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Growth Promoters and Novel Feed Additives Improving Poultry Production and Health, Bioactive Principles and Beneficial Applications: The Trends and Advances-A Review

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Abstract: A substantial growth in poultry industry has been observed mainly due to exploitation of various modern growth promoting strategies and appropriate disease preventive and control measures. The present review describes the various essential growth promoters and novel feed supplements, their salient features, classical examples, bioactive principles, pharmacological and modes of action and useful applications for improving poultry production and health. It highlights antibiotics, probiotics, prebiotics, synbiotics, organic acids, vitamins and minerals, oils, enzymes, amino acids, betaine, carnitine, L-arginine, ractopamine, nucleotides, electrolytes, herbs, panchgavya elements. Apart from boosting poultry production and safeguarding general health of birds some of these have been found to possess beneficial immunomodulatory and stress relieving properties and also have added advantages to help produce lean meat and designer poultry products taking into account health awareness and preferences of the consumers. It is a comprehensive and an updated review compilation focusing the salient aspects of various important growth promoters and feed additives having potential applications to promote poultry production and health. Due care has been taken to cover the ongoing trends and recent advances with a perspective vision and their holistic usages and beneficial applications in poultry production system. The contents of the review will be highly useful for researchers, scientists, pharmacists, veterinary professionals, pharmaceutical industries, poultry producers/owners and poultry industry as well as for perspective applications in livestock industry. It would enrich the knowledge of researchers and help the scientific community to conduct more research on such daily essential requirements for boosting poultry production in a better way. It will also shed light regarding the management and production aspects of poultry especially broilers which will enlighten farmers and poultry producers for better economic growth.

Key words: Growth promoters, feed additives, poultry production, health, antibiotics, organic acids, vitamins, minerals, prebiotic, probiotic, oils, enzymes, electrolytes, herbs

INTRODUCTION

There has been a phenomenal growth in poultry production in India during the last decade, which has been largely secluded to the large and small scale organized poultry industries. This has been primarily achieved due to the exploitation of various modern growth promoting strategies and appropriate disease prevention measures (Kataria *et al*., 2005; Angelakis *et al*., 2013). But the main constraint for an

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economic poultry rearing in especially the un-organized poultry sector is the threat posed by the pathogens that are present in and around the poultry dwelling units. This has lead to high cost treatment using antibiotics which has reduced the profitability of small scale poultry farming in the country and which if satisfactorily answered, can keep the country in a numero uno position in world poultry market. Hence, it has been thought to evolve newer trends and strategies to minimize the alarming farm inputs and maximize the outputs. For achieving the objective, several approaches have to be followed like genetic improvement by selective breeding, effective application of immunoprophylactic measures and better health cover with low cost growth promoting agents. As per the current global scenario, the demand for cheap and quality food is continuously increasing due to the growing world population and this highlights the importance of maximizing the efficiency of poultry production in a cost effective manner, through the application of growth promoters, which are non-nutrients aimed to maximize utilization of the nutrients present in feed (Patterson and Burkholder, 2003; Kocher, 2006; Akinleye *et al*., 2008; Huyghebaert *et al*., 2011).

Growth promoters are the substances that are added to a nutritionally balanced diet which provoke response towards the exploitation of maximum genetic potential of the host, in terms of growth as well as improvement in feed conversion efficiency. There are different types of growth promoters which are used to exploit the broiler industry like antibiotics, probiotics (bio-growth promoters), prebiotics, exogenous enzymes, antioxidants, coccidiostats etc. (Allen, 1999; Walker and Duffy, 1998; Dhama *et al*., 2007, 2011; Angelakis *et al*., 2013). Many other novel growth promoters include herbs, panchgavya elements and certain other nutritional substances (Mahima *et al*., 2012, 2013; Dhama *et al*., 2013a). In India, the use of growth promoters has been accepted in the broiler industry and they are usually included in the feed in very small quantities. Many antibiotics are used in animal and poultry feeds as growth promoters to improve the health and well being of animals and as a prophylactic agent for promoting growth. The withdrawal of these antibiotic growth promoters not only affect or reduce productive performance, but also increases morbidity and mortality in poorly maintained flocks (Dibner and Richards, 2005). Research has been conducted in an intensified manner in the last two decades for developing antibiotic alternative for maintaining health as well as performance of animals. Probiotics and prebiotics; acidifiers as well as extracts of plants; neutraceuticals viz., copper as well as zinc are the alternatives of antibiotics. At the same time the potential of antimicrobial peptides; clay minerals; antibodies from chicken egg yolk, essential oils, medium chain fatty acids (from eucalyptus oil), rare earth elements; as well as enzymes (recombinant) have been tested for their ability of replacing antibiotics as dietary feed additives (Han and Thacker, 2010; Jones *et al*., 2010; Han *et al*., 2011; Thacker, 2013). The cost factor and the possibility of evolution of antibiotic resistant microbes has made it necessary for the feed industry to use alternatives to antibiotics, such as probiotics, prebiotics, organic acids to maintain good production and health of poultry as well as livestock. High environmental temperature is responsible for imbalance of homeostasis in poultry resulting in reduction in plasma protein as well as elevation of concentration of blood glucose. Thus the role of vitamins (especially vitamins C, E and A) along with electrolytes ($NaHCO_3$, KCl) are of great concern in this aspect (Sahin *et al*., 2001; Mabelebele *et al*., 2014) which will be discussed along with the topics on other growth promoters in this review.

The present review describes the various essential growth promoters and novel feed supplements, their bioactive principles, pharmacological mechanisms, modes of action, classical examples and useful applications for improving poultry production and health. It is a comprehensive and updated review compilation covering most of the salient aspects of growth promoters and feed additives having potential applications to promote poultry production and health. It also highlights the trends and recent advances with a perspective vision and usage of growth promoters and feed additives in poultry production. The contents of the review will be highly useful for researchers, scientists, pharmacists, veterinary professionals, pharmaceutical industries, poultry producers as well as a perspective for livestock industry.

TYPES OF GROWTH PROMOTERS AND FEED ADDITIVES

During the last 2-3 decades, a substantial growth in poultry industry has been observed, largely secluded to large and small scale organized poultry farming. This is mainly due to exploitation of various modern growth promoting strategies and appropriate disease preventive and control measures. Many antibiotics are used in poultry feeds as growth promoters for improving health of animals. Others growth promoting agents and feed additives comprises of probiotics, prebiotics, synbiotics, organic acids, vitamins and minerals, herbs, panchgavya, betaine, carnitine, which have been used widely to promote poultry health and production (Mahima *et al*., 2012; 2013; Angelakis *et al*., 2013;

Dhama *et al*., 2011, 2013a). Antibiotics are given at sub therapeutic dosage for stabilization of the microflora of intestine and for improving the performance in general along with prevention of certain specific pathological conditions of the intestine (Dibner and Richards, 2005; Hassan *et al*., 2010). For neutralization of entero-toxins, probiotics play an important role. Supplementation of the diet with small fragments of carbohydrates manipulates the gut ecosystem (NRC, 1994; Patterson and Burkholder, 2003; Ashayerizadeh *et al*., 2009). The organic acids have got bacteriostatic properties as well as anti-mycotoxic effects (Gaglo-Disse *et al*., 2010; Wang *et al*., 2010; Cengiz *et al*., 2012). As premix in feed of poultry, multivitamin-minerals have been used for improving broiler growth and feed utilization thereby helping in realization of better return on production as well as economy (Peric *et al*., 2009). Various herbal products have got enhanced digestive activity, antimicrobial, antioxidant and immunomodulatory properties and can be used as alternative to chemotherapeutic agents (Fallah *et al*., 2013). ‘Panchgavya’ are rich source of elements that are essential along with minerals as well as hormones (Mahima *et al*., 2012, 2013). Betaine and L-arginine are also used in poultry industry as feed additives due to their beneficial effects on bird’s perfomance (Zimmermann *et al*., 1996). Health awareness among the consumers has been increased with more preference to lean meat hence the use of feed additives like L-carnitine, ractopamine, nucleotides have increased due to their lipolytic activity and better effect on growth performance of birds (Zuo *et al*., 2010; Yasmeen *et al*., 2013). Besides these, certain amino acids, essential oils and enzymes are also being tried with success (Wen and He, 2012). The additives like sodium bicarbonate, potassium chloride are more beneficial especially in heat stressed birds (Ahmad *et al*., 2006).

Antibiotic as growth promoter (AGP): Antibiotic Growth Promoters (AGP) are the antibiotics that are used in poultry feed continuously at a lower level to improve growth and feed conversion and not for the purpose of any therapeutic reasons. Antibiotic compounds commonly used as growth promoters include Bacitracin, Penicillin, Virginiamycin, Flavomycin, Chlortetracycline, Oxyteracycline, Colistin sulphate, Doxycycline, Erythromycin, Aureomycin, Avilamycin, Tiamulin, Furazolidone, Lincomycin, Enrofloxacin and Neomycin sulphate (Chowdhury *et al*., 2009). In germ-free birds, the use of antibiotics as growth promoters are not of much value regarding performance enhancement, which reflects that their mode of action is primarily due to antibacterial activity instead of having any direct effect on physiology of the birds (Stanley *et al*., 2004; Dibner and Richards, 2005).

Principal mode of action of antibiotics is the regulation and maintenance of optimal balance of avian intestinal microflora (between gram-negative and gram positive organisms). The well balanced intestinal microflora contains more than 90% Gram positive bacteria (mainly *Lactobacillus*). During stress or digestive disturbances, the number of pathogenic organisms like *Escherichia coli* or other gram-negative organisms is increased, leading to an imbalance of microflora. The gram-negative bacteria further colonize in the intestines, adhere to intestinal epithelium and cause inflammation of intestinal mucosa thus reducing the absorption of nutrients and in turn retarding the growth and productivity of birds. The AGP also has the ability to alter processes of mucin biosynthesis; and modifications in mucin dynamics influence the gut function and health and may change nutrient uptake. Hence, for eliminating the chances of imbalance under practical conditions, antibiotics are added to the feed or water as a prophylactic measure (Jones and Ricke, 2003; WHO, 2004). Use of anticoccidial drugs along with antibiotics as growth promoter increased the growth and immune status of chicken in contaminated environment (Lee *et al*., 2012). Antibiotics are given at sub therapeutic dosage for stabilization of the microflora of intestine and for improving the performance in general along with prevention of certain specific pathological conditions of the intestine. However, while using antibiotics as growth promoters it must be kept in mind that their use on long term basis must be avoided as it can give rise to resistance group of microorganisms viz., gram negative bacteria (*E. coli* and *Salmonella* spp.) (Gustafson and Bowen, 1997; Dibner and Richards, 2005; Hassan *et al*., 2010; Seniya *et al*., 2012).

