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Review: Sanguinarine as a growth promoter.

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ABSTRACT

The increased concern about the potential for antibiotic resistant strains of bacteria has compelled the researchers to utility of other non-therapeutic alternatives like enzymes, probiotics, prebiotics, herbs, essential oils, immunostimulants and organic acids as feed additives in animal production. Managerial and biosecurity measures, they can prove powerful in maintaining the health of the GI-tract of poultry, thus improving their zootechnical performances. Current review is introducing Sanguinarine as a plant extracts (phytogenics), its suggested efficiencies are reducing amino acid degradation, increasing feed intake, and promote growth in different species of animal. Many mods of actions have been reported to improve the protein retention by reducing intestinal decarboxylation of aromatic amino acids through the inhibition of L-amino acid decarboxylase. Furthermore, enhancement of feed intake by modulating effects on the tryptophanserotonine pathway.
Keywords: Sanguinarine, growth promoter, phytogenics

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INTRODUCTION

World population is expected to increase to more than 9 billion by the year of 2050 and agricultural sectors, specifically global poultry industry, have rapidly responded to meet the growing meat demand, which has already increased to more than 4-fold during last 4 decades (Godfray et al., 2010). In order to sustain the ever growing meat demand, it is true that the poultry production efficiency should be kept as high as possible. This statement however is based on the premises that the genetic potentials of chickens will be achieved and simultaneously any environmental challenges such as climate change, feed security, intensive production, or ban on antibiotics in poultry industry are effectively controlled (Lillehoj and Lee, 2012).

It is well understood that low-level inclusion of in-feed antibiotics as growth promoters has played a significant role in the growth and development of the poultry industry for more than 50 years. Their efficiency in stimulating growth, improving feed conversion and reducing mortality/morbidity from clinical disease is well recognized (Thomke and Elwinger, 1998). However, the consumers concerns have been raised on the drug residues in meat products and on the occurrence of drug-resistant bacteria due to frequent use of antibiotics in diets (Yang et al., 2009). As a result, the commonly practiced antibiotic inclusion into poultry diets has been banned in Europe since 2006, and this ban is further expected to affect the rest of the world. Consequently, alternative strategies to antibiotics have been mainstream of topics for researches in animal science to sustain the animal production. The most widely accepted alternatives (Grashorn, 2010) include probiotics, prebiotics, exogenous enzymes, and phytogenics including plant extracts in poultry.

High levels of production and efficient feed conversion are the need of the modern livestock industry which to a certain extent could be achieved by the use of specific feed additives. Antibiotic feed additives as growth promoters have long been supplemented to poultry feed to stabilize the intestinal microbial flora, improve the general performances, and prevent some specific intestinal pathology (Truscott and Al-Sheikhly, 1977; Miles et al., 1984; Waldroup et al., 1995). However, because of the growing concern over the transmission and proliferation of resistant bacteria via the food chain, the European Union (EU) in 2006 banned antibiotic growth promoters to be used as additives in animal nutrition. The antibiotic growth promoters have been under scrutiny for many years and have been removed from the market in many countries (Ratcliff et al., 2000). Antibiotic growth promoters and antibiotic resistance are closely related. The increased concern about the potential for antibiotic resistant strains of bacteria has compelled the researchers to explore the utility of other non-therapeutic alternatives like enzymes, probiotics, prebiotics, herbs, essential oils, immunostimulants and organic acids as feed additives in animal production. The focus of alternative strategies has been to prevent proliferation of pathogenic bacteria and modulation of indigenous bacteria so that the health, immune status and performance are improved (Ravindran, 2006). This publication presents a review on the growth promoting efficiency as well as mechanism of action of dietary organic acids in poultry.

