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Review on Natural Growth Promoters Available for Improving Gut Health of Poultry: An Alternative to Antibiotic Growth Promoters

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ABSTRACT

'Gut health' is a term currently gaining much more attentions in veterinary literature especially in poultry. It covers multiple positive aspects of the gastrointestinal (GI) tract, such as the effective digestion by absorption of food, absence of GI illness, normal and stable intestinal microbiota, effective immune status and a state of well-being. Any disturbance or imbalance in above said aspects may influence the gut health. Thus it is necessary to maintain the balance of all possible associated factors related to gut health. Although till date this is being achieved in poultry farming by Antibiotic Growth Promoters (AGPs). However, the growing concern over the transmission and the proliferation of resistant bacteria in human via the food chain has led to a ban of Antibiotic Growth Promoters (AGP) in livestock feed within the European Union since, 2006. As a result, new commercial additives derived from nature have been examined as part of alternative feed strategies for the future. Such products have several advantages over commonly used commercial antibiotics since they are residue free and recognized as safe items in the food industry. Certain natural alternatives recognized by scientific community as Natural Growth Promoters (NGPs) to preserve and maintain the balance of gut microbiota in poultry are summarized in present communication. The article is also enriched with possible mechanisms of action of NGPs with relevant examples by citing research results obtained by various authors in past and current years.

Key words: Poultry, antibiotic, antimicrobial, growth promoters, antioxidant

INTRODUCTION

The term ‘gut health’ is currently gaining much more attentions in veterinary literature especially in poultry and has been applied to coordinate the working efficiency of gut (Cummings *et al*., 2004; Laudadio *et al*., 2012). Although, the term is restricted to gastro-intestinal (GI) tract only and does not involve other organs (Bischoff, 2011). The gut is the primary site for multitude of processes such as, digestion, fermentation, nutrient absorption, nutrient metabolism, intestinal integrity, immune recognition, immune regulation and development of immune tolerance (Sommer and Backhed, 2013). Gut is mainly composed of physical, chemical, immunological and microbiological components and acts as a selective barrier between the tissues of the bird and its luminal environment (Yegani and Korver, 2008). The gut is the most extensive exposed surface and is constantly exposed to wide variety of potentially beneficial non-infectious as well as harmful infectious agents (Lievin-Le Moal and Servin, 2006). It has been reported that exposure of gut to such harmful infectious agents or pathogens cause an imbalance, which can lead to severe productivity loss, sudden dietary changes, intestinal disease (worm infestation, coccidiosis) and immune suppression (McDevitt *et al*., 2006). It is now well established that development of antibiotic resistance result from the use of Antibiotic Growth Promoters (AGPs) in animal feed, may be compromised the efficacy of similar antibiotics in therapy for human diseases. Hence, the European Union (EU) introduced a ban on AGPs in 2006, which is now followed in most of the other nations. Before the ban, gut of poultry was highly dependent on Antibiotic Growth Promoters (AGPs) to control intestinal pathogens (Wallace *et al*., 2010). In view of rising concerns on the extensive loss in poultry due to GI complaints and implementation of strict laws to use of harmful synthetic drug or antibiotics, creates demand of an alternative disease control resources to enhance gut health and to reduce the use of AGPs (Mirzaei-Aghsaghali, 2012). Interest and some useful research on various Natural Growth Promoters (NGPs) such as phytobiotics (essential oils, powders, extracts and phytochemicals), probiotics, prebiotics, synbiotics, organic acid, clay minerals, egg yolk antibodies, exogenous enzymes, recombinant enzymes, nucleotides, polyunsaturated fatty acids and miscellaneous compounds has increased the impetus for revisiting to look for new, useful additives that can enhance gut health and productivity of birds. Utilization of such Natural Growth Promoters (NGPs), as an alternative to AGPs are summarised and explored in the present work by reviewing all possible updated literature till date.

NGPs in poultry gut health: Many alternative substances obtained from nature and belonging to the groups of prebiotics, probiotics, organic acids, enzymes, silicates, herbs and spices etc., have been vigorously tested and evaluated for their potential to replace AGPs in poultry diets (Panda *et al*., 2006; Khan *et al*., 2012a, b). Such, alternative substances were referred as Natural Growth Promoters (NGPs). There are a number of such investigated NGPs that are mainly utilised for providing beneficial role for improving health of poultry against various infectious diseases rather than regular nutrition. The involvement of these NGPs in improving of intestinal morphology and nutrient absorption may also encourage the scientists to include these compounds in the diet to improve gut health, promote the growth and overall performance of birds.

Characteristics of ideal NGPs for gut health: Ideally, the NGPs alternatives to AGP should have the same beneficial actions as AGP. Some of key features identified from the most well-known hypothesized mechanism of AGPs to be fulfilled by proposed NGPs (Huyghebaert *et al*., 2011) that favours performance of gut are: (1) Antimicrobial action, (2) Reduces the incidence and severity of subclinical infections, (3) Reduces the microbial use of nutrients, (3) Improve absorption of nutrients, (4) Reduces the amount of growth-depressing metabolites, (5) Control microbiota shifts, (6) Inhibit the production and excretion of cytokines by immune cells (macrophages) and (7) Shifting the microbiota composition towards one that is less capable of evoking an inflammatory response (Humphrey and Klasing, 2003). Based on the suggested mechanism of action of none of the non-antibiotic NGPs is likely to compensate the loss of gut health. So, it must be emphasised that some strategies will only help to compensate partially by NGPs and will work through indirect mechanisms.

NGPs and their mode of action

Phytobiotics or botanical supplements: Many plants have been reported to possess beneficial multifunctional properties and have been used as feed additives for farm animals in ancient cultures for the same length of time as for human (Huyghebaert *et al*., 2011). There are many categories of plants products on the basis of physical characters and appearance viz., essential oil, crude or processed plant parts, processed extracts, mixtures of powders or extracts and phytochemicals used for the prevention and treatment of various diseases in farm animals (Sethiya *et al*., 2013; Dhama *et al*., 2015). Botanical or herbal extracts, flavours and essential oils (EO) are now fall within the scope of European Commission Regulation 1831/2003. However, unprocessed herbs are still regarded as feed materials and do not need any authorisation (Huyghebaert *et al*., 2011).

Essential oils: Essential oils are also known as volatile or ethereal oil, obtained from medicinal and aromatic plant materials, which have the characteristic odor or flavor of source plant and are mainly associated for essences and fragrances of plants (Stein and Kil, 2006; Tomer *et al*., 2010). The major actions exhibited by essential oils are: to increase the release of digestive enzymes and reduce the amount of nutrients available for the growth of bacteria in the lumen of gut (Pasteiner, 2006). The antimicrobial properties of EO have not been fully established but the majority of them shown their effect by changing in lipid solubility at the surface by hydrophobic constituents, which may rupture or disintegrate the outer membrane of bacteria (Dorman and Deans, 2000). A summary of promising EO proven to as a possible sources of NGPs have been shown in Table 1.

