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A review on gut health in chicken: Associated factors and nutritional strategies

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Abstract
Demand for chicken meat is rapidly increasing and human is becoming more adaptive towards chicken as potent animal protein source. Recent decade in the field of poultry science has observed a tremendous increase in interest for improving gut health of chicken for producing healthy food for humans and it improves health and performance of chicken. Gut health of chicken depend upon factors including environment, nutrition and genetic makeup of chicken. Chickens' gut health plays a major role in digestion, nutrient utilization and maintenance of proper immunity status of chicken. Hence, the maintenance of proper gut health in chicken may play a vital role in improving and maintenance of health and production of healthy chicken. Nutritional approaches such as supplementation of probiotics, prebiotics, synbiotics, exogenous enzymes, organic acids and phytobiotics have shown encouraging results in improving gut health of chicken. This review paper has been formulated to provide a better understanding of the factors associated with gut health and nutritional management to improve gut health of chicken.

Keywords: Chicken, gut health, nutrition, healthy food

Introduction
The total population of India is 1.21 billion according to 11th census and it is growing every year. Egg and chicken are accepted by all the communities and are available at the most reasonable prices. The poultry is most organized and rapidly growing sector in the animal agriculture. The poultry population is 851.81 million which is increasing by 16.81% from 2012 to 2019. The total egg production from poultry is 103.32 billion which has increased by 8.5% as compared to previous year, the total egg production from commercial poultry is 84.91 billion numbers and from backyard poultry is 18.41 billion numbers, with per capita availability of 79 eggs per annum. The meat production from poultry is 4.06 million tones, contributing about 50% of total meat production which has increased by 7.8% from previous year (BAHS 2019, 20th livestock census). India ranks third in egg production and sixth in broiler meat production in the world (FAOSTAT 2019) [31]. Human nutritionists recommended 180 eggs & 10 kg chicken per year. Most of the countries consume over 240 eggs and 20 kg of chicken. There is scope for enhancing the production. Production is getting more organized and move ahead of consumption resulting in optimum prices and with minimum profits (Kotaiah, 2016) [47].

Gut health defined as effective digestion and absorption of food, a stable gut microbial population, structure and function of the gut barrier, and effective function of the immune system, all of which play a critical and important role in gut physiology and the productivity of the animal (Kogut *et al*., 2017; Nagar *et al*., 2020; Singh *et al*., 2021a; Singh *et al*., 2021b) [46, 61, 75, 74]. Gut is mainly composed of physical, chemical, immunological and microbiological components and acts as a selective barrier. If gut health is compromised, digestion and nutrient absorption will be affected which leads to deteriorate the animal health and production (Bailey, 2013; Nagar *et al*., 2021) [98, 62].

Development of gut
Gut starts to develop when the fertilized egg is brooded and continues after the egg is hatched. During the last 3 day of incubation, the ratio of small intestinal weight to body weight increases from approximately 1% on day 17th of incubation to 3.5% at hatch (Korver and Yegani, 2008) [99]. Intake of good quality feed is accompanied by rapid development of the GI tract and associated organs. Early access to nutrients and water stimulate the activity of the

GIT and digestive organs (Noy and Sklan, 2001) [100]. The growth of the gut and digestive organs are affected by the establishment and growth of the microflora (Apajalahti *et al*., 2004) [1].