Organic acids are considered to be any organic carboxylic acid including fatty acids and amino acids, of the general structure R-COOH. Not all of these acids have effects on gut microflora. In fact, the organic acids associated with specific antimicrobial activity are short chain acids (C1-C7) and are either simple, monocarboxylic acids such as formic, acetic, propionic and butyric acids, or carboxylic acids bearing an hydroxyl group (usually on the alpha carbon) such as lactic, malic, tartaric and citric acids. Salts of some of these acids have, also, been shown to have performance benefits. Other acids, such as sorbic and fumaric acids which are short chain carboxylic acids containing double bonds, have been observed to possess antifungal activity (Dibner and Buttin, 2002). Generally, two types of acidifiers are used, feed acidifiers and gut acidifiers. Feed acidifiers are pure organic acids which can be added to the feed by direct spraying. However, pure organic acids corrode the G.I. tract of poultry, and are, also, difficult to handle. Gut acidifiers are organic acid salts, such as ammonium di-propionate, potassium di-formate, sodium formate, calcium propionate, calcium lactate, ammonium formate etc., and have little or no corrosive effect on the G.I. tract of poultry (Paul, 2007). Organic acids are not antibiotics but, if used correctly along with nutritional, managerial and biosecurity measures, they can be a powerful tool in maintaining the health of the GI-tract of poultry, thus improving their zootechnical performances (Abdel-Fattah et al., 2008). If applied correctly, organic acids work in poultry, not only as a growth promoter but also as a meaningful tool of controlling all enteric bacteria, both pathogenic and non-pathogenic (Naidu, 2000; Wolfenden et al., 2007). Table 1 shows list and properties of commonly used dietary organic acids in poultry.

Patten and Waldroup (1988) evaluated fumaric acid and reported that addition of 0.5 or 1.0% fumaric acid significantly improved body weights of broilers but did not influence feed utilization. Skinner et al. (1991) reported that addition of 0.125% fumaric acid significantly improved 49-day body weight of females and average weight gain of both sexes with no effect on feed utilization. Also, higher body weight gain, feed intake and better feed efficiency due to organic acid supplementation has been reported (Denli et al., 2003). Christian Luckstadt et al. (2004) observed that organic acid blend (3 kg inclusion rate per ton of feed) increased the growth of broiler chicken under controlled conditions without the use of anti-biotic growth promoters. The body weight of broilers at 6th wk. of age was significantly higher in the groups fed diet containing organic acid at 1 kg/ton or 1.5 kg/ton with a better feed conversion ratio noticed in the group containing organic acid at 1 kg/ton (Thirumeignanam et al., 2006). Paul et al. (2007) reported that ammonium formate or calcium propionate at the level of 3 g/kg feed increased the live weight and live weight gain and feed conversion ratio at day 21 in broiler chicken. Formic acid at the rate of 5,000 ppm and 10,000 ppm in the diet of chicken significantly improved feed conversion ratio and both levels were beneficial for improving the growth traits (Garcia et al., 2007). Vieira et al. (2008a) reported improved body weight and feed conversion ratio with diets supplemented with a blend of organic acids (40% lactic, 7% acetic, 5% phosphoric and 1% butyric). Owens et al. (2008) reported 12 % increase in total live weight gain and about 9 % improvement in gain feed ratio with diets supplemented with dietary organic acids. Improvement in live body weight, body weight gain and feed conversion ratio by organic acid supplementation (containing acetic acid, citric acid and lactic acid, each at 1.5 and 3.0 % in the diet) was also observed by Abdel-Fattah et al. (2008).