Botanicals powder and extracts: Plant-derived products are natural, less toxic, residue free and have been scientifically proven as ideal feed additives in food animal production due to presence of varying degree of growth promoting nutraceuticals components (Wang *et al*., 1998). The various research conducted to understand the proposed mechanisms by which the botanicals powder and extract mainly exert their beneficial effects are as follows: (1) Disrupt cell membrane of microbes, (2) Interfere with virulence properties of the microbes by increasing the hydrophobicity, which may influence the surface characteristics of microbial cells, (3) Stimulates and proliferate the growth of beneficial bacteria (e.g., lactobacilli and bifidobacteria) in the gut, (4) Act as an immunostimulants, (5) Protects intestine from microbial attack, (6) Stimulate the proliferation and growth of absorptive cells (villus and crypt) in the gastrointestinal tract and (7) Enhances the production and/or activity of the digestive enzymes (Jamroz *et al*., 2003; Vidanarachchi *et al*., 2006). Table 2 shows some examples of botanicals powder and extracts with their growth promoting effects on the gut.

Phytochemicals: Phytochemicals are purified single chemical compounds (primary and secondary metabolites) present in cell sap of the naturally occurring plants and may possess some biological significance (Sethiya *et al*., 2009). The primary mode of action of phytochemicals is to have a significant action on growth inhibition of harmful intestinal microflora in the GI tract. They likely to promote growth by stimulating function of digestive enzymes and organ, e.g., pancreas and small intestine. Changing permeability for cations such as H^+ and K^+ ions of microbial cell membranes of microorganisms, exhibit growth promotion by oxidation-resistant activity and improvement of the immune system are major proposed mechanisms reported by various researchers by which the phytochemicals exert their antimicrobial activity. A summary of recent update on the effect of some examples of phytochemicals on gut health, in chickens was shown in Table 3.

Table 1: Essential oils and their role on poultry gut health

Essential oils and their botanical sources	Major chemical constituents	Actions	References
Angelica (*Angelica archangelica*)	α-Pinene, δ-3-carene, α-phellandrene, myrcene, limonene, β-phellandrene and ρ-cymene	Effective against Necrotic enteritis	Brenes and Roura (2010)
Artemisia (*Artemisia absinthium*)	β-thujone, 1-8 cineol, ρ-cymene and sabinene	Antimicrobial properties against *C. perfringens* type A	Engberg *et al*. (2012)
Basil (*Ocimum basilicum*)	Citronellol, linalool, myrcene, pinene, ocimene, terpineol, linalyl acetate, fenchyl acetate, trans-ocimene, 1, 8-cineole, camphor, octanane, methyl eugenol, methyl chavicol, eugenol and β-caryophyllene	Active against *E. coli* including extended spectrum on β-lactamase positive bacteria	Sienkiewicz *et al*. (2013)
Bergamot (*Citrus bergamia*)	β-Pinene, limonene, β-phellandrene, -terpinene, linalool and lynalil acetate	Have potential bactericidal properties against food-poisoning bacteria	Deans and Ritchie (1987)
Black pepper (*Piper nigrum*)	α-Pinene, β-pinene, sabinene, δ-3-careen, limonene, β-cryophyllene and piperine	Stimulate the digestive enzymes of pancreas, thus to enhance the digestive capacity	Srinivasan (2007) and Brenes and Roura (2010)
Caraway (*Carum carvi*)	Carvone, limonene, myrcene, β-caryophyllene, thujone, anethole and pinene	Have antiulcerogenic, antiflatulent, antibacterial antifungal and laxative properties	El-Soud *et al*. (2014)
Cinnamon (*Cinnamomum zeylanicum*)	Cinnamaldehyde, eugenol and cinnamyl acetate	Phenylpropanes, such as cinnamaldehyde bind with proteins through their carbonyl group and preventing the action of important cell enzymes such as amino decarboxylases. It has been shown to inhibit the growth of *C. perfringens* and *B. fragilis*	Lee and Ahn (1998)
Clove (*Syzygium aromaticum*)	Eugenol and eugenyl acetate	It inactivates *C. perfringens* and other bacteria	Briozzo *et al*. (1988)
Coriander (*Coriandrum sativum*)	ρ-Cymene and linalool	Significantly effects on performance and blood biochemical parameters. It has also appetizing and stimulatory effects in the digestion process	Jang (2011)
Dill (*Anethum graveolens*)	Limonene, dihydrocarvone, carvone and dillapiole	Antimicrobial	Delaquis *et al*. (2002)
Eucalyptus (*Eucalyptus globulus*)	Citronellal and citronellol	Improved the production performance and stimulated the immunity in laying birds	Abd-El-Motaal *et al*. (2008)
Garlic (*Allium sativum*)	Allicin, 1-propene, 3, 3'-thibis-sulfide, methyl-trans-propenyl-disulphide, di-2-propenyl tri-sulphide, methyl 2-propenyl, di-2-propenyl and diallyl tetra sulphide	Improve growth performance and beneficial gut microbial population	Dieumou *et al*. (2009)
Geranium (*Pelargonium graveolens*)	Isomenthone, citronellol, geraniol and cytronellyl formate	Antioxidant and has potential immune modulating effects on natural killer cells. It further helpful for detoxification and indigestion	Saraswathi *et al*. (2011)
Ginger (*Zingiber officinale*)	Camphene, neral, geranial, bornyl acetate, β-bisabolene, Ar-curcumene and β-eudesmol	Improve growth performance and beneficial gut microbial population	Dieumou *et al*. (2009)

Table 1: Continue

Essential oils and their botanical sources	Major chemical constituents	Actions	References
Laurel (*Laurus nobilis*)	1, 8-cineole, terpenes, terpinyl acetate, sesquiterpene, methyl-eugenol, α- and β-pinene, phellandrene, linalool, geraniol and terpineol	Antimicrobial, antiviral and beneficial to promote the gut health of chickens	Baratta *et al*. (1998)
Lemon (*Citrus limon*)	α-Pinene, camphene, β -pinene, sabinene, myrcene, α-terpinene, linalool, β-bisabolene, limo-nene, trans-α-bergamotene, nerol and neral	Effects on coccidia oocyte output and the number of *Clostridium perfringens* in broiler	Lee *et al*. (2004)
Litsea (*Litsea cubeba*)	Citral, α-cis-ocimene, 3, 7-dimethyl-1, 6-octadien-3-ol and n-transnerolidol.	Help with indigestion and flatulence. It also acts as antimicrobial and antifungal	Wang *et al*. (1999)
Nutmeg (*Myristica fragrans*)	α-Pinene, β-pinene, sabinene and myristicin	Antioxidant and antimicrobial	Dorman *et al*. (1995)
Orange (*Citrus sinensis*)	Limonene and linalool	Antimicrobial	Caccioni *et al*. (1998)
Oregano (*Oreganum compactum*)	Carvacrol, thymol and -terpinene	Antimicrobial, antifungal, insect-cidal and antioxidant	Remmal *et al*. (2011)
Peppermint (*Mentha piperita*)	Menthol, menthone and 1-8 cineol	Destroy *Eimeria oocyst* (Anticoccidiosis)	Remmal *et al*. (2011)
Rosemary (*Rosmarinus officinalis*)	1-8 cineol, α-pinene, camphor, carnosal, carnosic acid, caffeic acid, bornyl acetate and rosmarinic acid	Powerful antioxidant and improve gut health	El-Latif *et al*. (2013)
Sage (*Salvia officinalis*)	1, 8-Cineole, α-thujone and β-thujone	Increase thickness of the mucus layer in the duodenum and number of goblet cells containing acidic and neutral mucins was significantly decreased in the duodenum and jejunum and increased in the ileum	Capkovicova *et al*. (2014)
Savory (*Satureja khuzistanica*)	Carvacrol, p-cymene, myrcene, -terpinene and terpinene-4-ol.	Effective against both gram-positive and gram-negative bacteria	Farsam *et al*. (2003)
Tea tree (*Melaleuca alternifolia*)	Terpinen-4-ol and -terpinen	Antimicrobial and active against *Staphylococcus aureus*	Cox *et al*. (2000)
Thyme (*Thymus vulgaris*)	Thymol, carvacrol and ρ-cimène	Monoterpene phenols, such as thymol and carvacrol, interact with the cell membrane by hydrogen bonding, rendering the membranes and mitochondria more permeable and disintegrating the outer cell membrane. They can inhibit the growth of *E. coli* O157:H7, *S. aureus*, *S. enterica*, *P. fluorescens* and *B. thermosphacta*	Di Pasqua *et al*. (2010)
Turmeric (*Curcuma xanthorrhiza*)	α-Phellandrene, δ-3-carene, eucalyptol, β-caryophllene, β-farnesene, Ar-curcumeme, β-bisabolene, sesquiphellandrene, Ar-tumerone and curlone	Caused a decrease in coliform counts in ileum and modify intestinal traits. It also inhibits the growth of *C. septicum*, *C. novyi* and *C. sporogenes*	Singh *et al*. (2011)