Salient features of AGPs:

- Modifies intestinal microflora and help to improve bird’s performance and health status
- Have inhibitory effect on enzymes released by microorganisms and also on enzymes involved in microbial metabolism
- Reduces the growth-depressing metabolites produced by microorganisms (Feighner and Dashkevicz, 1987; Knarreborg *et al*., 2004; Huyghebaert *et al*., 2011)
- Addition of antibiotics to feed results in increased amino acid levels in the gut and improved nitrogen balance

- Improves absorption of feed nutrients because of thinning of intestinal wall, feed conversion ratio, weight gain, performance and productivity. Increases egg production and hatchability
- Reduces the damage caused by dietary fluctuations and destroy the harmful bacteria, keeping and minimize the adverse effects of dietary changes
- Prevents exponential multiplication of common pathogenic bacteria (*E. coli*, *Salmonella* spp., *Streptococcus* spp., *Hemophilus* etc.), reduce incidences of non-specific diarrhoea or enteritis of chicken (George *et al*., 1982; Brennan *et al*., 2003; Huyghebaert *et al*., 2011)
- Reduces stress and mortality in chicks by boosting body defense
- Reduces the microbial use of nutrients (Snyder and Wostmann, 1987; Huyghebaert *et al*., 2011)

The use of antibiotics through feed or drinking water when the birds are not infected can be disadvantageous, in certain aspects. It can lead to the development of antibiotic resistant strains of pathogenic microorganisms like *Staphylococcus aureus* and *Streptococcus* spp. of bacteria. The continued use of antibiotics as routine feed additives may also result in the presence of antibiotic residues in poultry products. Certain antibiotics even as residues can cause allergic or hypersensitive reactions in consumers. The continuous application of antibiotics can suppress sensitive natural microflora in the gastrointestinal tract like saprophytes, commensals, non-pathogenic bacteria, fungi and yeasts or can show a compensatory growth and few can even increase their virulence. Those activated microorganisms invade the host causing complications as generally seen in infections caused by *Proteus*, *Pseudomonas*, *Aspergillus* and *Candida albicans*. Also, the elimination of microorganisms in gastrointestinal tract by the continuous use of antibiotics may result in losses of B and K vitamins. Due to the above mentioned disadvantages, its utility as a growth promoter has not been permitted in many countries. Since 1999, some of the antibiotics growth promoters like spiramycin, tylosin, bacitracin and virginiamycin are banned in European Union due to development of resistance among bacteria of man and animals (McNamee *et al*., 2013). Apart from that, many other commonly used feed antibiotics had been banned by European commission due to development of resistant bacteria (Huyghebaert *et al*., 2011; Devirgiliis *et al*., 2013; Koluman and Dikici, 2013). At present use of antibiotics as growth promoter in food animals has become a great concern (Devirgiliis *et al*., 2013). World health organization along with World Organization for Animal Health (WOAH) encourages the health, agriculture, veterinary sector for reducing the injudicious use of antibiotics as growth promoters and further to decrease the spread of resistant bacteria (Aidara-Kane, 2012). Therefore, other non-therapeutic alternatives such as probiotics, prebiotics, symbiotics, antimicrobial peptides, enzymes, etheric oils, essential oils, eucalyptus oil, medium chain fatty acids, clay minerals, egg yolk antibodies, rare earth elements, recombinant enzymes and immunostimulants have been introduced as an alternative to the antibiotic growth promoters (Partanen and Mroz, 1999; Engster *et al*., 2002; WHO, 2002, 2003; Castanon, 2007; Cross *et al*., 2007; Yang *et al*., 2008; Windisch *et al*., 2008; Nava *et al*., 2009; Huyghebaert *et al*., 2011; Wen and He, 2012; Tellez *et al*., 2012; Mookiah *et al*., 2014; Thacker, 2013).

In edible tissues as well as products, the antibiotic residue involved risks are the allergic and toxic reactions but such reactions in consumers are negligible as only those antibiotics that can not undergo absorption in the digestive tract are permitted to be used as growth promoters. However, in the long term the use of antibiotics in wider sense as feed additives use to contribute to development of bacteria that are resistant to drugs and such antibiotics can not be used for treating diseases that are infectious in nature. But it must not be forgotten that such microbials bearing resistant genes have potential safety concern as the genes can get transferred to persons during the course of treatment (Donoghue, 2003; Castanon, 2007).

Under good environmental conditions of production and sound health status of birds it has been shown that it is possible to attain good as well as competitive results of production for poultry rearing without continuous use of antibiotic in feeds (Wierup, 2001; Engster *et al*., 2002; WHO, 2002). Studies conducted concerning antimicrobials that are safer as alternatives for antibiotic replacement for interaction with the microflora of intestine include: Prebiotics and probiotics; enzymes or dietary acidifications (Bedford, 2000; Patterson and Burkholder, 2003; Ricke, 2003; Diebold and Eidelsburger, 2006; Hruby and Cowieson, 2006; Kocher, 2006; Niewold, 2007). Pedroso *et al*. (2013) reported that withdrawal of antibiotics or using alternatives to antibiotic growth promoter could alter the microbial flora of body.

Probiotics: Extensive use of antibiotics has led to imbalance between pathogenic and normal microflora as well as emergence of antibiotic resistant strains of bacteria. So, there is an increased interest in finding antibiotic alternatives for production of poultry. In poultry natural feed additives like live probiotics have got the potential of reduction of poultry enteric diseases subsequently causing contamination of poultry products (Dhama and Singh, 2010; Gupta and Das, 2013). Probiotics are the live microbial feed supplements which are used for balancing the microbial population in the intestine through the production of various compounds, competitive exclusion and displacement of pathogens from enterocytes, as well as maintenance of gut pH and thereby improving the health and immune status of the birds. Along with this, the broiler production factors are also improved. This helps in production of healthy meat without having any drug residues (Alavi *et al*., 2012). From a practical point of view, knowledge on the potential use of probiotics to optimize the balance of microflora in avian gut is essential. The idea that intestinal bacteria play a role in maintenance of health was originated by Metchnikoff in 1907 when he studied "lactic acid bacteria" in fermented milk products and their use to increase longevity and maintenance of youthful vigor in humans. The gastro-intestinal microflora of the host is responsible for the natural resistance of animals against infection (Fuller, 1989; Bengmark, 1998; Anandakumar and Lakshminarayan, 1997). Soon after birth, young ones acquire microflora from the surrounding environment. With the increase in the age, the microflora stabilizes themselves in the intestinal environment and a balance comes into existence between host's favorable and harmful microflora (Fuller, 2001; Ivanov, 2003; Gibson and Roberfroid, 1995; Manjunatha, 2005; Dhama *et al*., 2007, 2008). If the microbes, which contribute to the proper microbial balance, are added to the feed, then the host receives a 'boost' to establish a proper microbial population in its gut and beneficially affect the host by improving the properties of the indigenous gastrointestinal microbiota (Kumar *et al*., 2011a). This finding has given rise to the concept and development of probiotic mediated growth promoters. Apart from establishing a balance in the gut environment/microflora, they specifically generate antibacterial substances (e.g., bacteriocins or colicins, lactoferrin, hydrogen peroxide, lactoperoxidase), competes for nutrients and make nutrients non-available to pathogens, modulate immune responses and compete with pathogenic bacteria (competitive exclusion) for adhesion receptors to intestinal epithelium (Jin *et al*., 1997; Balevi *et al*., 2001; Gao *et al*., 2008; Haghighi *et al*., 2006; Mountzouris *et al*., 2007; Modesto *et al*., 2009; Dhama *et al*., 2011; Tellez *et al*., 2012). Probiotics have also been found to improve digestion and utilization of nutrients and help in metabolism of minerals and synthesis of vitamins (Biotin, Vitamin-B_1, B_2, B_{12} and K), which are responsible for proper growth and metabolism. These can neutralize toxins released by pathogenic bacteria by releasing anti-enterotoxin substances (acidolin, acidophilin and lactin) and are also proved to bind mycotoxins present in feed. This has been found useful in reducing ammonia production in litter by their antagonistic action towards ammonifying bacteria and reducing urease activity and thus prevents developing of keratoconjunctivitis (NRC, 1994; Zoppi, 1998; Patterson and Burkholder, 2003; Ashayerizadeh *et al*., 2009). The feeding of probiotic culture of *L. acidophilus* and *L. casei* alone or in combination through the poultry feed or even through the water significantly decreased the triglycerides level in serum (Mansoub, 2010). This reduction in lipid content attributed to the change in fat digestion and gallbladder acids (Moharrery, 2006). Dietary *Bacillus subtilis* in broiler chickens, reduced the triglyceride levels in serum, liver and carcass due to their effectiveness in limiting the rate of synthesis of fatty acids by reducing the activity of acetyl coenzyme A carboxylase.

The most commonly used probiotics contain one or a mixture of harmless microbes. The microbes generally considered for developing probiotic growth promoters are *Lactobacillus acidophilus*, *L. sporogenes*, *L. bulgaricus*, *L. casei*, *L. plantarum*, *L. cellobiosus*, *L. salivarius*; *Streptococcus faecium*, *S. thermophilus*; *Bacillus coagulans*; *Bifidobacterium bifidum*; *Saccharomyces cerevisiae*, *Enterococcus faecium*, *Torulopsis* spp. *Aspergillus oryzae* and *Bacillus licheniformis* (Owens and McCracken, 2007; Dhama *et al*., 2011; Tellez *et al*., 2012; Liu *et al*., 2012; Lv *et al*., 2012; Mookiah *et al*., 2014).