The undissociated organic acid pass through the cell membrane of the bacteria and dissociate to form H+ ions which lower the pH of bacterial cell, causing the organism to use its energy, trying to restore the normal balance. Whereas RCOO- anions produced from the acid can disrupt DNA, hampering protein synthesis and putting the organism in stress. As a result the organism cannot multiply rapidly and decrease in number (Nursey, 1997). The antibacterial effect of organic acids has been reported by many researchers. Sofos et al. (1985) reported that the broilers on sorbic acid-containing feed had lower coliform counts in the duodenum, lower yeast and mold counts in the caeca, and higher Bacteroides counts in the caeca. Humphrey and Lanning (1988) observed that 0.5% formic acid resulted in significant reduction in the isolation rate of Salmonella from laying hens, and also, a reduction in the incidence of infection in newly hatched chicks. Use of organic acid mixture containing formic and propionic acid decreased the Salmonella and lactic acid producing bacteria counts in hen's crop (Thompson and Hinton, 1997). Alp et al. (1999) reported that inclusion of antibiotic and an organic acid mixture containing lactic, fumaric, propionic, citric and formic acid separately or in combination reduced the Enterobacteriacae count in the ileum of broilers. Ramarao et al. (2004) studied the efficacy of gut acidifier in broiler diets at the rate of 300 g/100 kg feed vis-à-vis use of antibacterial compounds. They observed that the total bacterial, coliform, and Escherichia coli counts in crop and caecal contents were low in broilers fed gut acidifier and opined that gut acidifier can safely replace antibacterial compounds in broiler chicken diets with beneficial effects on the intestinal bacterial colonization and resistance to E. coli challenge. Moharrery and Mahzonieh (2005) described that malic acid have the potential for reduction of E. coli population in the intestines of broiler chicken. Thirumeignanam et al. (2006) reported a decrease in the total bacterial load with concomitant increase in lactobacilli load as a result of dietary acidification. Organic acids mixture at the level of 0.2% in the diet of broilers significantly decreased total bacterial and gram negative bacterial counts compared to the basal diet (Gunal et al., 2006). Fumaric and sorbic acid lowered the numbers of lactic acid bacteria and Coliforms in the ileum and caeca (Pirgozliev et al., 2008; Adil et al., 2011). Due to antimicrobial effect, organic acids result in inhibition of intestinal bacteria leading to the reduced bacterial competition with the host for available nutrients and diminution in the level of toxic bacterial metabolites as a result of lessened bacterial fermentation resulting in the improvement of protein and energy digestibility; thereby ameliorate the performance of bird.

Organic acids have direct stimulatory effect on the gastro-intestinal cell proliferation as has been reported by various workers with short chain fatty acids. The short chain fatty acids are believed to increase plasma glucagon-like peptide 2 (GLP-2) and ileal pro-glucagon mRNA, glucose transporter (GLUT2) expression and protein expression, which are potential signals mediating gut epithelial cell proliferation (Tappenden and McBurney, 1998). Le-Blay et al (2000) and Fukunaga et al (2003) also reported that short chain fatty acids can accelerate gut epithelial cell proliferation, thereby increase intestinal tissue weight and changing mucosal morphology. The beneficial effect of organic acids on the gastro-intestinal tract was observed by Denli et al (2003) who reported that organic acids resulted in remarkable increase in the intestinal weight and length of broiler chicken. Also, Hernandez et al. (2006) reported that formic acid increased the crypt depth of small intestines. Senkoylu et al. (2007) reported increased villus height with combination of formic and propionic acids in broilers but found no effect on the thickness of lamina muscularis mucosae. Paul et al. (2007), also, reported that the propionate, formate and lactate supplementation improved duodenal villus height. Similar results were observed by Garcia et al. (2007) who found improved villus height with formic acid and also greater crypt depth but villus surface area was not influenced. Abdel-Fattah et al. (2008) reported that the addition of any level and source of organic acids increased feed digestion and absorption as a result of increased small intestine density which is an indication of the intestinal villi dimension. The increased villus height in the small intestines has been related to a higher absorptive intestinal surface (Loddi et al., 2004) which facilitates the nutrient absorption and hence, has a direct impact on growth performance.

Dietary supplementation of organic acids has been found to reduce the pH of crop, gizzard and duodenal contents (Thirumeignanam et al., 2006). Abdel-Fattah et al. (2008) reported that the pH values in different gastro-intestinal tract segments were decreased, although insignificant, with supplementation of organic acids irrespective of type and dose used. As per Bolton and Dewar (1964) the effects of organic acids down the digestive tract gets diminished because of reduction in the concentration of acids as a result of absorption and metabolism. The lowered pH is conducive for the growth of favourable bacteria while it simultaneously hampers the growth of pathogenic bacteria which grow at relatively higher pH. This reduces bacterial competition with the host for available nutrients, thereby increasing the nutrient absorption. The acid anion has been shown to complex with calcium, phosphorus, magnesium and zinc, which improves the digestibility of these minerals (Li et al., 1988; Edwards et al., 1999). Organic acids serve as substrates in the intermediary metabolism (Kirchgessner et al., 1982) and lower chyme pH, consequently, enhancing the protein digestion (Gauthier, 2002). Reduction in gastric pH occurs following organic acid feeding which may increase the pepsin activity (Kirchgessner and Roth, 1982) and the peptides arising from pepsin proteolysis trigger the release of hormones, including gastrin and cholecystokinin, which regulate the digestion and absorption of protein (Hersey, 1987).