Table 2: Medicinal plants powders/ extract/combinations and their role on poultry gut health

Medicinal plants and their botanical sources	Major chemical constituents	Dose (feed)	Actions	References
Intact plants/parts/powders				
Asthma plant (*Euphorbia hirta*)	Afzelin, quercetin, myricetin, rutin, euphorbin, β-amyrin, β-sitosterol, choline, camphol and quercitol	7.5 g kg^{-1}	Increased the villus height, crypt depth, ratio of villi to crypt and overall enhanced maintenance and function of the small intestine	Kumar *et al*. (2010), Hashemi *et al*. (2014)
Button mushroom (*Agaricus bisporus*)	Protein, carbohydrate, fat, fiber, linoleic acid and palmitic acid	10-20 g kg^{-1}	Exerted changes in intestinal microbial communities, intestinal integrity and antioxidant protective activity	Nasiri *et al*. (2013), Giannenas *et al*. (2011)
Corn (*Zea mays*)	β-ionone	38%	Effective against Clostridium and *Eimeria* species	Annett *et al*. (2002)
Cumin (*Nigella sativa*)	Cuminaldehyde, cymene and terpenoids	25-200 mg kg^{-1}	Enhanced immune responsiveness in broiler chickens against NDV vaccine	Al-Mufarrej (2014)
Edible mushroom (*Pleuratus florida*)	β-glucan	50-100 g t^{-1}	Immunomodulator on the innate immune responses in broiler	Ganguly (2013)
Gel (*Aloe vera*)	Acemannan-a mannose polymer	2%	Improve villus height, villus height to crypt depth ratio, improve immune response and improved intestinal microflora	Darabighane *et al*. (2011)
Ginger rhizome (*Zingiber officinale*)	Gingerol, shogaols, gingerdiol and gingerdione	240 ppm	Enhances nutrient digestion and absorption because of its positive effect on gastric secretion, enterokinesia and digestive enzyme activities	Khan *et al*. (2012)
Green tea leaves (*Camellia sinensis*)	Polyphenols (catechins and flavanoids), alkaloids (caffeine, threobromine, theophylline), polysaccharides, amino acids, lipids, vitamin C and minerals	0.50-1.50%	Effective against necrotic enteritis, salmonellosis, dermatitis, colibacillosis and coccidiosis	Ishihara *et al*. (2001), Jang *et al*. (2007) and Khan (2014)
Guar gum (*Cyamopsis tetragonolobus*)	Galactomannans and saponins.	50 g kg^{-1}	Anticoccidial effect by interfering cell membranes.	Abbas *et al*. (2012)
Huang Qi (Mandarin) (*Astragalus membranaceus*)	Polysaccharides, saponin, flavonoids, isoflavonoids, sterols, amino acids and volatile oils	9-30 g kg^{-1}	Increases the white blood cell count, mainly through the contribution of CD_4^+ lymphocytes	Yuan *et al*. (2006) and Agyemang *et al*. (2013)
Neem leaves (*Azadirachta indica*)	Nimbin, nimbanene, nimbandiol, nimbolide, ascorbic acid and nimbiol	10 g kg^{-1}	Had favourable influences on immune responses of broiler chicken	Landy *et al*. (2011)
Olympus tea (*Sideritis scardica*)	Carvacrol, thymol and others	2.5-5 g kg^{-1}	Anti-inflammatory/antioxidant properties	Bozkurt *et al*. (2013)
Oregano (*Oreganum compactum*)	Carvacrol and thymol	2.5-5 g kg^{-1}	Suppression of oocyst production of *E. tenella*	Bozkurt *et al*. (2013)

Table 2: Continue

Medicinal plants and their botanical sources	Major chemical constituents	Dose (feed)	Actions	References
Papaya (*Carica papaya*)	Papaine	150 g kg^{-1}	Lysis of sporozoites of *E. tenella*	Bozkurt *et al*. (2013)
Peppermint (*Mentha piperita*)	Menthol, menthone and 1-8-Cineol	70 mg kg^{-1}	Growth promoter	Ocak *et al*. (2008)
Purple coneflower (*Echinacea purpurea*)	Caftaric acid, chlorogenic acid, cynarin, echinacoside and cichoric acid	2.0%	Enhance immune stimulation	Lee *et al*. (2012)
Tulsi leaves (*Ocimum sactum*)	Eugenol, ursolic acid, oleanolic acid, rosmarinic acid, carvacrol, linalool, β-caryophyllene and germacrene D	10 g kg^{-1}	Activates the cell mediated immune response and therefore, creates an enhanced response to any future challenges occurred by disease organisms	Eevuri and Putturu (2013)
Extracts				
Anise fruit (*Pimpinella anisum*)	Anethol, eugenol, anethole, coumarins, scopoletin, umbelliferone and estrols	200 mg kg^{-1}	Antibacterial, antifungal, digestion stimulant and overall performance GI tract.	Shojaii and Fard (2012) and Kamel (2001)
Artemisia leaf (*Artemisia annua*)	Artemisin	30-300 mg kg^{-1}	Anti-inflammatory, anticoccidial and antioxidant	Abbas *et al*. (2012)
Acacia (*Acacia senegal*)	Arabinose, galactose, rhamnose glucuronic acid and diferulic acid	50 g kg^{-1}	Increased the number of lactobacilli and caused reduction in coliform counts in the ileum	Vidanarachchi *et al*. (2013)
Babylon willow (*Salix babylonica*)	Tritetracontane, octadecenoic acid and hexadecanoic acid methyl ester	100 mL day^{-1}	Improve heat tolerance, weigh gain and feed conversion rate	Salem *et al*. (2011), Al- Fataftah and Abdelqader (2013)
Black poplar (*Populus nigra*)	Caffeic and p-coumaric acids	100 mL day^{-1}	Improve heat tolerance, weigh gain and feed conversion rate	Dudonne *et al*. (2011), Al-Fataftah and Abdelqader (2013)
Broccoli (*Brassica oleracea*)	Glucoraphanin and sulforaphane	3694 mg kg^{-1}	Improve intestinal microflora by antioxidation	Mueller *et al*. (2012)
Capsicum fruits (*Capsicum annuum*)	Capsaicin, fatty acids, rutin, vitamins (A and C), B-complex vitamins, minerals and proteins	1-2%	Antidiarrhoeic, anti-inflammatory, stimulant and gut health tonic	Kamel (2001) and Aziz (2010)
Cardamom seed (*Elettaria cardamomum*)	Cineol, α-pinene and spathulenol	0.5-1.5 g kg^{-1}	Appetite and digestion stimulant	Kamel (2001)
Celery fruits and leaves (*Apium graveolens*)	Polyacetylenes, apiin, apigenin and phtalides.	200 mg kg^{-1}	Appetite and digestion stimulant	Kamel (2001) and Bazafkan *et al*. (2014)
Chinese Sumac (*Galla Chinensis*)	Pentagalloylglucose, gallotannin and gallic acid	4 -8 µg mL^{-1}	Anti-*Escherichia coli* and antiparasitic activity	Xie *et al*. (2008) and Ho *et al*. (2013)
Cinnamon Bark (*Cinnamomum zeylanicum*)	Coumarin, cinnamaldehyde, 2-hydroxy cinnamaldehyde and cinnamyl acetate	0.5-3 g kg^{-1}	Appetite and digestion stimulant and antiseptic	Kamel (2001)
Clove (*Syzygium aromaticum*)	Eugenol	10-100 mg mL^{-1}	Destruction of *Eimeria* oocysts	Abbas *et al*. (2012)