Factors affecting gut health

There are so many factors that affect the gut health in poultry which include various factors like Age, Sex, Breed, Gut Region, Maternal Factor, Feed, Hygiene, Housing, Medication, Temperature, Litter Materials and Location of Poultry Farm, but Diet and Infectious agents have more impacts on gut health of poultry. Material ingested by a bird can contain nutrients, non-nutrients, and beneficial and potentially harmful organisms. In other words, the digestive tract of the chicken is a major site of potential exposure to pathogens. The lumen normally contains feed and its constituents, resident and transient microbial populations, endogenous nutrients, and secretions from the GI tract and its accessory organs such as the liver, gall bladder, and pancreas. The GI tract must selectively allow the nutrients to cross the intestinal wall into the body while preventing the deleterious components of the diet from crossing the intestinal barrier. So to improving gut health diet is one of major factor, there are so many nutritional strategies in which feed additives are one of the most important one that we can use to improve the health of the gut and increasing the animal productivity. Di*et al*so affects the gut microbiota of birds. Factors such as pellet size, choice of food grains, and the microbiota of those foods can cause shifts in birds' microbial communities (Tellez *et al*., 2014; Haberecht *et al*., 2020; Thakur *et al*., 2020a; Thakur *et al*., 2020b; Singh *et al*., 2021) [83, 33, 84, 85, 79] Various types of feed additives have been evaluated under commercial conditions and in experimental trials with the objective to achieve improvements on growth performance and
the best economic return. Some of the alternatives that have been studied include herbs, spices and various plant extracts/essential oils, probiotics or direct fed microbials, prebiotics, synbiotics, organic acids and dietary enzymes. Combinations of two or more of these additives have been used in various trials in order to maximize the benefits from using them. Herbs, spices and various plant extracts/essential oils can be used as alternatives to replace antibiotic growth promoters as they rich of phytochemicals (active compounds) that can be used to stimulate growth and health of the animals. In "one health" approach the issue of uncontrolled using of antibiotic in poultry can lead to development of antibiotic resistance not only in animal's nut in human also (Popov *et al*., 2021) [66]. So, recently feed additives which are alternative to antibiotics are mainly used as growth promoters.

Probiotics

Probiotics are viable micro-organisms used as feed additives, which lead to beneficial effects on the microbial balance in the gut of animal (Yang *et al*., 2009) [92]. There are two basic mechanism of action of probiotics which are "competitive exclusion" and "immune modulation".

A variety of microbial species have been used as probiotics, including species of *Bacillus*, Bifidobacterium, Enterococcus, Escherichia, Lacto *Bacillus*, *Lactococcus*, Streptococcus, a variety of yeast species, and undefined mixed cultures. Spore forming probiotics also gaining popularity in poutry industry (Ruiz *et al*., 2021) [71]. Spore forming species includes Clostridium and *Bacillus* found not only in gut like other species but also found in soil, dust and water (Mingmongkolchai *et al*., 2018) [57]. These species preferably used among novel growth promoters because of their many beneficial effects. Spore forming probiotics are highly accessible than Lacto*Bacillus* species, they are having higher survivability rate during probiotic manufacturing process like fermentation, freezing, drying, thawing, and rehydration. Although they proliferate and survive more than any other probiotics in the gut of animal (Popov *et al*., 2021) [66]. Some important effects of spore forming probiotics:

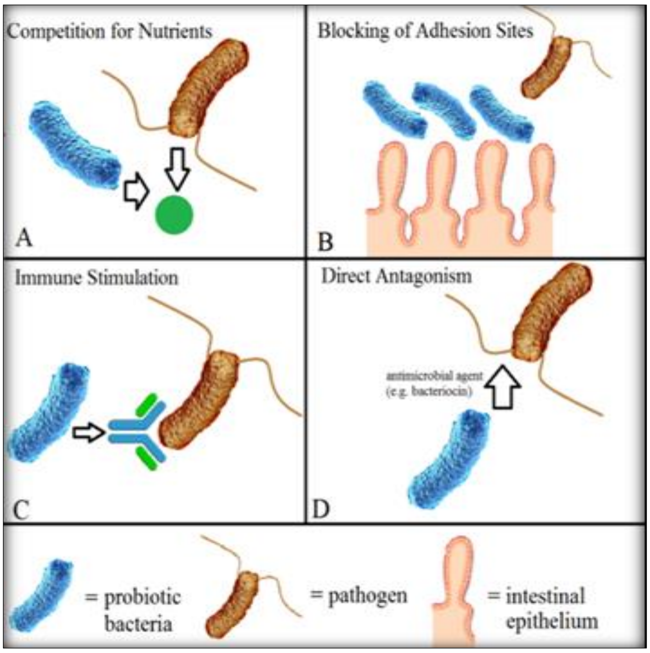

Fig 1: mechanism of action of probitoics

Immunomodulation

Bacillus species as probiotics in poultry were reported to play a role in immune modulation, cytokine production, and macrophage activation without cytotoxicity. Duc *et al*. (2004) [27] and Sebastian *et al.* (2013) [73] reported that serum concentration of IgA and IgG were increased in poultry groups treated with Bacilli spp, indicating modulation of the humoral immune response.