Probiotic supplementation plays a crucial role in countering enteric bacterial infections, especially inhibiting pathogens such as *Staphylococcus aureus*, *Escherichia coli*, *Salmonella enteritidis*, *S. typhimurium*, *Clostridium perfringens*, *Listeria monocytogenes*, *Campylobacter jejuni*, *Yersinia enterocolitica*, *Candida albicans* and the coccidian parasites *Eimeria* sp. (Mulder, 1991; Nava *et al*., 2009; Van Coillie *et al*., 2007; Vicente *et al*., 2007; Willis and Reid, 2008; Tellez *et al*., 2012; Dhama *et al*., 2011, 2013b, 2013c). Different *Lactobacillus* strains have protective effects on raw chicken meat against *Listeria monocytogenes* and *Salmonella enteriditis* (Maragkoudakis *et al*., 2009). Supplementation of *L. johnsonii* FI9785 strain had reduced the necrotic enteritis caused by *Clostridium perfringens* (La Ragione *et al*., 2004;

Rai *et al*., 2013). *Bacillus longum* have capability to survive in gastrointestinal tract of chicken and have considerable antimicrobial activity against *Campylobacter* infection and therefore helpful in reducing the contamination of the intestinal pathogen at the farm level and in the chicken meat (Santini *et al*., 2010). *Bacillus licheniformis* have been found beneficial in increasing the productivity and meat quality in broilers poultry (Liu *et al*., 2012). Dietary probiotics have been found beneficial in increasing the performance of broiler chickens experimentally challenged with *E. tenella* (Giannenas *et al*., 2012).

In broiler chick's diet, probiotics improved the immune response significantly (Cotter *et al*., 2000; Panda *et al*., 2000). Probiotics feeding also have been reported to improve antibody titres against viral diseases like Newcastle Disease (ND) and Infectious Bursal Disease (IBD) (Talebi *et al*., 2008). Probiotics augment the bird's resistance to fight off infectious pathogens and limit the negative growth effects of pathogenic microbes. By reducing the intestinal pathogenic microbial load, probiotics lower the pathogen spread in the poultry house via fecal contamination. A multi strain probiotic need to be used timely and regularly in feed for preventing various infectious agents including bacterial, fungal, protozoan and viral agents. Probiotics can reduce the flock mortality occurring due to immunosuppressive diseases (IBD, chicken infectious anemia, reoviral infections, Marek's disease, mycotoxins etc) (Dhama *et al*., 2011).

Use of probiotics is recommended in newly hatched chicks to establish gut microbial balance and prevent early chick mortality; stressful conditions like during de-worming, overcrowding, vaccination, temperature and environmental stresses, change of feed/ingredients, management (shifting/transportation, contamination, gastro-intestinal disturbances (scouring, loss of appetite, poor digestion and absorption of nutrients). Nowadays, application of probiotics is being recommended during antibiotic therapy for maintaining the required intestinal balance of microflora and reducing diarrhea, without affecting the efficacy of antibiotics. Probiotics have been considered as good alternatives to antibiotic growth promoters which help in limiting antibiotic residues in poultry products and the development of drug resistant microorganisms (Dhama *et al*., 2011).

Probiotics formulations include bacteria, fungi and yeast, therefore the use of term "Direct Feed Microbials (DFM)" has been preferred now-a-days than the former. The addition of probiotics to poultry diet has been found to improve growth performance and feed conversion in broilers, egg production in layers and modulates the immune system of the birds to fight against various pathogens (Salim *et al*., 2013). Seeing the residual effect of antibiotics observed in poultry products and generation of antibiotic resistant strains, both having public health significance, nowadays, the use of probiotics as substitute for antibiotics in poultry production has become an area of great interest (Yang *et al*., 2009; Dhama *et al*., 2011; Salim *et al*., 2013).

Advantages of probiotics:

- Inhibits growth of diseases producing organisms
- Prevents digestive upsets and diarrhoea due to bacterial invasions
- Improves intestinal ecology by creating a balance in the gut microbial population
- Harmonize functions of digestive system and improves absorption of nutrients
- Improves feed intake and feed conversion efficiency
- Increases growth rate, body weight gain and productivity
- Regulates the lipid metabolism and reduces the body cholesterol content
- Improves fertility, egg quality and reduces cholesterol concentration
- Enhances survival and significantly help lowering of chick mortality
- Helps to maintain healthy gastrointestinal tract after antibiotic therapy
- Reduces stress after vaccination, antibiotic therapy, transportation, change of feed etc
- Stimulates immunity and also augment the effects of drugs and vaccines
- Helps in quicker detoxification of mycotoxins
- Improves litter condition by reducing ammonia and faecal water contents
- Synthesis of the vital B group vitamins
- Production of short chain fatty acids. Much safer without any side effects
- No residue carry-over in meat or eggs
- Cost effective and reduces expenditure on antibiotics

(Seema and Johri, 1992; Bengmark, 1998; Pal and Chander, 1999; Dhama *et al*., 2011; Mookiah *et al*., 2014).

Prebiotics: Supplementation of the diet with small fragments of carbohydrates (such as oligosaccharides) is another method used to manipulate the gut ecosystem. Prebiotics selectively fermented by beneficial microflora into Short Chain Fatty Acids (SCFA) which effectively excludes the pathogenic microbes due to a lowered pH in

GI tract through lactic acid production and thus inhibiting colonization of pathogenic bacteria. But the effect is specific for the type and dose of carbohydrate and also the rate of fermentation by the beneficial organisms. Aside to this, the SCFA produced by fermented prebiotics have strong effect on the metabolism of the host. The acetate and propionate are having gluconeogenic effects while butyrate is a major source of energy for intestinal epithelial cells. Also, the non-digestible oligosaccharides have been found to stimulate absorption of several minerals like calcium, magnesium, zinc and iron (Fallah and Rezaei, 2013).

The term ‘prebiotics’ was introduced by Gibson and Roberfroid (1995), who defined them as “a non-digestible food ingredient/supplement that beneficially affects the host by selectively stimulating the growth of some or all of the non-pathogenic organisms (bacteria) in the gut/colon.” The commercially available prebiotic products mainly including oligosaccharides of galactose, fructose or mannose viz., galacto-oligosaccharides (GOS), mannan oligosaccharides (MOS) and fructo-oligosaccharides (FOS) have been tried in poultry with much success (Gibson and Roberfroid, 1995; Dhama *et al*., 2007, 2008; Roberfroid, 2007). These non-digestible substrates (oligosaccharides) are considered as ‘food for beneficial microbes’, which on fermentation inhibit pathogens while simultaneously stimulating the absorption of several minerals in intestine. Prebiotics exert their beneficial effects on the host by selectively feeding the harmless bacteria at the expense of the harmful ones. *Salmonella*, *E. coli* and many other gram-negative harmful microbes are unable to utilize these oligosaccharides and therefore their growth is inhibited (Nisbet *et al*., 1993). Bacteria use lectins on their cell surface to bind to mannan on the intestinal epithelial cells to initiate attachment and colonization and during such a scenario, the MOS itself binds to receptors on bacterial pathogens and prevent their attachment to epithelial cells and prevent their colonization. Later the MOS pass through the gut with the pathogens attached, thus assisting in their effective clean up. Prebiotics such as FOS on the other hand, serves as a fiber source for certain microbial populations and enhance production of organic acids in the gut (Dhama *et al*., 2007). Feeding of MOS and FOS was found to increase immune status and enhance the macrophage activity along with T-helper cell activities (Hofacre *et al*., 2003; Shohani *et al*., 2013).

It has been reported that mannan oligosaccharides from yeast cell wall works by providing specific binding sites to enteric pathogens, thus reduces their chances to attach to the intestinal tract and these oligosaccharides being not digested by the endogenous enzymes of the bird pass through the gut with the pathogens attached thus producing a cleaning up effect (Zopf and Roth, 1996). The mannans also help in changing the acidity of intestine via increasing lactic acid density as well as decreasing activities of harmful bacteria of intestine (that include: *Escherichia coli*, *Salmonella*, *Clostridium* etc). They also help in colonization of *Lactobacillus* thus improve their activities (Elwinger *et al.,* 1998; Roberfroid, 2000; Al-Ghazzewi and Tester, 2012; Khan *et al*., 2012c). Nowadays, combination of probiotics and prebiotics (synbiotics), having shown synergistic effects, are effectively used to counter the impact of stress factors or pathogens in poultry production systems (Mookiah *et al*., 2014).

Salient features of prebiotics:

- Beneficially affects the host by stimulating the growth/activity of harmless bacteria, indicating a synergistic effect with probiotics
- Provides substrates for the bacterial fermentation in colon or caecum to produce vitamins and antioxidants that further benefit the host animal by indirectly providing energy, metabolic substrates and essential micro nutrients
- Prebiotics can provide energy and other limiting nutrients to the intestinal mucosa
- Simultaneously produce systemic effect on utilization of feed ingredient, stimulation of immunity and neutralization of toxins
- Prebiotics help inhibiting colonization of pathogenic bacteria
- Because of their organ as well as organism specific action, the prebiotics are potential candidates for incorporation in diet of chicken
- Additionally, some prebiotics can provide specific members of the native microflora such as Bifidobacteria and Lactobacillus (probiotics), a competitive advantage that can exclude pathogenic bacteria from the intestine (Dhama *et al*., 2007)