Table 2: Continue

Medicinal plants and their botanical sources	Major chemical constituents	Dose (feed)	Actions	References
Coriander leaf and seed (*Coriandrum sativum*)	Linalol, coriandrin, γ -terpinene, α-pinene, camphor, limonene, geraniol, camphene and D-limonene	8 mg mL^{-1}	Digestion stimulant and improve gut health	Kamel (2001) and Shahwar *et al*. (2012)
Cumin seed (*Cuminum cyminum*)	Cuminaldehyde	1-2%	Digestion stimulant and improve gut health	Yılmaz *et al*. (2013)
Dessert banana root (*Musa paradisiaca*)	Anthocyanidins such as dephindin, cyanidin, petunidine, pelargonidin, peonidine, malvidin, sterols, triterpenes, polysaccharides, xylose, arabinose, galactouronic acid, galactose, rhamnose, mannose and arabinogalacton type I pectin.	1000-4000 mg kg^{-1} b.wt.	Reduced severity of clinical symptoms and *Eimeria* oocyst count per gram of faeces and gradually increased packed cell volume in a dose-dependent pattern	Anosa and Okoro (2010) Mondal *et al*. (2001)
Eucalyptus leaves (*Eucalyptus globulus*)	Cineole, α-pinene, d-Limonene, oxysesquiterpene	100 mL day^{-1}	Wide spectrum of antimicrobial activity	Pereira *et al*. (2014)
False Daisy (*Eclipta alba*)	Coumestans, polyacetylenes, steroids, triterpenes and flavonoids	120-180 ppm	Act as therapeutic or prophylactic agent against avian coccidiosis	Kumari *et al*. (2006) and Michels *et al*. (2011)
Fenugreek seeds (*Trigonella foenumgraecum*)	Trigonelline, neurin, trimethylamine, biotin, minerals and vitamins (A, D)	5.33 kg ton^{-1}	Appetite stimulant and growth promoters	Kamel (2001) and Abdel-Rahman *et al*. (2014)
Garlic (*Allium sativum*)	Disulphide derivatives, allicin	35 mg kg^{-1}	Inhibition of parasite reproduction	Abbas *et al*. (2012)
Grape seed (*Vitis vinifera*)	Tannins	10–20 mg kg^{-1}	Oxidative stress	Abbas *et al*. (2012)
Green chirayta leaves (*Andrographis paniculata*)	Deoxyandrographolide, andrograp-holide, neoandrographolide and deoxydidehydroandrographolide	0.1-0.4 %	Reduce mortality and effective against bacterial dysentery (reduction of intestinal tract movements and diarrhea)	Deng *et al*. (1978) Gupta *et al*. (1990)
Long pepper (*Piper longum*)	α-Pinene, β-pinene, sabinene, δ-3-carene, limonene, β –caryophllene and piperine	15-30 mg kg^{-1}	Effective against necrotic enteritis, salmonellosis and coccidiosis	Griggs and Jacob (2005)
Mojave yucca or spanish dagger (*Yucca schidigera*)	Saponins, resveratrol, larixinol and spirobiflavonoid	50-200 ppm	Lower intestinal urease activity, enzymes involved into metabolic urea cycle, reduced intestinal and faecal urease activities	Killeen *et al*. (1998) and Cheeke *et al*. (2006)
Nutmeg seed (*Myristica fragrans*)	Myristicin, safrole, 4-terpineol and sabinene	0.1-0.3 mL $bird^{-1}$	Digestion stimulant and antidiarrhoeic	Kamel (2001) and Muchtaridi *et al*. (2010)
Oak (*Quercus infectoria*)	Carbohydrates (starch), fibre, protein, sugar and soluble nutrients	25-100 g kg^{-1}	Antibacterial and growth promoter	Basri and Fan (2005) and Kutlu *et al*. (2001)

Table 2: Continue

Medicinal plants and their botanical sources	Major chemical constituents	Dose (feed)	Actions	References
Olive leaves (*Olea europaea*)	Oleanenoic acid	90 mg kg^{-1}	Anti-inflammatory/antioxidant properties	Abbas *et al*. (2012)
Orange peel (*Citrus sinensis*)	Tannin, saponin, oxalate, flavonoids, limonene and linalool	1000 ppm	Caused a decrease in coliform counts in ileum and modify some microbial and intestinal traits	Pourhossein *et al*. (2014)
Parsley seeds (*Petroselinum crispum*)	Apiol and vitamins such as A, C, thiamine, riboflavin and niacin.	3 g kg^{-1} feed 1000 mg mL^{-1}	Appetite and digestion stimulant, antiseptic	Kamel (2001) and Abbas (2010)
Pine (*Pinus sabiniana*)	Condensed tannins		Anticoccidial effect by damaging cytoplasm	Abbas *et al*. (2012)
Shiitake mushroom (*Lentinus edodes*)	Eritadenine, amino acid, protein and fat	100 g L^{-1}	Promoted bifidobacteria growth in the gut of broiler chickens	Willis *et al*. (2007)
Siberian Ginseng (*Acanthopanax senticosus*)	Triterpenoid saponins, coumarins, flavones and phenolic compounds (syringin and eleutheroside E)	0.1%	Enhances the digestion and absorption of dietary protein and amino acids	Huang *et al*. (2011) and Kong *et al*. (2009)
Sweet chestnut wood (*Castanea sativa*)	Hydrolyzable tannins (castalagin)	0.25%	Enhance digestibility, growth performance, carcass quality and N balance of broiler chick.	Schiavone *et al*. (2008)
Thyme (*Thymus vulgaris*)	Thymol	10-100 mg mL^{-1}	Destruction of Eimeria oocysts	Abbas *et al*. (2012)
Turmeric (*Curcuma longa*)	curcumin (diferuloylmethane)	35 mg kg^{-1}	Attenuate Eimeria-induced, inflammation-mediated gut damage	Kim *et al*. (2013)
Whiteweed (*Ageratum conyzoides*)	Ageratochromene, β-caryophyllene, β-sinenesal, β-sesquiphelandrene and τ-cadinene	500-1000 mg kg^{-1} b.wt.	Destruction of Eimeria oocysts	Ranaa and Blazquezb (2003) and Nweze and Obiwulu (2009)
Combinations *Curcuma longa*, *Capsicum annuum* and *Lentinus edodes*		35+35+5 mg kg^{-1}	Enhanced innate immune responses, as easured by transcript levels of the cytokines interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-5 (IL-5) and interferon-γ (IFN-γ), at the intestinal site and produced a high level of protective immunity against *E. acervulina* infection	Lee *et al*. (2010)
Lentinus edodes, Tremella fuciformis and *Astragalus membranaceus*		10+2+2 g kg^{-1}	Stimulated the number of bifidobacteria and lactobacilli and reduced the number of the potentially harmful bacteria (*Bacteroides* spp. and *E. coli*)	Guo *et al*. (2004)
Use of *Agrimonia eupatoria*, *Echinacea angustifolia*, *Ribes nigrum* and *Cinchona succirubra*		0.5-1.0 g kg^{-1}	Exerted a coccidiostatic effect against *E. tenella*	Christaki *et al*. (2004)