Active compounds obtained from plants have been used for a variety of human needs for centuries; however, many commercially available additives based on natural extracts lack a definite mode of action in animal feeds (Dickens & Ingram, 2001).

Natural compounds extracted from plants, such as quaternary benzo[c]phenanthridine alkaloids (QBA) sanguinarine and chelerythrine, are known to have antimicrobial (Newton et al., 2002), anti-inflammatory (Tanaka et al., 1993), and immunomodulatory (Chaturvedi et al., 1997) effects. Sanguinarine has been incorporated into swine, bovine, and poultry diets to reduce amino acid degradation, increase feed intake, and promote growth (Tschirner, 2004). Improvements in protein retention by reducing intestinal decarboxylation of aromatic amino acids through the inhibition of L-amino acid decarboxylase (Drsata et al., 1996), and enhancement of feed intake by modulating effects on the tryptophanserotonine pathway have also been suggested as part of their a mode of action (Mellor, 2001).

Sanguinarine (SGV) as a phytogenicis a quaternary benzo [c]phenanthridine alkaloid (Dvorak and Simanek, 2007) and is an active component in the powdered stems, leaves, capsules and seeds of Macleaya cordata. With the well-established biological properties (Franz et al., 2005), it has been added into diets for bovine, swine and poultry intended to promote growth and to increase feed intake. It is known that sanguinarine possess various biological activities such as analgesic, anti-inflammatory, anti-microbial and immunomodulatory activities (Niu et al., 2012). In addition, it is reported that SGV stimulates the secretion of enzymes in the intestine (Franz et al., 2005) which is often regarded as one of characteristic properties of herbs and spices (Lee et al., 2003). Furthermore, SGV is not metabolized into potentially harmful metabolite (e.g., benz[c]acridine) and is excreted without being absorbed through the small intestine (Zdarilova et al., 2008). It has been reported that dietary SGV affected growth performance (Vieira et al., 2008b,c), cholesterol concentration (Yakhkeshi et al., 2011), fatty acid profiles of breast meats, and cecal microflora (Juskiewicz et al., 2011) in broiler chickens and the inclusion levels in diets ranged from 12.5 to 50 ppm. It is of note that dietary sanguinarine stimulated growth at early ages of chickens (Vieira et al., 2008a, b). At this stage, the effect of SGV on meat quality in broiler chickens has not been studied albeit that there is indication on its antioxidant property (Vrba et al., 2004). Sangrovit contains a mixture of the intact aerial parts and the fraction of quaternary benzo[c]phenanthridine alkaloids from Macleaya cordata (Willd). The recommended dietary level of this preparation for broilers and growing turkeys has been reported as 20 to 50 ppm. It has even been observed that male Wistar rats fed Sangrovit at 7,000 mg/kg of feed for 90 d showed no changes in hematology markers, oxidative stress parameters, or the morphological structure of selected organs (Zdarilova et al., 2008). The main activity of sanguinarine is exhibited in the lower part of the gastrointestinal tract because of its modulatory effect on microbial activity (Jankowski et al., 2009). It should be pointed out that the sensory quality of meat can be influenced by several factors, including direct transfer of aroma-active components from feed to meat, changes in the composition of fatty acids, and the production of aroma-active microbial metabolites in the gastrointestinal tract, which are absorbed and deposited in meat (Hansen et al., 2002).

In view of the concern for increased drug resistance among pathogens and drug carry over effects following use of subtherapeutic antibiotic growth promoters as feed additives, the non-therapeutic alternatives like enzymes, probiotics, prebiotics, herbs, essential oils, immunostimulants and organic acids are the potential candidates as feed additives in animal production. Organic acids have shown versatility under experimental conditions. They exert growth promoting effect mainly because of their antibacterial activity, trophic effects, ph reducing property besides improving protein and mineral digestibility.

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