Organic acids: In recent years, the use of acidifiers has been increased many fold and are found to have the ability to reduce many pathogenic and spoilage organisms by lowering the gut pH. Because of the development and emergence of antibiotic resistant microbes (Tiwari *et al*., 2013), the utilization of organic acids has been increased as growth promoters in animal agriculture, which could help in providing protection from adverse human health implications. In poultry diets, the use of organic acids elicits a positive response in performance of broiler growth. In order to inhibit growth of bacteria of intestine (those which compete with host for the nutrients that are available) there is requirement of dietary acidification thereby causing reduced possibility of availability of bacterial metabolites which are toxic in nature. In the ceaca as well as small intestine it has been suggested by a number of studies that organic acids affect the bacterial concentration. In the crop of the poultry birds they are bactericidal for *Salmonellae* (Gaglo-Disse *et al*., 2010; Wang *et al*., 2010; Cengiz *et al*., 2012). In the young ones, acid production in the gut is insufficient and acidifiers are sometimes used in feeds to compensate it. The use of organic acids such as formic, lactic, propionic, citric, sorbic and phosphoric acids optimizes the balance of the microflora of the gastrointestinal tract (Byrd *et al*., 2001; Griggs and Jacob, 2005; Van Immerseel *et al*., 2006; Nava *et al*., 2009; Emami *et al*., 2013). They lower the pH, at which the activity of proteases and beneficial bacteria is optimized and proliferation of pathogenic bacteria is minimized by a direct antibacterial effect destroying their cell membranes (Partanen and Mroz, 1999; Chowdhury *et al*., 2009; Nava *et al*., 2009). In experimental studies, organic acids have been found suitable growth promoters in pigs (Partanen and Mroz, 1999; Overland *et al*., 2000; Partanen *et al*., 2002) and poultry (Gauthier, 2005). Supplementation of organic acid also increases intestinal colonization of *Lactobacillus* spp. in chicks (Nava *et al*., 2009). They are widely used to inhibit pathogens like salmonellae and in their undissociated forms are able to pass through their cell membrane. Inside the bacterial cell, the acid dissociates to produce H^+ ions, which lower the pH causing the organism to use its energy in trying to restore the normal balance. It also disrupts DNA and protein synthesis and thus the bacteria are unable to replicate or its replication slows down. Lower pH conditions thus protect the bird from infection especially at young ages. In addition to direct microbial action, recent studies have shown that salt form of organic acids including butyrate, propionate and acetate have shown their ability in reducing *Salmonella* colonization in chicken cecum by enhancing innate immune defense via increased synthesis of host defense peptides (Sunkara *et al*., 2011, 2012). Furthermore, organic acids also reduce the contamination of litter with the harmful microorganisms, neutralize ammonia production and diminish the risk of re-infection. The effectiveness of organic acids in poultry may also depend on the composition of the diet and its buffering capacity. The combination of citric, lactic, formic and orthophosphoric acid at doses of 2-8 kg ton^{-1} of feed are found effective. Propionic acid suppresses the growth of moulds and prevents the formation of mycotoxins. Short-chain fatty acids such as butyrate are considered potential alternatives to antibiotic growth promoters. Butyric acid at 0.2% level of incorporation can help to maintain the performance and carcass quality of broilers (Leeson *et al*., 2005). The Medium-chain Fatty Acids (MCFA), caproic, caprylic and capric acid, are also capable of inhibiting the growth of pathogenic bacteria at low concentrations *in vitro*. The organic acidifiers are thus considered effective and recognized as safe, with no concern over getting into human food chain.

The bacteriostatic effects of organic acids are well known and as *Salmonella* control agents they have been used in the feed as well as water supply of poultry (Ricke, 2003). Explanation has been given by Brul and Coote (1999) regarding the salient basic principle of the mechanism of action of organic acids on bacteria which indicates that organic acids that are non-dissociated undergo penetration of the cell wall of bacteria that is otherwise known as pH sensitive which means that a wide margin of external as well as internal pH can not be tolerated. Various organic acids viz., formic, fumaric, propionic, lactic as well as sorbic acids acidify the diet and help to decrease pathogen colonization as well as toxic metabolite production; digestibility of protein as well as calcium and phosphorus; magnesium and zinc are improved. Various studies have demonstrated that organic acid supplementation in diet of broilers improves the growth performance and reduces diseases as well as problems associated with management (Vlademirova and Sourdjiyaska, 1996; Runho *et al*., 1997; Gunal *et al*., 2006; Islam *et al*., 2008; Ao *et al*., 2009).

With the advancement of research in exploiting the usage of organic acids, certain volatile short-chain fatty acids like butyric acid, are identified as a bacteriostatic agents against the gram-negative bacteria (Hirshfield *et al*., 2003) without altering the normal intestinal microflora of the birds (Ricke, 2003). The bacteriostatic activity of these acids is more in its undissociated state, through their ability to pass through the intact bacterial cell wall (Warnecke and Gill, 2005) and causes increased acidity inside the cell. Because of decreased intracellular pH, purine bases are disintegrated, resulting in reduced DNA synthesis and cell proliferation. The more positive effects of acidifiers are noticed when they are either partially protected as sodium butyrate or as gastric coated form. Fernandez-Rubio *et al*. (2009) reported a significant reduction in shedding of *Salmonella* through the feaces in *Salmonella enteriditis* infected birds fed partially protected butyrate.

Table 1: Organic acids and their pKa value

Acid	Chemical name	Formula	Molecular weight	pKa
Formic	Formic acid	$HCOOH$	46.03	3.75
Acetic	Acetic acid	CH_3COOH	60.05	4.76
Propionic	2-propionic acid	CH_3CH_2COOH	74.08	4.88
Butyric	Butanoic acid	$CH_3CH_2CH_2COOH$	88.12	4.82
Lactic	2-hydroxypropanoic acid	$CH_3CH(OH)COOH$	90.08	3.83
Sorbic	2,4hHexandienoic acid	$CH_3CH:CHCH:CHCOOH$	112.14	4.76
Fumaric	2-butenedienoic acid	$COOHCH:CHCOOH$	116.07	3.02
HMB	2-hydroxy-4-methylthio butanoic acid	$CH_3SCH_3CH_2CH(OH)COOH$	149.00	3.86
Malic	Hydroxybutanedioic acid	$COOHCH_2CH(OH)COOH$	134.09	3.40
Tartaric	2,3-dihydroxy-butanedioic acid	$COOHCH(OH)CH(OH)COOH$	150.09	2.93
Citric	2-hydroxy-1,2,3-propanetricarboxylic acid	$COOHCH_2C(OH)(COOH)CH_2COOH$	192.14	3.13

Now-a-days, formaldehyde, a potent mold inhibitor (Spratt, 1985) is being used to protect the feed from fungal or mold attack and also improves the keeping quality of the feed. The formaldehyde is sprayed in the form of fine mist over the finished feed before the feed is packed or shifted into bulk conveyer tankers. The keeping quality of the feed increased without any fungal growth for a period of 20 days. Moreover, addition of formaldehyde did not affect the feed intake or growth rate of birds (Regal, 2014).

The selection of appropriate acidifiers plays an important role in its usage as an alternate to antibiotics and the pKa value in range of 3-5 was found optimal. The pKa values of different organic acids were presented in Table 1.

Vitamins and minerals: As premix in feed of poultry (particularly in feed of broilers), multivitamin-minerals have been used for improving the broiler growth as well as feed utilization thereby helps in realization of better return of production as well as economy. Their performance level is optimum when there is poor health condition of the birds (Prescott and Baggot, 1993; Peric *et al*., 2009). They also exert beneficial effect on health of gut as well as immunity along with immune performance. Positive effect is exerted via better appetite even though there is variation in mechanism of action. Along with this, there is improved conversion of feed, immune system stimulation, growing vitality as well as regulation of the microflora of intestine. In terms of improvement of utilization of feed as well as metabolism and minimization of various stresses all the vitamins (especially vitamin C) have essential roles to play (Sahin *et al*., 2003). Ascorbic acid or vitamin C is also having the ability to reduce the weight loss in birds due to heat stress. It resulted in enhanced performance in broiler chicks exposed to multiple concurrent environmental stressors (McKee and Harrison, 1995). In addition to ascorbic acid, tocopherols or vitamin E-supplemented diets resulted in better growth performance, by improving the feed conversion efficiency. Vitamin E is available in two forms: Tocopherols and tocotrienols. After absorption, vitamin E is hydrolyzed in its unesterified form. L-arginine can also be supplemented with vitamin C for obtaining better meat quality. There is reduction in the effect of diet that is modified on the iron concentration in the liver as well as spleen and in heart of copper (Al-Darajih and Salih, 2012a, b; Suliburska *et al*., 2014).

According to NRC (1994), in normal conditions for satisfactory performance of the birds, the recommended dose of vitamin E ranges from 5-25 IU kg^{-1} of feed. However, higher doses than this have been tested to improve the performance of the poultry. Vitamin E is added into the animal feed to enhance performance, to improve immune response and to increase the vitamin E content in animal meat (McDowell, 1989). Vitamin C or L-ascorbic acid is an antioxidant vitamin which is naturally synthesized by the birds (Khan, 2011). Avian species synthesize ascorbic acid by an enzyme, gulonolactone oxidase, which is required for the biosynthesis of this vitamin and is lacking in humans and some other species (Lin *et al*., 2006; Khan, 2011). Hence no recommendation for this vitamin has been established by NRC for birds (NRC, 1994) but it has been recommended in poultry feed to alleviate stress on the assumption that during stress the requirements may exceed the synthesizing ability (Gous and Morris, 2005). Chickens require vitamin C for the metabolism of amino acid and absorption of minerals especially for maintaining dietary iron in reduced (ferrous) form and for the synthesis of hormones (McDowell, 1989). Recently, there is a considerable interest in a possible nutritional role of ascorbic acid on the basis that the requirement of this vitamin may augment during heat stress (Lin *et al*., 2006). Supplementation of heavy metals such as zinc has some beneficial effect by influencing intestinal microflora but may lead to spread of antimicrobial resistance (Bednorz *et al*., 2013). Similarly, iron is also having dual role as growth inhibitor as well as growth promoter (Visca *et al*., 2013). The role of dietary phosphorus for body weight gain in broilers is quiet noteworthy (Abudabos, 2012).

Antimicrobial peptides: Antimicrobial peptides (AMPs), also known as host defense peptides (HDPs) are small peptides (30-60 amino acids) and can be isolated from all living organisms. They are essential components of the innate immune system and possess antimicrobial and immunomodulatory properties (Li *et al*., 2012; Parachin *et al*., 2012). These can directly kill broad range of microbes including bacteria, fungus and viruses (Koczulla and Bals, 2003). Till date more than 700 antimicrobial peptides have been identified. After identification, some of these peptides are synthesized and tested for their antimicrobial and immunomodualtory functions. Studies have been conducted on fowlicidin 1 and 3 peptides (Bommineni *et al*., 2007; 2010). These antimicrobial peptides interact with surface membrane of bacteria either by forming discrete pores or by disrupting the membrane bilayer, leading to loss of membrane function, resulting in cell leakage and, consequently, cell death (Brogden, 2005; Li *et al*., 2012; Parachin *et al*., 2012). In relation to the full length peptide fowl-1(6-26), an analog from which five-amino terminal amino acid residues have been omitted, has helped in maintaining the antibacterial potency against a wide range of Gram-negative as well as Gram-positive bacteria that include strains which are resistant to antibiotic (Bommineni *et al*., 2010). Recently, other modes of action like inhibition of the synthesis of nucleic acids, proteins, cell-wall components and essential enzymatic activities have also been proposed (Nguyen *et al*., 2011). AMPs can be obtained from natural sources, chemical synthesis or by recombinant technology (Li *et al*., 2008). Some of the antimicrobial peptides such as colicin and cecropin, particularly cecropin A (1-11)-D (12-37)-Asn (CADN), act as growth promoter in poultry and have been suggested as possible alternate to antibiotic growth promoters (Wen and He, 2012).