Table 3: Phytochemicals and their role on poultry gut health

Phytochemicals and their botanical sources	Actions	References
Alkaloids sanguinarin and chelerythrin (*Sanguinaria canadensis*)	Improved daily weight gain and feed conversion ratio	Wallace *et al*. (2010)
Artemisinin (*Artemisia annua*)	Decreased the number of oocysts in the faeces of chickens challenged with Eimeria	Arab *et al*. (2006)
Astaxanthin (*Haematococcus pluvalis*)	Inhibits *C. perfringens* caecal colonisation	Waldenstedt *et al*. (2003)
Astragalan and achyranthan Chinese herbal polysaccharides	Increased micro hem agglutination inhibition (HI), antibody titres and bursa of *Fabricius index.* Increased IL-2 production and proliferation of splenocytes in chicken.	Chen *et al*. (2003)
Betaine (*Beta vulgaris*)	*E. acervulina* (and *E. tenella*, but less effective) invasion and development when used in combination with salinomycin	Allen and Fetterer (2002)
Caffeic acid (Coffee, tea, sweet potatoes and sunflower seeds)	Caffeic acid is a natural antioxidant phenolic acid possesses antibacterial properties	Marinova *et al*. (2009)
Cardamom oleoresins (*Amomum subulatum*)	Antifungal and antioxidant activities	Kapoor *et al*. (2008)
Carvacrol (Oregano and Thyme)	Improve antioxidant enzyme activities, fatty acid composition, digestive enzyme activities and immune response	Hashemipour *et al*. (2013)
Chestnut tannins (*Castanea sativa*)	Inhibit the *in vitro* growth of *Salmonella typhimurium*, but had no effect on the excretion of the bacteria in an infection model in pigs	Van-Parys *et al*. (2010)
Cinnamaldehyde	Improve growth performance, nutrient digestibility, fecal microbial shedding and fecal noxious gas content	Yan and Kim (2012)
Condensed tannins (Green tea or quebracho)	Have proven to have antimicrobial activity and affect gastrointestinal bacteria colonization in chickens	Elizondo *et al*. (2010) and Hara (1997)
Eugenol	Improve growth performance, nutrient digestibility, fecal microbial shedding and fecal noxious gas content	Yan and Kim (2012)
Grape seed proanthocyanidin (*Vitis vinifera*)	Inhibit *E. tenella* infection and improve weight	Wang *et al*. (2008)
Lupulone (*Humulus lupulus*)	Inhibits intestinal *C. perfringens.*	Siragusa *et al*. (2008)
Maslinic acid (found in the leaves and fruits of olive tree)	Act as a natural coccidiostatic in animal infected with *Eimeria tenella*, decrease in lesion index and oocyst index	De-Pablos *et al*. (2010)
Plant extracts containing; 5% carvacrol, 3% cinnamaldehyde and 2% capsicum	Villi-related protective activity	Jamroz *et al*. (2003)
Thymol	Improve antioxidant enzyme activities, fatty acid composition, digestive enzyme activities and immune response	Hashemipour *et al*. (2013)
Tocopherol (*Linum usitatissimum*)	*E. maxima* lesions, weight gain, *E. acervulina* (not *E. tenella*) and antioxidant	Allen and Fetterer (2002)

Probiotics: Probiotics are strains of various microbial species, currently has been gained attention as a substitute of antibiotics for poultry production as growth promoters with feed additives (Ahmad, 2006). The various proposed mechanisms by which probiotics act to maintain a beneficial microbial population are: (1) Promote balance of bacteria in the gut by competitive exclusion and antagonism, (2) Involved in gut maturation and integrity, (3) Immune enhancement and preventing inflammation use (4) Improves digestive enzyme activity, (5) Improves feed intake and digestion, (6) Neutralise enterotoxins, (7) Stimulates immune response and (8) Act as growth stimulator (Jin *et al*., 1997; Simon *et al*., 2001). Table 4 summarize some examples of probiotic strains and their effects on the gut microbial population of the chicken.

Prebiotics: Prebiotic has been defined as “a non-digestible dietary supplement or feed ingredient that beneficially affects the host by selectively stimulating the growth by altering the composition and metabolism of the gut microbiota” (Gibson and Roberfroid, 1995). The proposed mechanism by which prebiotics exert their effects are: (1) Growth inhibition of harmful intestinal microbes (through competition for substrates and mucosal attachment sites), (2) Increased intestinal acidity