Effect on metabolic activities

Spore forming probiotics help in various metabolic activities which include, removing of free radicles (Kaushik *et al*., 2009) [41], production of mucin (Aliakbarpour *et al*., 2013) [7] and bacteriocin (Cotter *et al*., 2013) [22] and other antimicrobial substance for pathogenic microbes (Mohan 2015) [58]. Mucin is an important source of carbohydrates and exogenous nutrients for the growth and maintenance of intestinal flora (Deplancke *et al*., 2001) [25]. Aliakbarpour *et al.* (2012) [6] reported that birds fed a diet containing a probiotic strain of *Bacillus subtilis* significantly increased gene expression of intestinal MUC 2 mRNA in comparison to the control group. The higher the expression of the MUC2 gene, the more growth performance and improved intestinal morphology were found in the B. subtilis probiotic-fed chicks. Ammonia emissions also related to the composition of microbial community in the gut. Zhang *et al.* (2013) [95] reported that dietary supplementation of *B. subtilis* has been reported to enhance the enzymatic activity of the intestinal microflora, increasing their nitrogen utilization and eventually reducing ammonia emission in poultry faeces. Several studies reported that the some of *Bacillus* species had the capability to produce beneficial enzymes such as proteases, lipases, cellulases, xylanases, phytases, and amino acids (Latorre *et al*., 2014; Adeola *et al*., 2011) [83, 3]. Commonly used spore-forming Bacilli as probiotics commercially are B. subtilis, B. licheniformis, and B. cereus (Larsen *et al*., 2014) [49]. Recently, B. *amyloliquefaciens* B-1895 was reported to have positive health effects on poultry, increasing meat mass as well as food digestion and absorption in broilers (Chistyakov *et al*., 2015; Chen *et al*., 2014) [102, 19].

Table 1: Biological activity of various strains of probiotics

Strains of probiotic	Biological activities	References
L. acidophilus, L. casei, B. bifidum, A. oryzae, S. faecium and *Torulopsis spp.*	Lowered numbers of coliform and Campylobacter in the gut	(Khaksefidi and Rahimi, 2005) [42]
L. salivarius	Reduced the number of *S. enteritidis* and *C. perfringens* in the gut	(Kizerwetter-Swida and Binek, 2009) [45]
Commercial probiotics containing *L. plantarum, L. bulgaricus, L. acidophilus, B. bifidum, S. thermophilus, E. faecium, A. oryzae*	Increased antibody titre against Newcastle disease (ND).	(Khan *et al*., 2011) [43]
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) [59]

Table 2: Several studies of spore forming probiotics effects on poultry performance

Spore forming probiotic strain	Probiotic administration (Way)	Results	Reference
B. amyloliquefaciens BLCC1-0238 at 0.01%, 0.03%, or 0.06% levels	with standard diet	Egg production increase by 0.06% in comparison to control group in poultry	Zhou *et al.*, 2020 [96]
B. subtilis C-3102 spores at 9.3 × 109 CFU/kg	With standard diet	No significant difference were seen in egg weight, average daily feed intake but feed conversion ratio significantly decrease from 2.15 in the control group to 2.08 in the treatment group	Wang *et al.*, 2021 [89]
Clostridium butyricum at 2.5 × 104 (CB1), 5 × 104 (CB2), 1 × 105 (CB3), and 2 × 105 (CB4) CFU/g	Supplementing standard corn–soybean basal diet	Egg production significantly increase from 85.4 in the control group to 91.4 in CB2, with no significant difference in feed intake and feed conversion ratio	Zhan *et al.*, 2019 [94]

Prebiotics

Prebiotics are non-digestible feed ingredients that beneficially affect the host by selectively altering the composition and metabolism of the gut micro flora. It provides energy for the growth of endogenous favourable bacteria like bifidobacteria and lactobacilli, results in improving the host microbial balance (Sugiharto 2014) [103]. Prebiotics provide energy and a carbon source for microorganisms, which generally live in the colon, where some of the bacterial fermentation of nutrients occur (Dankowiakowska *et al*., 2013) [24]. Prebiotic which are commonly used in poultry industry are FOS, GOS, yeast cell wall and MOS.