Exogenous enzymes: The exogenous enzymes through the feeds include Non-Starch Polysaccharides (NSP) degrading enzymes, proteases and phytase that would help in better utilization and reduction in environmental pollution. In poultry feeding, the fiber component of the feed is considered as waste as these compounds are often called as NSP, an anti-nutritive factor. Barley, wheat and rye contain β-glucans, arabinoxylans or pentosans as NSPs, respectively. Most of the grain endosperm cell walls consist of mixed-linked arabinoxylan and β-glucan (Chesson, 1993). These NSPs have a negative effect on broiler performance (Choct and Annison, 1992) and depressed the growth rate (White *et al*., 1981) by encapsulating the nutrients, increasing the intestinal viscosity; increase endogenous nitrogen flow and bacterial fermentation in the gastrointestinal tract, reduced feed passage rate resulting in overall reduced feed intake to depress production in broilers and cause sticky droppings, vent pasting and dirty eggs (Yin *et al*., 2004). Arabinoxylan and β-glucans present in rice grain also interferes with nutrients digestion and absorption (Graham *et al*., 1988) and also decreases the production of digestive enzymes (Ikegami *et al*., 1990) in gastro-intestinal tract. The digestibility of starch, nitrogen (Hesselman and Aman, 1986) and fat (Edney *et al*., 1989) were reduced as a result of increased intestinal viscosity. The addition of β-glucanase along with the barley helps to overcome these depressive effects. Hence, these Non-Starch Polysaccharides (NSPs) are degraded using enzymes such as xylanases and beta-glucanases, play an important role in reducing the pathogenic bacteria such as *Clostridium perfringens* (Jackson *et al*., 2003). These enzymes also reduce the harmful effect of NSPs such as (hemi) celluloses, pectins and oligosaccharides, arabinoxylans and β-glucans. NSPs have anti-nutritive effect by increasing the bulk and viscosity of intestinal content ultimately reduces the digestion and absorption of nutrients in intestine (Choct *et al*., 1996; Ao *et al*., 2009; Hedemann *et al*., 2009; Huyghebaert *et al*., 2011).

Shifting the focus into the protein, the digestibility of proteins is high in typical corn-soybean meal-based diets. However, the soaring prices of conventional protein sources, the poultry producers are forced to use unconventional protein or animal by-product protein sources to run the farm in economical manner. Here comes the problem with proteins, as the digestibility of protein is variable among different ingredients due to their amino acids composition and structure (Parsons *et al*., 1997; De Coca-Sinova *et al*., 2008). These undigested or poorly digested proteins can be better utilized by using the exogenous protease enzyme (a protein degrading enzyme) (Lemme *et al*., 2004). Supplementation of protease enzyme resulted in improved crude protein digestibility and fat also (Freitas *et al*., 2011).

Phosphorus (P) is an essential mineral for poultry to aid several functions. The phosphorus in naturally occurring plants is in the form of Phytate Phosphorus (PP) or organic complex as phytic acid with about 60-80% of phosphorus present in cereal grains and oilseeds are as phytic acid (Simons *et al*., 1990). These PP reduces the utilization of minerals like calcium, zinc, copper, etc., by forming a complex with them (Cheryan, 1980) in gut. In earlier days, the produces were forced to include inorganic phosphorus sources to overcome this phytate effect and meet the bird's phosphorus needs. Moreover, due to low activity of endogenous phytase, more than two third of plant PP were excreted. These conditions lead to higher production cost (P being a costlier mineral) and also more environmental pollution (Paik, 2001). Hence, the poultry producers had to reduce the phosphorus excretion by improving their utilization by the birds. Supplementation of phytase enzyme, degrades insoluble, phytate to soluble inositol monophosphate and orthophosphate to mono phosphates (Liu *et al*., 1998). This increases the availability of minerals not only phosphorus but also the calcium, zinc, copper and reduced the need for dietary inorganic P supplementation (Saylor, 2000). Studies have shown that the addition of phytase enzyme reduces the P excretion upto 50% and also lessen environmental pollution (Vohra *et al*., 2006).

Essential oils: Essential oils are a mixture of oily aromatic compounds obtained from different plant materials such as their flowers, buds, seeds, leaves, twigs, bark, herbs, wood, fruits and even their roots (Gopi *et al*., 2014). These are also called as volatile or ethereal oils, which are obtained from plants. It is a mixture of low-boiling-phenylpropenes and terpenes. Till date, about 3000 essential oils are known and they are having beneficial effect in lipid metabolism, stimulation of digestion and have antimicrobial, antioxidant and anti-inflammatory effect (Bishop, 1995; Mourey and Canillac, 2002; Botsoglou *et al*., 2004; Rota *et al*., 2004; Platel and Srinivasan, 2004; Acamovic and Brooker, 2005; Brenes and Rourab, 2010). Dietary supplementation of essential oils like capsaicin, cinnamaldehyde, carvacrol, garlic powder, thymol powder etc., improved the performance of broilers and carcass yield (Jamroz *et al*., 2003; Demir *et al*., 2003; Lewis *et al*., 2003; Cross *et al*., 2004; Alcicek *et al*., 2003, 2004; Toghyani *et al*., 2011; Mehdipour *et al*., 2013). In turkey, the feed conversion ratio was increased by supplementation of oregano leaves (Bampidis *et al*., 2005). Essential oils from *Euphorbia hirta* reduced the concentration of *Clostridium perfringens* in the intestines of broiler chickens (Mitsch *et al*., 2004). Essential oils such as oregano and garlic oil inhibit microorganisms like *E. coli* and other Enterobacterial counts, Clostridium count, *Staphylococcus aureus, Salmonella typhimurium* and *Listeria monocytogenes* (Singh and Shukla, 1984; Kumar and Berwal, 1998; Aligiannis *et al*., 2001; Ross *et al*., 2001; Friedman *et al*., 2002; Oussalah *et al*., 2007; Kirkpinar *et al*., 2011). For the animals, essential oils not only act as anti oxidants *in vivo* but their anti-oxidant action help to prolong the feed shelf life (Gopi *et al*., 2014).

Clay minerals: Clay minerals containing molecules like silicon, aluminum and oxygen, are formed by tetrahedral and octahedral layers. There can be binding as well as immobilization of materials that are toxic in nature in the gastrointestinal tract when there is addition of clay. This causes reduction in biological activity as well as toxicity. Aflatoxins can be bound by clay minerals and so also metabolites of plants; heavy metals as well as toxins. The chemistry of clay minerals determines the degree of adsorption. Along with these exchangeable ions, surface properties as well as the fine structure of the clay particles also determine the absorption rate (Vondruskova *et al*., 2010). Clay after addition in diet binds with toxic substances such as aflatoxins, plant metabolites and heavy metals etc. Therefore, these substances may be useful in case the feed contain some amount of mycotoxins. Research is going on for exploiting the use of clay mineral (especially silicate minerals) in diet of animals for improving the growth (Safaei *et al*., 2014).

Herbs as growth promoters: Since ancient times aromatic plants/phytobiotics have been used because of their preservative as well as medicinal properties along with the characteristic of imparting aroma as well as flavour to food. Utility of plant extracts as perfume fumigations had been done by the father of medicine: Hippocrates. In traditional as well as veterinary medicine for centuries long aromatic plants (also called as herbs and spices), their essential oils as well as extracts from herbs has originated from sources like ethno veterinary medicine or even from folkloric sources (Fallah *et al*., 2013; Midrarullah *et al*., 2014). Now-a-days, natural products obtained from plants and fungi are gaining interest of consumers as natural additives (Toghyani *et al*., 2010). Natural medicinal products originating from herbs, spices and their products including essential oils have been used as feed additives in poultry production (Hashemi and Davoodi, 2011; Khan *et al*., 2012a). Supplementation of *Aspergillus niger* fermented *Ginkgo biloba* leaves in diet of broiler enhanced the growth performance (Zhang *et al*., 2012). Compared with antibiotics or inorganic chemicals, these plant-derived products have proven to be natural, less toxic and are thought to be the ideal feed additives in the feed of poultry. Now-a-days, there is an increasing interest in the use of medicinal plants as feed additives in poultry diet to enhance the performance of poultry birds (Khan *et al*., 2010, 2012b).

Through the use of phytobiotics, enhancement of growth is probably found as the result of synergistic effects among molecules that are active as well as complex and those that exists in phytobiotics. Well known antimicrobial activities are possessed by phytochemicals in phytobiotics (Cowan, 1999). The antimicrobial activities of phytochemicals vary. For instance tannins act by deprivation of iron; binding with hydrogen or via interactions non-specifically with proteins of the virus such as enzymes (Scalbert, 1991).

Garlic (*Allium sativum*), Turmeric (*Curcuma longa*), Thyme (*Thymus vulgaris* L.) Aloe vera, onion (*Allium sepa*), Ginger (*Zingiber officinale*, Rosc.), *Astragalus membranaceus*, Noni (*Morinda citrifolia*) etc., are some of the major plant additives which have been extensively reported in poultry feed for enhanced growth effect in broiler and better egg production in laying hens (Guo *et al*., 2004; Sunder *et al*., 2013, 2014). The active components of the medicinal plants are chemical compounds present in the entire plant or some parts of the plant that confer therapeutic activity or beneficial effects. The positive effects of these herbs are due to the presence of essential oils, fatty acids, alkaloids, flavanoids, fats, minerals fibers, vitamins, protein and carbohydrates. Plant's effects may be due to greater efficiency in the utilization of feed which result in enhanced growth. However, the exact mechanism of action of these medicinal plants is not clear, but experimental studies have suggested that they have increased gut microflora, which positively affects host nutrition, health and growth by better utilization of nutrients (Hashemi and Davoodi, 2011). It has been reported that curcumin in turmeric enhances the activities of digestive enzymes like pancreatic lipase, amylase, trypsin and chymotrypsin (Khan *et al*., 2012a). There are evidences that plant contents have digestion-stimulating properties that have intrinsic bioactivities on animal physiology and metabolism (Hernandez *et al*., 2004). Al-Kassie *et al.* (2011) suggested that dietary feeding of essential oil extracted from herbs improve the secretion of digestive enzymes, so improve the digestibility of the feeds and enhance the performance of broiler. Zhao *et al.* (2011) reported that ginger enhances nutrient digestion and absorption because of the positive effect on the gastric secretion, enterokinase and digestive enzyme activities.