Table 4: Probiotics and their role on poultry gut health

Probiotics strains	Activities	References
Single strains		
Suspension of gut contents derived from healthy adult chickens	Used for protection against colonization by *Salmonella enteritidis*	Nurmi and Rantala (1973)
Lactobacillus acidophilus	Competed with pathogenic *E. coli* in the gut of gnotobiotic chicks, immune enhancement, balance intestinal microflora and decrease fecal enzyme activity	Sanders (1999)
Salmonella gallinarum	Competed with pathogenic *Salmonella enteritidis* in the gut	Rabsch *et al*. (2000)
Yeast *Saccharomyces boulardii*	Used for the treatment of *Eimeria* infected chickens and prevents the recurrence of *Clostridium difficile* infections and some colibacillosis. It is reported to significantly mitigate the effect of decreasing haemoglobin and total protein (albumin, globulin) in chickens whose diet contained ochratoxin A at levels of 0.5 ppm	Czerucka and Rampal (2002) and Czerucka *et al*. (2007)
L. salivarius CTC2197	Reduced *S. enteritidis* C-114 colonization of the gut	Pascual *et al*. (1999)
L. salivarius	Reduced the number of *S. enteritidis* and *C. perfringens* in the gut. It also produces bacteriocins with antagonistic activity against gram-positive bacteria and *Campylobacter jejuni*	Kizerwetter-Swida and Binek (2009) and Stern *et al*. (2006)
Lactobacillus GG	Increased serum IgA response to *Salmonella typhi* in IgA secreting cells in the intestine, prevent rotavirus diarrhoea and prevent antibiotic associated diarrhoea	Sanders (1999) and Edens (2003)
L. casei Shirota	No effect on NK cell numbers, phagocytosis or cytokine production	Sanders (1999)
A protein called BIF, secreted by *B. longum* BL 2928	Active agents against gram-negative bacteria and known to inhibit the interaction between *E. coli* and epithelial cell lines	Fujiwara *et al*. (1997)
Bifidobacterium strains (CA1 and F9)	It secretes a lipophilic compound with a strong antimicrobial activity against *S. typhimurium* SL1344 and *E. coli* 1845	Lievin *et al*. (2000)
Bifidobacterium bifidum	Treat rotavirus diarrhoea and balance intestinal microflora	Sanders (1999) and Edens (2003)
B. lactis	Increased IgA levels	Sanders (1999) and Edens (2003)
Bacillus subtilis	Keep birds free from specific pathogens challenged with *C. perfringens*	La Ragione and Woodward (2003)
Wild mushroom, *Ganoderma lucidum*	Treatment of *Eimeria tenella* infected chickens.	Ogbe *et al*. (2009)
Lactic acid bacteria	Reduced 95% of the number of colonization of *S. heidelberg*, 4-76% of the number of colonization of *S.* enteritidis and 92-96% of *Salmonella typhimurium*	Higgins *et al*. (2010)
Bacillus subtilis	Reduced 58% of the number of colonization of *S. heidelberg*	Knap *et al*. (2011)
Mixtures of probiotic strains		
L. acidophilus, L. casei, B. bifidum, Aspergillus oryzae, Streptococcus faecium and fungus species like *Torulopsis*	Lowered numbers of *Coliform* and *Campylobacter* in the gut	Khaksefidi and Rahimi (2005)
L. agilis JCM 1048 and *L. salivarius* subsp. (*salicinius* JCM 1230)	Enriched the diversity of *Lactobacillus* flora in jejunum and caecum, restored microbial balance and maintained the natural stability of indigenous bacterial microbiota in the gut	Lan *et al*. (2004)
Lactobacillus, Bifidobacterium, Enterococcus and Pediococcus strains	For maintenance of above bacteria in intestine	Mountzouris *et al*. (2007)
L. reuteri C1, C10 and C16; *L. gallinarum* I16 and I26; *L. brevis* I12, I23, I25, I218 and I211 and *L. salivarius* I24	Increased the caecal populations of lactobacilli and bifidobacteria and decreased the caecal *E. coli*	Mookiah *et al*. (2014)
L. acidophilus, L. casei, B. thermophilus and *Enterococcus faecium*	Improvement of quality as well quantity of egg production	Davis and Anderson (2002)

Table 4: Continue

Probiotics strains	Activities	References
E. faecium, *L. case* and *L. plantarum*	Early use establishes a balance in microbial flora against pathogenic bacteria.	Leandro *et al*. (2010)
L. acidophilus, *B. bifidum* and *S. faecalis*	It stimulates the production of antitoxin α IgA from *C. perfringens* in the intestine of non-vaccinated chicks	Haghighi *et al*. (2006)
Yeast (*S. cerevisiae*) and fungi (*A. oryzae*)	Used to control pathogenic bacteria infection in chickens	Woo *et al*. (2006)
Mixture of *Bacillus mesentericus*, *E. faecalis* and *Clostridium butyricum*	Reduced the harshness of diarrhoea	Rodriguez-Fragoso *et al*. (2012)
Lactic acid bacteria (*Lactococcus lactis* CECT 539 and *Lactobacillus casei* CECT 4043) and their products of fermentation (organic acids and bacteriocins)	Used as a replacement for antibiotics in stimulating health and growth of broiler chickens	Fajardo *et al*. (2012)
Mixture obtained from crop (*Lactobacillus reuteri*), jejunum (*Enterococcus faecium*), ileum (*Bifidobacterium animalis*) and cecum (*Pediococcus acidilactici* and *Lactobacillus salivarius*) of healthy adult chicken	It increased integrity of the gastrointestinal tract associated with a higher surface area of the villi, resulted in improved production results and could reduce both the damage of enterocytes and the need for cell renewal in the gut	Peric *et al*. (2010)
Live yeast culture (*Yea Sacc*1026, *L. acidophilus* 108 and *Streptococcus faecium* 108)	Yielded positive effects on growth performance of gut	Singh *et al*. (2009)
L. acidophilus, *B. bifidum* and *S. faecalis*	Utilised to increase in the natural antibody production in the serum and gut for some antigens. It also induces changes in the gastrointestinal tract in terms of histological structure and regulation of mucus secretion	Deplancke and Gaskins (2001)
L. salivarius and *L. reuteri*	Increased the growth performance and improved intestinal nutrient absorption with an associated improvement intestinal architecture	Awad *et al*. (2010)

(through production of short-chain fatty acids), (3) Growth stimulation of intestinal absorptive cells and (4) Stimulation of the enteric immune system, thus facilitating better performance and health status of the birds (Gibson and Roberfroid, 1995; Collins and Gibson, 1999; Huyghebaert *et al*., 2011; Chen *et al*., 2014). Table 5 summarize some examples of prebiotic and their effects on the gut microbial population of the chicken.

Synbiotics: Synbiotic has been defined as “any combination, which is formed by adding both probiotics and prebiotics to provide the beneficial effects on the gut of birds” (Huyghebaert *et al*., 2011). This combination could improve the survival and persistence of the health-promoting organism in the gut of birds and can be utilised as alternative to AGP due to its availability as a specific substrate for fermentation and having synergistic action of both probiotics and prebiotics (Yang *et al*., 2009; Adil and Magray, 2012; Aziz Mousavi *et al*., 2015). Table 6 summarize some examples of synbiotics with their potential benefits on the intestinal microbial ecosystem of chicken.

Organic acids: Organic acids are group of organic chemicals, composed of carboxylic acid, including fatty acids and amino acids, of the general structure R-COOH (Dibner and Buttin, 2002). In recent years, the use of organic acid has been increased many fold due to its potential to reduce many pathogenic and spoilage organisms by lowering the gut pH (Huyghebaert *et al*., 2011). They lower the pH, at which the activity of proteases and beneficial bacteria is optimized and proliferation of pathogenic bacteria is minimised by a direct antibacterial effects destroying their