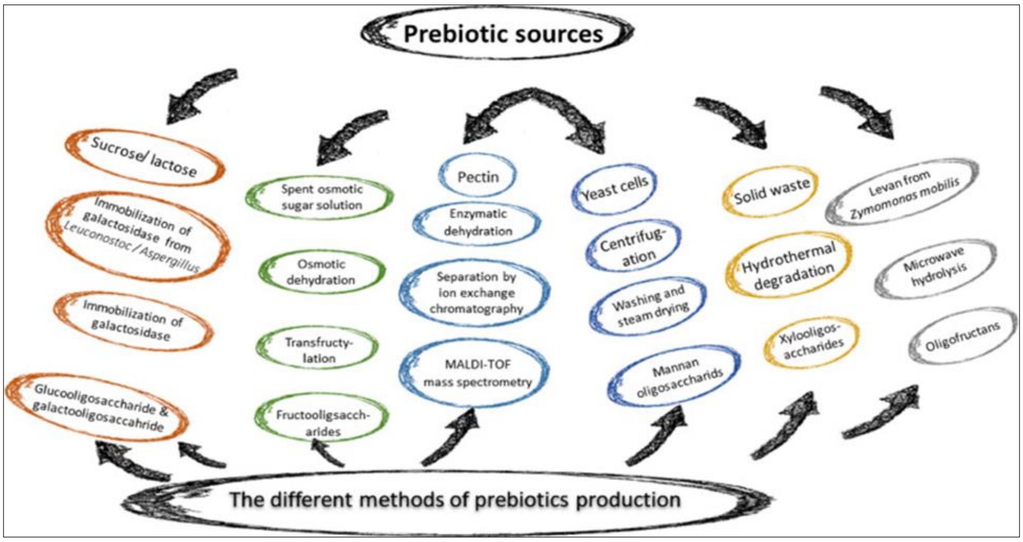

Fig 1: Different prebiotic sources

Prebiotics affect the multiplication of bifidobacteria species, reduce the growth of pathogenic microorganisms, remove of toxic metabolites and enzymes, enhance birds' performance, show Hypocholesterolemia effect, and lower blood pressure, and prevent carcinogenesis processes (Mateova *et al*., 2008) [54]. Kannan *et al.* 2005 [40] and Pilarski *et al.* 2005 [65] reported that prebiotics affects the synthesis of vitamins such as nicotinic acid, folic acid, B1, B2, B6, and B12.

FOS (Fructooligosaccharides) can act as substrates for specific microorganism in intestine and are not hydrolyzed in the upper gastrointestinal tract thus, they (Kumar *et al*., 2019). FOS is fermented by *Lacto Bacillus* and *Bifidobacteria* species, which improves the host's gut health (Ricke 2018) [70]. FOS may increase the concentration of SCFA and lactic acid and inhibits the growth of pathogenic bacteria such as *Clostridium* perfringens which is one of the major causes of high mortality rate in poultry (Kumar *et al*., 2019) [48]. Oyarzabal and Conner 1996 [64] reported that colonization of *Salmonella* species was reduced by 19% in broilers with the addition of FOS in the drinking water. FOS increase the enzymatic activity of protease, amylase and leucine amino peptidase which was positively associated with improvement in feed conversion ratio (FCR) (Ricke, 2015,2018; Micciche *et al*., 2018; Kim *et al*., 2019) [69, 70, 56, 48] MOS (Manna oligosaccharides) it is a component obtained from the outer cell wall of *Saccharomyces cerevisiae*. They are outer layer of yeast cell walls, including glucan 30%, mannan 30%, and protein 12.5%. Mannan oligosaccharides contain a high-affinity ligand for bacteria and provide a competitive binding site. So pathogens attach to the MOS instead of the intestinal wall and move through the intestine without colonization (Benites *et al*., 2008) [14]. Rehman *et al.* (2020) [68] reported that on dietary supplementation of prebiotics improved the growth performance of broiler and may be increasing the antibody titre against infectious bursal disease.