Studies have shown that the active agents in the herbs have a strong capability for scavenging superoxide radicals, hydrogen peroxide and nitric oxide from activated macrophages, reducing iron complex and inhibiting lipid peroxidation (Gowda *et al*., 2009; Khan *et al*., 2012a, b). It has been shown that plant phenolic components like carvacrol and thymol are responsible for the antioxidant activity (Schwarz *et al*., 1996). Apart from these compounds, other phenolics in thyme leaves such as caffeic acid, p-cymene-2,3-diol and biphenylic as well as flavonoid compounds have been found to exhibit antioxidant activity (Bolokbasi *et al*., 2006). Zhang *et al.* (2009) stated that supplementation of ginger at the rate of 5 g kg^{-1} significantly increased activities of SOD and GSHPx and reduced MDA in broilers at the age of 21 and 42 days.

Apart from the digestive and antioxidant prosperities, the herbs and plant additives may exert the beneficial influence through antimicrobial, immunomodulating and antiparasitic effects. Several natural adjuvants as well as synthetic agents are found to have immunostimulatory properties but various side effects are possessed by them. But the plant immunomodulators that are conventional are cheaper and safe to use. This is the reason why herbal medicines are used as immunomodulatory substances thereby providing alternative potential for the conventional chemotherapy. Patents have been filed regarding several plant extracts as well as compounds and formulations that include: Polysaccharides and lectins; peptides and flavonoids and tannins. Various *in vitro* models have been used to assess their immunomodulatory characteristics. Plants like Ashwagandha (*Withania somnifera*), Neem (*Azadirachta indica*), Guduchi (*Tinospora cordofolia*) and others are widely used these days due to their potent immunomodulatory and health beneficial properties (Barnes *et al*., 2007; Kumar *et al.*, 2011b; Sengupta *et al.*, 2011; AbdElslam *et al*., 2013; Bhatt *et al*., 2013; Lateef *et al*., 2013; Latheef *et al*., 2013; Tiwari *et al*., 2014a, b). In broilers leaves of nishyinda (*Vitex negundo*); black pepper (*Piper nigrum*) and cinnamon (*Cinnamomum verum*) have been used as growth promoters and such polyherbal extracts are found to be safe as growth promoters in production of broilers without any effect on health of chicken adversely (Chowdhury *et al*., 2009; Mode *et al*., 2009; Molla *et al*., 2012). Helander *et al.* (1998) suggested that thymol and carvacrol, the active ingredients in thyme exert their antibacterial action through penetration of these components into the Gram negative bacteria. Juven *et al.* (1994) postulated that the active ingredients of the thyme bind to the amine and hydroxylamine groups of bacterial membrane protein and results in the cell lysis. Lee *et al.* (2010) reported that fecal oocyst shedding from birds experimentally infected with *E. acervulina* was significantly decreased when broiler chickens were fed with a diet containing *C. longa*. Khalafalla *et al.* (2011) reported that Curcumin has considerable effects on *Emeria tenella* sporozoite morphology and viability in a dose-dependent manner after incubation. Hanieh *et al.* (2010) suggested that immunomodulating effect of garlic is associated with its ability to enhance phagocytosis of peritoneal macrophages, increased production of interleukins, interferon (INF-γ) and tumor necrosis factor (TNF-α) secretary metabolism of macrophages and antigen presenting cells.

The current review of literature suggests that medicinal plants may be a useful alternative to antibiotics in poultry production due to its wide range safety margin. However, meager work has been conducted on the mechanism of action through which they beneficially affect poultry productivity. Therefore, further investigations on the medicinal plants are suggested to clarify the mode of action as well as the exact dose, duration or both for more efficacious use.

Panchgavya: In the Vedas, the utility of products derived from cows have been mentioned (Dhama *et al*., 2005). Several researchers as well as scientists have proven them as rich source of elements that are essential along with minerals as well as hormones. The use of Panchgavya thereby is gaining popularity day by day as the therapy associated with it helps in maintaining poultry health. There is continuous increase in antibiotic resistance (evolution of drug resistance) to microbes due to their indiscriminate use and in this regard panchgavya therapy is found essential to combat the same. When plants like *Andrographis paniculata* is used along with panchgavya use to act as an alternative to antibiotic growth promoter thereby enhancing broiler industry productivity. It furthermore possesses antiviral activity such as against New Castle disease in layer birds (Mathivanan *et al.,* 2006; Mahima *et al*., 2012, 2013; Dhama *et al*., 2005; 2013a, 2013d; Sumithra *et al.,* 2013).

Additives to promote growth in heat stress conditions: A constant challenge is being faced in tropical countries in case of production of poultry due to stresses caused by the hot climate. The comfort of broiler birds is affected badly by heat stresses thereby causing suppression of production efficiency. It has been postulated for long that there is reduction in growth performance due to heat stresses (Lara and Rostango, 2013; Norain *et al*., 2013).

Electrolytes: With the increasing global temperature, the birds are becoming more susceptible to heat stress that to more pronounced in tropical climatic conditions. The birds will be under heat stress when they are exposed to a temperature of above 25°C (above thermoneutral zone). These birds exhibit panting, a rapid, shallow breathing (Mushtaq *et al*., 2005), to reduce the body temperature because of the lack of sweat glands (Mushtaq, 2004). Panting causes excessive loss of carbon dioxide (CO_2) and leads to respiratory alkalosis (Calder and Schmidt-Nielsen, 1967) due to loss of bicarbonate ions along with potassium (K) or sodium (Na) from the body (Da Silva *et al*., 1994). These metabolic alterations lead to reduced feed intake, growth rate, survivability and in turn profitability (Deaton *et al*., 1986). Dietary manipulations like increasing the supplemental level of vitamins and minerals along with the altered energy and protein content in the diet were tried to compensate the reduced feed intake in this climatic conditions (Baghel and Pradhan, 1989). Loss of electrolytes can be prevented by dietary cations and anions as dietary cation anion difference (DCAD) (Hurwitz *et al*., 1973); which describes the supplementation of electrolytes (sodium bicarbonate ($NaHCO_3$), potassium chloride (KCl), calcium chloride ($CaC1_2$) and ammonium chloride (NH_4C1) either through feed or water (Ahmad *et al*., 2005). Sodium salts (NaCl, $NaHCO_3$) through diet had resulted in better body weight gain, feed intake and feed to gain ratio and also increased water intake (Ahmad *et al*., 2006).

Betaine: Betaine nowadays getting more importance in poultry industry as a feed additive due to its sparing effect on essential amino acids like methionine and choline, reducing heat stress associated mortalities and muscle drip loss (Zimmermann *et al*., 1996). It has a sparing effect on methionine as a labile methyl donor and also protect the cells from osmotic stress (osmotic protectant), maintaining their regular metabolic activities (Kidd *et al*., 1997). They are found widely in variety of plants and also synthesized by microbes (Boch *et al*., 1994). Although, betaine is not a dietary essential component for poultry but its supplementation helps in maintaining the osmolytic protective property especially in heat stressed birds (Zulkifli *et al*., 2004). Betaine supplementation promotes higher water retention in the cells especially resulting in more carcass yield (Mooney *et al*., 1998) and improves meat quality (Matthews *et al*., 2001). In addition, it plays a role in lean meat production by positively affecting the lipid metabolism with increased fatty acid's catabolism via carnithine synthesis pathway and thus reduces carcass fat deposition (Saunderson and MacKinlay, 1990).

Medicinal herbs: Leaf extracts of *Salix babylonica* as well as *Populus nigra* used to improve heat tolerance; intake of feed; body weight gain; feed conversion rate as well as reduction in mortality of those broilers which are heat stressed. Extracts of these plants can be used as an alternative in the nature for replacement of the synthetic acetylsalicylic acid thereby controlling temperature of the body of the broiler birds which are heat stressed (Mohammed, 2010; Al-Fataftah and Abdelqader, 2013).

Trace minerals like chromium: It is beleived currently that there are no National Research Council (NRC) recommendations for the use of chromium in diets of poultry. Basically most of the diets of poultry are composed of plant origin ingredients. It has however been proved that chromium nicotinate (an organic source of chromium) when supplemented proves to be beneficial to broiler chickens under the condition of stress due to hot weather inspite of lowering of consumption of feed (Zha *et al*., 2009; Moeini *et al*., 2011; Toghyani *et al*., 2012).

Additives for growth and better carcass quality products antioxidants: Antioxidants exert beneficial health effects by protecting the biologically important cellular components, like cell membrenal lipids, DNA, cellular proteins, etc., from reactive oxygen species (Su *et al*., 2007; Rahal *et al*., 2014). Synthetic antioxidants like butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT) and tertiary butyl hydroquinone (TBHQ) have been used in poultry diets to retard or minimize the oxidative deterioration along with natural antioxidants like vitamin C, vitamin E and phenolic compounds, etc. Dietary antioxidants have a beneficial effect in lowering the oxidative status of the meat (Fasseas *et al*., 2008). Moreover, oxidation products decrease the nutrient content of the diet by reacting with them like destruction of vitamin A or deterioration of fats. The feeding of broilers with oxidized oil based feeds leads to an increased drip loss in muscles (Zhang *et al*., 2011). Antioxidants increase body weight gain and feed intake as it protects dietary lipids from further oxidizing and hence improved broiler performance and shelf life of their products. Studies suggested that using blends of antioxidants improved broiler performance better than the use of individuals alone (Tavarez *et al*., 2011).

Ractopamine: The carcass fatness is one of the major concerns among the chicken consumers. The broiler body fat content can be manipulated by feed additives like Ractopamine hydrochloride and L-Carnitine by their lipolytic and growth promoter properties. They are used to improve the feeding efficiency, carcass leanness and animal growth hence termed as repartitioning agents (Darlymph *et al*., 1985). Ractopamine, clenbuterol and salbutamol, a β-agonists improved the body weight gain and reduces the body fat content (Carr *et al*., 2009). Clenbuterol can be exploited as nutrient repartitioning agent as it diverts the nutrients from fat deposition to the muscle tissues deposition (Sillence, 2004; Zuo *et al*., 2010). Salbutamol incorporation had favoured higher body weight gain with improved feed efficiency (Yasmeen *et al*., 2013). Hence, the addition of salbutamol during finisher stage in broilers, can favor more uniform carcass finishing.