Table 5: Prebiotics and their role on poultry gut health

Prebiotics	Actions	References
Individual prebiotics		
Fructo-oligosaccharides (FOS)	Reduced intestinal colonization of *Salmonella*, *C. perfringens* and *E. coli*. It provided nutrients for the growth of beneficial bacteria in the gut and increased the population of *Bifidobacterium* and lactobacilli in the intestine. It is reported to improve body weight, FCR and larger crypts size	Bailey *et al*. (1991), Williams *et al*. (2008) and Li *et al*. (2008)
Fructans	Increase mineral absorption of calcium and phosphorous and improve hardness of the egg shell and cholesterol diminishing of the yolk	Curbelo *et al*. (2012)
Manan-oligosaccharides (MOS)	Prevents adherence of pathogens to intestinal wall	Sinovec and Markovic (2005)
Bio-MOS	Increased body weight, FCR, villi lengths, RNA/DNA ratios and crypts depth	Iji *et al*. (2001) and Yang *et al*. (2008)
Oligo-fructose	Increase cecal and colonic macrophages	Gaskins *et al*. (1996)
Purified indigestible dextrin (5 % w/w)	Increase content of IgA-positive cells in small intestine and cecal mucosa	Kudoh *et al*. (1998)
Galacto-oligosaccharides (GOS)	Increased *Bifidobacterium* spp. and decreased *Campylobacter* spp. in the faecal samples	Baffoni *et al*. (2012)
Transgalacto-oligosaccharides (TOS)	Improve weight gains and FCR	Biggs *et al*. (2007)
Isomalto-oligosaccharides (IMO)	Increased the caecal populations of lactobacilli and bifidobacteria and decreased the faecal *E. coli*	Mookiah *et al*. (2014)
Inulin	Improve intestinal microflora and gut morphology. Increased Bifidobacterium counts and decreased *E. coli* counts in faecal contents	Nabizadeh (2012)
Purified natural lactose or whey powder (70-80% lactose)	It has inhibitory effects on *Salmonella* and other pathogenic bacteria in the digestive tract of broiler chickens by production of short chain fatty acid (SCFA) and lactic acid from lactose as a substrate for host bacteria enzymes, with deep reduction in cecal pH	Szczurek (2008)
Partially hydrolysed guar gum (PHGG)	Improve both feeding behaviour and food passage from the crop in growing chicks	Hajati and Rezaei (2010)
Wheat	Increase relative amounts of bifidobacteria and lactobacilli, which may affect Fe bioavailability in long-term use	Tako *et al*. (2014)
β-glucan from an edible mushroom (*Pleuratus florida*)	Act as an immunomodulator on the innate immune responses	Paul *et al*. (2013)
Non-starch polysaccharides (NSP) from chicory	Cause changes in gut micro-environment and gut morphology	Lindberg (2014)
Combinations of prebiotics		
Mannan oligosaccharide and *Saccharomyces cerevisiae*	Significantly improves the gut health of broiler chickens	Padihari *et al*. (2014)
Mannan oligosaccharide (MOS) and Organic acid (OA)	Successfully reduces bacterial load in the intestine of broiler birds and increase higher villi in the jejunum	Pelicano *et al*. (2005)
MOS and BMD (basal metabolic diet)	Turkeys showed significantly lower *Clostridium perfringens* population in the gut	Sims *et al*. (2004)
FOS and *B. subtilis*	Better growth promoting effects with effects on reducing diarrhoea rate	Li *et al*. (2008)
Extract from the cell walls of yeasts (β-glucans, mannans and polysaccharides) and sodium salt of n-butyric acid	Beneficial effect on microbial intestinal state and decrease of total number of the heterotrophic bacteria and the low coli/lacto index was achieved	Gajewska *et al*. (2012)
Retrograded resistant corn starch, fibersol-2, inulin and oat β-glucan	Affect gut and the whole body health status via influencing the alkaline phosphatase detoxification	Ontario (2012)
Xylo oligosaccharides (XOS) and arabinoxylooligosachride (AXOS)	Increased Bifidobacterial populations	Courtin *et al*. (2008)
FOS and MOS	Decrease Clostridia and *E. coli* populations and increase in lactobacilli populations and diversity, as well as total bacterial populations	Kim *et al*. (2011)

Table 6: Synbiotics and their role on poultry gut health

Synbiotics	Actions	References
Bifidobacterium-based products	Reduced *C. jejuni* concentration in poultry faeces.	Baffoni *et al*. (2012)
MOS and *Saccharomyces cerevisiae*	Significantly improves the gut health of broiler chickens.	Padihari *et al*. (2014)
IMO and *Lactobacillus* strains	Increased the caecal populations of lactobacilli and bifidobacteria and decreased the caecal *E. coli*	Mookiah *et al*. (2014)
FOS and *E. faecum*	Reduced the intestinal colonization by *C. perfringens*	El-Ghany (2010)
Raffinose and *L. lactic*	Stimulated the expression of IL-6 and IFN-	Sugiharto *et al*. (2014)
MOS and organic acid (OA)	Successfully reduces bacterial load in the intestine of broiler birds and increase higher villi in the jejunum	Pelicano *et al*. (2005)
MOS and BMD (basal metabolic diet)	Turkeys showed significantly lower *Clostridium perfringens* population in the gut	Sims *et al*. (2004)
FOS and *B. subtilis*	Better growth promoting effects with reducing diarrhoea rate	Li *et al*. (2008)
Cell walls of yeasts (β-glucans, mannans and polysaccharides) and sodium salt of n-butyric acid	Beneficial effect on microbial intestinal state and decrease of total number of the heterotrophic bacteria and the low coli/lacto index was achieved	Gajewska *et al*. (2012)
Lactobacillus, *Bifidobacterium* and oligosaccharides	Improved the antibody response	El-Sissi and Mohamed (2011)
Enterococcus faecium (DSM 3530), a prebiotic (derived from chicory) and immune modulating substances (derived from sea algae)	Shows positive effect on performance and blood parameters	Awad *et al*. (2008)
Bacillus subtilis and inulin	Colonization of the beneficial microflora along with increasing the villi-crypts absorptive area	Abdelqader *et al*. (2013)

Table 7: Organic acids and their role on poultry gut health

Organic acids and chemical formula	pKa	Actions	References
2, 3-dihydroxybutanedioic acid (tartaric) $COOHCH(OH)CH(OH)COOH$	2.93	Increases in weight gain	Vogt *et al*. (1982)
2-butenedioic acid (fumaric) $COOHCH:CHCOOH$	3.02	Improve ileal digestibilities	Blank *et al*. (1999)
2-hydroxy-1,2,3-propanetricarboxylic acid (citric) $COOHCH_2C(OH)(COOH)CH_2COOH$	3.13	Enhance performance in respect of live weight gain, feed conversion and degrade aflatoxins in young broiler chickens	Salgado-Transito *et al*. (2011)
Hydroxybutanedioic acid (malic) $COOHCH_2CH(OH)COOH$	3.40	Improve feed efficiency	Vogt *et al*. (1982)
Formic acid $HCOOH$	3.75	Improve ileal digestibility of nutrients	Hernandez *et al*. (2006)
2-hydroxypropanoic acid (lactic) $CH_3CH(OH)COOH$	3.83	Increases in weight gain and feed-to-gain ratios.	Dibner and Buttin (2002)
2-hydroxy-4-methylthio butanoic acid (HMB) $CH_3SCH_3CH_2CH(OH)COOH$	3.86	Used as a source of dietary methionine in poultry nutrition and protects intestinal epithelial barrier function by increased production of taurine and reduced glutathione level	Martin-Venegas *et al*. (2013)
Acetic acid CH_3COOH	4.76	Potent anticoccidial	Abbas *et al*. (2011)
2,4- hexadecanoic acid (palmitic) $CH_3CH:CHCH:CHCOOH$	4.76	Improve intestinal absorption of fatty acids by simple or facilitated diffusion	Casanovas *et al*. (1994)
Butanoic acid $CH_3CH_2CH_2COOH$	4.82	Maintained performance, intestinal tract health, villi development, crypts depth in jejunum and carcass quality in broiler chickens	Antongiovanni *et al*. (2007)
2-propionic acid CH_3CH_2COOH	4.88	Reduce abdominal fats of male broilers	Izat *et al*. (1990)

cell membranes (Partanen and Mroz, 1999; Chowdhury *et al*., 2009). Table 7 summarize some examples of organic acids and their effects on the gut microbial population of the birds.

