystem and normal gut function, improve overall poultry performances. However, essential oils which mostly contain lipophilic and aromatic active substances have several limiting factors for applications such as low water solubility, low stability and presenting limited delivery routes. Nanoemulsion is one of the potential technologies to facilitate the application of essential oils as a candidate of the alternative to the antibiotic in poultry production. Further studies need to be done to verify the potency of essential oil nanoemulsion as a candidate of the alternative to the antibiotic in poultry production.

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