L-carnitine: L-carnitine, a zwitter ion compound (Bremer, 1983), plays an important role in transportation of long chain fatty acids across the mitochondrial membrane (Owen *et al*., 2001). In poultry, it is primarily concerned with fatty acid metabolism. L-carnitine improved body weight gain and feed conversion in diets marginally deficient in lysine and methionine plus cystine respectively, indicative of sparing effect on lysine (remember carnitine is endogenously synthesized from lysine) (Schuhmacher *et al*., 1993). L-carnitine increased the yield of breast and leg muscles and also reduced the abdominal fat content (Rabie and Szilagyi, 1998; Xu *et al*., 2003; Kheiri *et al*., 2011). In breeder birds, the dietary inclusion of L-carnitine improved hatching rate of eggs (Leibetseder, 1995). Dietary carnitine resulted in increased yolk's carnitine content and will be beneficial to the developing embryo especially in fat utilization for its energy purpose (Rinaudo *et al*., 1991). It also showed positive effects on improving the egg hatchability in birds exposed to aflatoxicosis (Smith *et al*., 1993; Leibetseder, 1995).

Nucleotides in broiler diet: Nucleotides are essential to cellular metabolism as they participate in many intracellular biochemical processes (Lerner and Shamir, 2000) like in biosynthetic pathways, energy transfer system, as co-enzyme components and as well as biological regulators (Cosgrove, 1998). During periods of rapid growth phase, certain disease states or limited nutrient intake resulted in disturbed endogenous synthesis of nucleotides (Leleik *et al*., 1983; Van Buren and Rudolph, 1997; Lerner and Shamir, 2000). Nucleotides alter the cellular lipid metabolism, particularly of long-chain polyunsaturated fatty acids and the lipoprotein synthesis (Fontana *et al*., 1999). They perform many functions:

- They enhance the activity of Δ-5-desaturase enzyme, which results in increased protein synthesis and also facilitate protein synthesis by increasing the precursors of RNA synthesis (Gil *et al*., 1986; Garcia-Molina *et al*., 1991)
- They changes the intestinal microflora that affect long-chain polyunsaturated fatty acids levels, as those bacteria's possess necessary enzymes for fatty acid elongation and desaturation (Cosgrove, 1998)
- They modulate fatty acid chain elongation and desaturation in the enterocyte or in the hepatocyte (Cosgrove, 1998) and also increased phospholipid synthesis in liver (Garcia-Molina *et al*., 1991)
- Nucleotides promote intestinal absorption of iron (Cosgrove, 1998) by conversion of purine

nucleotides (AMP, GMP) to inosine, hypoxanthine and uric acid which increase the absorption of iron

Supplemental nucleotides had beneficial effects on growth performance and intestinal morphology. Increased body weight gain and feed conversion ratios were reported on nucleotide inclusion (Esteve-Garcia *et al*., 2007). But conflicting results on effectiveness of dietary nucleotides to regulate tissue desaturase have been reported and hence stimulate the accumulation of both n-6 and n-3 long chain polyunsaturated fatty acids (Gibson *et al*., 2005). With all these reports, currently the nucleotides are not considered as essential nutrients for use in poultry (Jung and Batal, 2012), but it has the potential to be used for better growth and product quality improver for poultry.

A list of important growth promoters and feed additives along with their modes of action and useful applications is given in Table 2. An illustration representing an overview of their mechanism of actions and beneficial applications is presented in Fig. 1.

Table 2: Growth promoters and novel feed additives in poultry production and health at a glance

Growth promoters	Examples	Mechanism of action	References
Antibiotic as growth promoter	Bacitracin, Penicillin, Virginiamycin, Flavomycin, Chlortetracycline, Oxyteracycline, Colistin sulphate, Doxycycline, Erythromycin, Aureomycin, Avilamycin, Tiamulin, Furazolidone, Lincomycin, Enrofloxacin and Neomycin sulphate	Regulation and maintenance of optimal balance of avian intestinal microflora (between gram-negative and gram positive organisms)	Gustafson and Bowen (1997), Jones and Ricke (2003), Stanley *et al*. (2004), Dibner and Richards (2005), Chowdhury *et al*. (2009), WHO (2004) and Hassan *et al*. (2010)
Probiotics	*L. acidophilus*, *L. casei*, *Bacillus subtilis*, *Lactobacillus acidophilus*, *L. sporogenes*, *L. bulgaricus*, *L. casei*, *L. plantarum*, *L. cellobiosus*, *L. salivarius*, *Streptococcus faecium*, *S. thermophilus*, *Bacillus coagulans*, *Bifidobacterium bifidum*, *Saccharomyces cerevisiae*, *Enterococcus faecium*, *Torulopsis* spp., *Aspergillus oryzae* and *Bacillus licheniformis*	Host receives a 'boost' to establish a proper microbial population in its gut and beneficially affect the host by improving the properties of the indigenous gastrointestinal microbiota due to addition of probiotics	Owens and McCracken (2007), Dhama *et al*. (2011), Kumar *et al*. (2011a), Liu *et al*. (2012), Lv *et al*. (2012), Tellez *et al*. (2012) and Mookiah *et al*. (2014)
Prebiotics	Oligosaccharides of galactose, fructose or mannose viz., galacto-oligosaccharides (GOS), mannan oligosaccharides (MOS) and fructo-oligosaccharides (FOS)	Effective clean up of harmful pathogens, act as a source of fibre for certain microbial population, enhance production of organic acids in the gut, they also help in colonization of *Lactobacillus* thus improve their activities	Gibson and Roberfroid (1995), Roberfroid (2000), Nisbet *et al*. (1993), Hofacre *et al*. (2003), Dhama *et al*. (2007), Roberfroid (2007) and Al-Ghazzewi and Tester (2012)
Organic acids	Formic, lactic, propionic, citric, sorbic and phosphoric acids	They lower the pH, at which the activity of proteases and beneficial bacteria is optimized and proliferation of pathogenic bacteria is minimized by a direct anti bacterial effect destroying their cell membranes	Partanen and Mroz (1999), Byrd *et al*. (2001), Griggs and Jacob (2005), Van Immerseel *et al*. (2006), Chowdhury *et al*. (2009), Nava *et al*. (2009), Nava *et al*. (2005) and Emami *et al*. (2013)
Vitamins and minerals	Vitamin C	Improvement of utilization of feed as well as metabolism and minimization of various stresses, has antioxidant	McKee and Harrison (1995), Sahin *et al*. (2003) and Khan (2011)
	Vitamin E	property Enhances performance, improve immune response	McDowell (1989)
	Zinc	Influences intestinal microflora but may lead to spread of antimicrobial resistance	Bednorz *et al*. (2013)
	Iron	Dual role as growth inhibitor as well as growth promoter	Visca *et al*. (2013)
	Chromium	As feed supplement proves to be beneficial to broiler chickens under the condition of stress due to hot weather inspite of lowering of consumption of feed	Zha *et al*. (2009), Moeini *et al*. (2011) and Toghyani *et al*. (2012)
Antimicrobial peptides	Fowlicidin 1 and 3	These antimicrobial peptides interact with surface membrane of bacteria either by forming discrete pores or by disrupting the membrane bilayer, leading to loss of membrane function, resulting in cell leakage and, consequently, cell death, Inhibition of the synthesis of nucleic acids, proteins, cell-wall components and essential enzymatic activities	Brogden (2005), Bommineni *et al*. (2007), (2010), Li *et al*. (2012), Parachin *et al*. (2012) and Nguyen *et al*. (2011)

Table 2: Continue

Growth promoters	Examples	Mechanism of action	References
Exogenous enzymes	Non-starch polysaccharides, (NSP) degrading enzymes, proteases and phytase, β-glucans, arabinoxylans or pentosans	Negative effect on broiler performance and depressed the growth rate by encapsulating the nutrients, increasing the intestinal viscosity, increase endogenous nitrogen flow and bacterial fermentation in the gastrointestinal tract, reduced feed passage rate resulting in overall reduced feed intake to depress production in broilers and cause sticky droppings, vent pasting and dirty eggs	White *et al.* (1981), Edney *et al.* (1989), Ikegami *et al.* (1990), Choct and Annison (1992), Yin *et al.* (2004), Ao *et al.* (2009), Hedemann *et al.* (2009) and Huyghebaert *et al.* (2011)
Essential oils	Essential oils from *Euphorbia hirta*	Reduces the concentration of *Clostridium perfringens* in the intestines of broiler chickens	Singh and Shukla (1984), Kumar and Berwal (1998) and Mitsch *et al.* (2004)
	Oregano and garlic oil	Inhibit microorganisms like *E. coli* and other Enterobacteria counts, Clostridium count, *Staphylococcus aureus, Salmonella typhimurium* and *Listeria monocytogenes*	Aligiannis *et al.* (2001), Ross *et al.* (2001), Friedman *et al.* (2002), Oussalah *et al.* (2007) and Kirkpinar *et al.* (2011)
Herbs	*Aspergillus niger* fermented *Ginkgo biloba* leaves	Enhances the broiler growth performance	Hashemi and Davoodi (2011), Khan *et al.* (2012a) and Zhang *et al.* (2012)
	Garlic (*Allium sativum*), Turmeric (*Curcuma longa*), Thyme (*Thymus vulgaris* L.) Aloe vera, onion (*Allium sepa*), Ginger (*Zingiber officinale*, Rosc.), *Astragalus membranaceus*, Noni (*Morinda citrifolia*)	Greater utilization of feed	Guo *et al.* (2004) and Sunder *et al.* (2014)
	Curcumin in turmeric	Enhances the activities of digestive enzymes like pancreatic lipase, amylase, trypsin and chymotrypsin	Khan *et al.* (2012a)
	Ashwagandha (*Withania somnifera*) and Guduchi (*Tinospora cordofolia*)	Potent immunomodulators	Barnes *et al.* (2007), Kumar *et al.* (2011b) and Sengupta *et al.* (2011)
	Nishyinda (*Vitex negundo*), black pepper (*Piper nigrum*) and cinnamon (*Cinnamomum verum*)	Enhance feed conversion efficiency	Chowdhury *et al.* (2009), Mode *et al.* (2009) and Molla *et al.* (2012)
	Leaf extracts of *Salix babylonica* as well as *Populus nigra*	Improve heat tolerance , intake of feed, body weight gain, feed conversion rate as well as reduction in mortality of those broilers which are heat stressed	Mohammed (2010) and Al-Fataftah and Abdelqader (2013)
Electrolytes	Sodium bicarbonate ($NaHCO_3$), potassium chloride (KCl), calcium chloride ($CaC1_2$) and ammonium chloride (NH_4C1)	Results in better body weight gain, feed intake and feed to gain ratio and also increased water intake	Hurwitz *et al.* (1973), Baghel and Pradhan (1989), Ahmad *et al.* (2005), Mushtaq *et al.* (2005) and Ahmad *et al.* (2006)
Additives for growth and better carcass quality products			
Antioxidants	Butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT) and tertiary butyl hydroquinone (TBHQ)	Retard or minimize the oxidative deterioration along with natural antioxidants like vitamin C, vitamin E and phenolic compounds	Fasseas *et al.* (2008), Su *et al.* (2007), Tavarez *et al.* (2011) and Zhang *et al.* (2011)
Ractopamine	Ractopamine hydrochloride and Salbutamol	Manipulation of the broiler body fat content by lipolytic and growth promoter properties	Darlymph *et al.* (1985), Sillence (2004), Carr *et al.* (2009) and Zuo *et al.* (2010)
L-carnitine		Favours higher body weight gain with improved feed efficiency	Yasmeen *et al.* (2013)
		Improves body weight gain and feed conversion in diets	Schuhmacher *et al.* (1993)
		Improves hatching rate of eggs	Leibetseder (1995)
		Increases yolk's carnitine content and will be beneficial to the developing embryo especially in fat utilization for its energy purpose	Rinaudo *et al.* (1991)
		Positive effects on improving the egg hatchability in birds exposed to aflatoxicosis	Smith *et al.* (1993) and Leibetseder (1995)
Nucleotides		Essential to cellular metabolism as they participate in many intracellular biochemical processes like in biosynthetic pathways, energy transfer system, as co-enzyme components and as well as biological regulators	Leleik *et al.* (1983), Van Buren and Rudolph (1997), Cosgrove (1998) and Lerner and Shamir (2000)