Clay minerals: Clay minerals are natural clay formed by a net of stratified tetrahedral or octahedral layers and mainly composed by molecules of silicon, aluminum and oxygen (Vondruskova *et al*., 2010). Clays added to the diet can bind and immobilize toxic materials such as aflatoxins and heavy metals etc., may present in the gastrointestinal tract of chicken and thus, reduce toxicity (Owen *et al*., 2012). As a result of their binding properties, clay minerals have been widely used in poultry diets to improve chicken performance when diets are supposed to contain mycotoxins (Zhou *et al*., 2014). Some of the molecules of clay minerals such as, bentonites, zeolite, kaolin, montmorillonite, smectite, illite, kaolinite, biotic and clinoptilolite, etc., have been reported to exhibit beneficial effects on the intestinal health of chicken due to additional toxin binding action (Thacker, 2013).

Egg yolk antibodies: Egg yolks antibodies (IgY) are find its application as a potential alternative to antibiotics for growth promotion and have ability to neutralise specific pathogens of gut (Thacker, 2013). In order to produce these antibodies, hens are exposed (usually injected) to antigens of choice to induce desirable immune responses. Normally, these antibodies are then transferred to the egg yolk. Booster dose of immunisation (second exposure) is usually given at a later time to ensure the continued transfer of antibodies from hen to the egg yolk. These antibodies are then extracted from the egg yolk and further processed to be administered directly to the animal or included in the feed (Schade *et al*., 2005).

Exogenous enzymes: Exogenous enzymes including β-glucanase, xylanase, amylase, α-galactosidase, protease, lipase, phytase, etc., have been supplemented in poultry diets and reported to modulate the gut microbiota of birds (Adeola and Cowieson, 2011). The effects of enzymes on gut microflora were classified into two phases: an ileal phase and a caecal phase. In the ileum, enzymes simply reduce the number of bacteria by increasing the rate of digestion and limiting the amounts of substrates available to the microflora. While, in the caecal phase enzymes produce soluble, poorly absorbed sugars which feed beneficial bacteria. However, the effects of enzymes on the gut microflora may be far more than those two phases (Bedford and Cowieson, 2011).

Recombinant enzymes: The application of genetic engineering allows us to develop targeted enzymes at molecular level for specific purposes. Recently, several enzymes have been developed, which have considerable potential for animal feed application (He *et al*., 2010). These enzymes have special properties such as, active over a broad pH range, exhibit thermostability, resistant to pepsin and trypsin and viable under simulated gastric conditions. Some typical example includes inclusion of a recombinant carbohydrases and β-mannanase in corn soybean meal diets cause magnitude of the improvement (Pettey *et al*., 2002).

Nucleotides: Nucleotides are essential components of body involves in cellular metabolism and all intracellular biochemical processes such as, biosynthetic pathways, energy transfer system, as co-enzyme components and as well as biological regulators. Nucleotides alter the cellular lipid metabolism, particularly of long-chain polysaturated fatty acids and the lipoprotein synthesis. Nucleotides changes the composition of intestinal microflora that affect long-chain polyunsaturated fatty acids levels, as some bacteria's possess necessary enzymes for fatty acid elongation and denaturation and also promote intestinal absorption of iron by conversion of purine nucleotides (AMP, GMP) to inosine, hypoxanthine and uric acid which increase the absorption of iron (Cosgrove, 1998).

Polyunsaturated fatty acids: Polyunsaturated fatty acids (PUFAs) are lipids in which the constituent hydrocarbon chain possesses two or more carbon-carbon double bonds, such as en-3 and n-6 fatty acids which were found to be essential components for the immune function of body's. Fish oil and corn oil are the main source of feed additive in poultry, contain n-3 and n-6 type polysaturated fatty acids. There are various reports which reflect the utility of these oil for improving gut and overall immunity of the poultry. In another study combination of tuna oil, sunflower oil and palm oil (contain n-3 PUFAs) improves immune responses of birds, as evidenced by the increase in spleen weight, Infectious Bronchitis Disease (IBD), Newcastle Disease (ND), antibody titres, IL-2 and IFN-concentrations (Maroufyan *et al*., 2012). Conjugated linoleic acid (CLA) is another type of PUFA that has been used as feed supplement to poultry diets and reported for enhancing the immune response, growth of immune tissue, stimulated T-lymphocyte proliferation, elevate, antibody production and maintain the number of LAB in the gut of chicken (He *et al*., 2007).

Miscellaneous compounds: Many additional compounds have been tested and reported in animals such as spray-dried porcine plasma, yeast culture, bacteriophages, lysozyme, bovine colostrum, lactoferrin and seaweed extract etc. for their potential to replace AGP (Thacker, 2013).

Marketed product survey: Table 8 reported various marketed product thoroughly sold globally as replacement of AGP. Many products from extensive survey were found to full fill the need of

Table 8: Market product as a source of NGP and their role on poultry gut health

Marketed products	Company	Action	References
Aerocid	Herbavita Bvba, Belgium	Antibacterial and stress reducing action	Hashemi and Davoodi (2010)
Aminofree	Indian Herbs, India	Enhances the intestinal enzyme system	Hashemi and Davoodi (2010)
Anihom	Herbavita Bvba, Belgium	Stimulated the immunity system, and give beneficial for the intestinal tract	Hashemi and Davoodi (2010)
Avericox	Mercordli Belgium	Combat coccidiosis	Hashemi and Davoodi (2010)
AV/AGP/10	Ayurvet, India	Improve height of intestinal villi of duodenum, ileum and jejunum	Debnath *et al*. (2014)
Bio-Mos®	Alltech, USA	Improve performance, small intestinal microflora and the immune response of broiler chicks. Modifying the bacterial community of the gut and promote maturation of the GI tract	Baurhoo *et al*. (2009)
Colinex	Mercordli Belgium	Immune stimulator and can be used successfully to prevent *E. coli* infections	Hashemi and Davoodi (2010) Grashorn (2010)
EV-herbaliq 100®	Möhnesee, Germany	Improve gut and immune function	Amirdahri *et al*. (2012)
Fermacto®	Pet Ag, USA	At a level of 1.5 g kg^{-1} improved the apparent organic matter, digestibility and decreased serum total cholesterol and abdominal fat percentage	
Gutsol	Regen Biocorps, India	Improve overall gut performance	No citation
Herban liquid and powder	Kelanv, Belgium	Promote poultry health	Hashemi and Davoodi (2010)
Immon®	Regen Biocorps, India	A comprehensive immuno-strengthen and gut health promoter containing nucleotides, spirulina, glucans, amino acid (arginine and glutamic acid), chelated minerals and vitamins	No citation
NuPro®	Alltech, USA	Rich source of nucleotides as well as amino acids including glutamic acids. Used in poultry nutrition as a functional protein source to improve gut health and found effective in reducing intestinal *C. perfringens* levels	Thanissery *et al*. (2010)

AGP in some extent. However, there is still need to set some standards for the replacement of antibiotic compounds in poultry, in terms of product type, identification of suppliers, poultry response criteria, regulatory status and veterinary definition.

CONCLUSION

The potentials of NGPs to AGPs are only of practical significance when they improve animal performance by maintaining gut health and immune functions in given time slot levels. Such thoroughly tested microbiota modulating and immunomodulatory compounds have potential to be used as feed stuff of feed additives for poultry productions. Although market is flooded with numerous products, some of them shown their potential, but at the same time there are many more objectionable products, where efficacy is still questionable. Therefore, there is an urgent need of further studies to develop larger datasets for product based mechanisms of action of each compound in a scientific way. The paper presented list of various NGPs are by no means of exhaustive and there are also many other products design and screened using these requirements day to day claiming to be of value added NGPs in gut health.

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