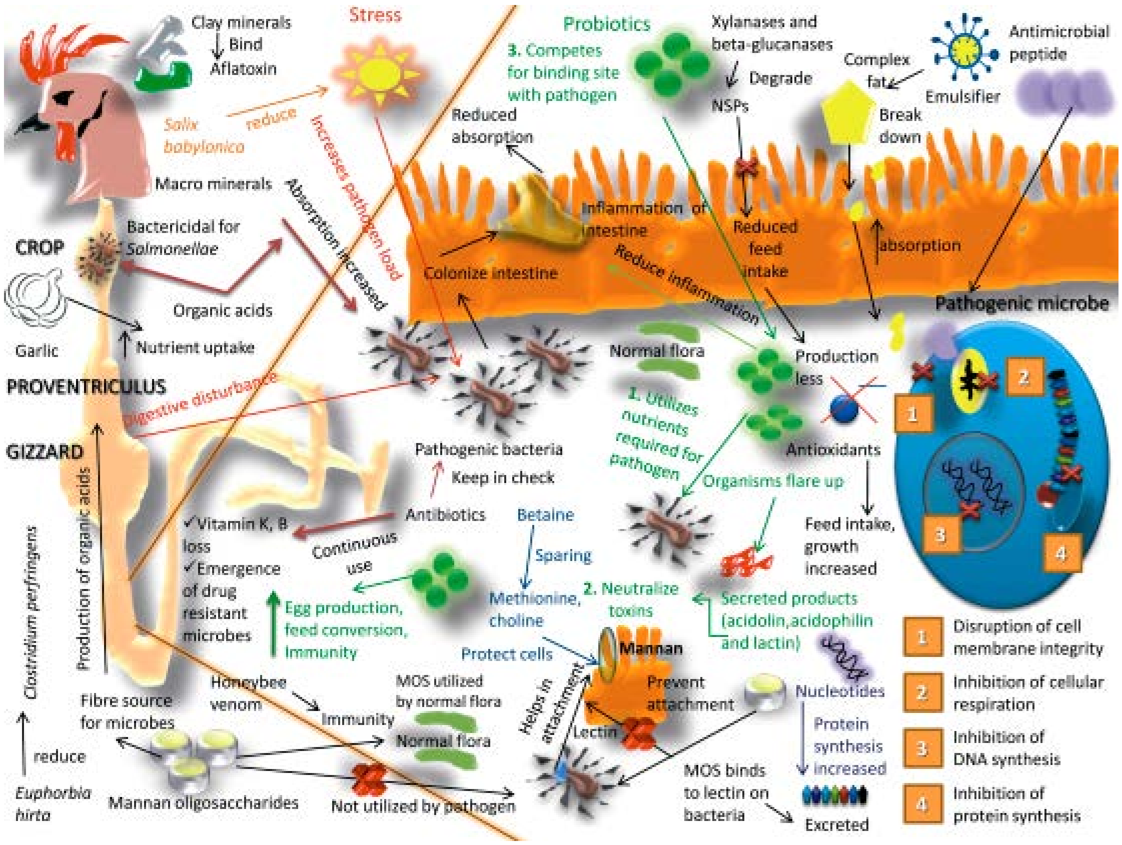

Fig. 1: An overview of mechanism of actions and beneficial applications of growth promoters and feed additives in poultry production and health

Miscellaneous growth promoting agents: In the current era of one world one health concept, care need to be taken regarding feeding of good nutritional elements and balanced food, which play crucial role in maintaining sound health of animals including of poultry as well as of humans (Dhama *et al*., 2013e, 2014). Apart from using AGPs, probiotis, prebiotics, organic acids, essential oils, vitamins and minerals, certain other growth promoting factors like antimicrobial peptide (cecropin), amino acids, enzymes and mushrooms (*Lentinus edodes* and *Tremella fuciformis*) are also tried with success (Guo *et al*., 2004; Wen and He, 2012). L-arginine is an essential amino acid for chickens, as well as the substrate for biosynthesis of Nitric Oxide (NO), a bioregulatory free radical molecule known to have antimicrobial activity. Broiler chicks fed a diet containing 4% of either corn oil or fish oil from 3-14 days of age have the ability to modify eicosanoid metabolism and attenuate the growth-depressing effects of infections, especially coccidiosis. Also, the improved digestion of the Non-starch Polysaccharides (NSP) is facilitated by addition of enzymes like xylanases, pectinases, gluconases cellulases etc., along with the feed, which complements to the endogenous enzymes and reduces the intestinal viscosity and bacterial load thereby enhancing the nutrient utilization and production performance. Honeybee (*Apis melifera*) venom has prophylactic effect against *Salmonella* gallinarum by stimulating non-specific immune response of birds suggesting it as an alternative to antibiotic in the poultry industry (Jung *et al*., 2013). Inclusion of eucalyptus oils obtained from the leaves of the eucalyptus, improved the production performance and stimulated the immunity in laying birds (Abd-El-Motaal *et al*., 2008).

The use of dietary emulsifiers are important for fat digestion and absorption especially in young birds as their digestive tract is not yet fully developed (Al-Marzooqi and Leeson, 1999). Emulsifier improved the utilization of fats in birds (Roy *et al*., 2010) especially in lower digested saturated fat sources by size reduction and enhancing micelles formation in the intestine. The need for exogenous emulsifiers in broiler diets becomes inevitable as feeding system has changed into high nutrient dense diets added high levels of vegetable or animal fat to exploit full growth potential. Soy lecithin, a natural emulsifier promotes incorporation of fatty acids into micelles and increase fat digestion in chicks (Polin, 1980). Lecithin contains choline in its structure which will be helpful to prevent perosis in poultry as additional benefit (Schaible, 1970). In the form of lecithin, choline is particularly effective. Polyoxyethylene glycol mono and dioleates, a synthetic emulsifier also showed promising results in fat digestion and utilization (Frobish *et al.*, 1969). Emulsifier in the diet increases the total surface area for enzymatic digestion of fats (Jones *et al.*, 1992).

CONCLUSION

A new era has been brought about in poultry production by growth promoters and novel feed additives. They are considered as powerful weapons to materialize improvement in health status and production performances of poultry flocks, thereby increasing the net economic returns. The achievement and maintenance of optimal balance of beneficial microflora in the avian gastrointestinal tract can be obtained with the use of growth promoters including antibiotics, probiotics, prebiotics, enzymes and organic acids. A lot of success had been achieved in poultry production initially by the use of antibiotics but they present some negative aspects with development of microbial resistance, due to their indiscriminate use. On the contrary, probiotics and organic acids offer the best viable alternatives to antibiotics as growth promoters to produce antibiotic free organic poultry meat. The use of probiotics in a daily supplementation regimen has become a popular routine method in the commercial poultry industry, particularly following an antibiotic therapy. The use of probiotics and other growth promoters have many potential benefits including the modification of host metabolism, immunostimulation, exclusion and inhibition of pathogens in the intestinal tract, enhanced nutrient absorption and performance and ultimately decreased human health risk. Studies have also proved the health promoting benefits of prebiotics coupled with probiotics, which can in turn result in a better and scientific management of poultry enterprises. In addition, performance of future studies on evaluation of antimicrobial peptides expression in birds by prebiotic and probiotic mediated short chain fatty acids are interesting to reveal the additional beneficial mechanisms of these compounds. Moreover, exploiting genetic engineering approaches, it is possible to strengthen or create completely novel probiotics which may have revolutionary potentials in oral immuno-therapeutic applications. Hence, considering the developments in the field of feed additives research, it is to be highlighted that, if properly and legitimately selected and exploited, the future for probiotics and prebiotics appears to be very strong for the poultry industry. Combined with good hygiene and management, these alternatives have shown to be effective in maintaining growth and production of birds by controlling the stress factors and commonly encountered infectious and non-infectious diseases. The use of organic acids, vitamins and minerals; herbs are found to be more effective than many of the antibiotic growth promoters in reducing the load of harmful GI pathogens and to combat heat stress respectively to maintain the normal homeostasis. In the present day context herbal therapy is one of the best alternative to prevent emerging multiple drug resistance. Natural medicinal products are also ideal feed additives and are gaining their popularity nowadays, but their future as feed additive will depend on knowledge of chemical structure, characteristics, physiological need, owner's preferences and expectations. With recent improvement in science, like betaine, carnitine, ractopamine and nucleotides can be used for better meat quality which will be more consumer friendly and health conscious. The use of dietary antioxidant both synthetic and natural becomes essential as the dietary inclusion of various fats and oils are increased. These antioxidants are not only promoting the keeping quality of feed but also the poultry carcass. On the productivity as well as immune response heat stress has got immense effect for which intervention strategies are required for dealing with conditions like heat stress. As the provision of healthy and competitive food supply is the primary goal of the Indian poultry industry, in order to keep its economical stability and prosperity, we must be able to exploit the utility of these viable alternatives, which could make it a most successful enterprise in the years to come.

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