Table 3: Biological activity of various types of prebiotics

Type of prebiotics	Biological activities	References
FOS	Reduced intestinal colonization by Salmonella	(Bailey *et al.*, 1991) [12]
	Enhanced the IgM and IgG antibody titres in plasma	(Janardhana *et al.*, 2009) [39]
	Provided nutrients for the growth of beneficial bacteria in the gut	(Alloui *et al.*, 2013) [9]
Commercial prebiotic (Fibregum and Raftifeed- IPE)	Increased serum concentration of IgA and IgM, and enhanced systemic immune capacity in chickens	(Vidanarachchi *et al.*, 2013) [87]
IMO	Increased the caecal populations of l*actobacilli* and *bifidobacteria* and decreased the caecal *E. coli*	(Mookiah *et al.*, 2014) [59]

Synbiotics

Synbiotics is defined as combination of prebiotics and probiotics. This combination could improve the survival and persistence of the health-promoting organism in the gut of birds because its specific substrate is available for fermentation (Yang *et al*., 2008) [104]. The composition of the newly elaborated synbiotic preparations of Lacto *Bacillus* spp. and *Saccharomyces cerevisiae* strains and inulin (as prebiotic) were used. Synbiotics when added in the broiler diet significantly increased the short chain fatty acids and lactic acid and significant decrease in the branch chain fatty acid in the gut of broiler so it improves the health of a broiler chicken (Śliżewska *et al.*, 2020) [78]. The Synbiotic was more effective in reducing Salmonella colonization than FOS or probiotic alone. While applying the combination of FOS and *Bacillus* to a corn-soybean basal diet, observed that average daily gain (ADG) and feed conversion ratio (FCR) were improved by 6% and 2%, respectively; diarrhoea and mortality rate were reduced by 58% and 67%, respectively (Li *et al*., 2008) [51].

Table 4: Biological activity of various strains of synbiotics

Type of Synbiotics	Biological activities	References
Commercial Synbiotics (Biomin IMBO)	Increased the LAB population and reduced E. *coli* and total coliform populations in the intestine	(Dibaji *et al.*, 2014) [26]
	Increased antibody production	(Hassanpour *et al.*, 2013) [34]
Synbiotic (11 *LactoBacillus strains* plus IMO)	Increased the caecal populations of *lactobacilli* and *bifidobacteria* and decreased the caecal *E. Coli*	(Mookiah *et al.*, 2014) [59]
Synbiotic (*S. cerevisiae* plus MOS)	Reduced the number of *E. coli* in the small intestinal and caecaldigesta	(Abdel-Raheem *et al.*,2012) [2]
Synbiotic (*LactoBacillus*, *Bifidobacterium* and oligosaccharides derived from yeast cell wall)	Improved the antibody response to NDV and infectious bronchitis virus (IBV)	(El-Sissi and Mohamed, 2011) [29]

Exogenous Enzymes

Enzyme is a substance that increase velocity or rate of chemical reaction without itself undergoing any change in the overall process. Various exogenous enzymes including β-glucanase, xylanases, amylase, α-galactosidase, protease, lipase, phytases, etc. have been supplemented in poultry diets (Bedford and Cowieson, 2012) [13]. Exogenous enzymes help in digestion of certain nutrients of feedstuffs for which endogenous enzymes cannot do this by own and also helps in hydrolyse anti-nutritional factors in feed ingredients. Enzyme supplementation is also important for to reduce the pollutant potential of excreta and reduce the environmental issues (Costa *et al*., 2008) [21]. Poultry, when fed with cereals, cannot hydrolyze the starch-free polysaccharides present in the cell wall due to the lack of enzymes, which causes low feed efficiency; these effects can be counteracted by modifying the diet or adding exogenous enzymes. Ojha *et al*., (2019) [63] reported that in organoleptic tests, egg yolk color, specifically, has been better observed when xylanases and β-glucanases are added to the diet, and a greater energy generation and a better production of meat and eggs with diets supplemented with α-amylases. Café *et al.* (2002) [16] supplemented a multienzyme complex (Avizyme) composed of xylanases, proteases and amylases into the poultry diet, observed an increase in body weights, a decrease in mortality and a greater amount of net energy compared to the group without Avizyme. On the other hand, Babalola *et al.* (2006) [11] observed that on adding xylanases in poultry diet the absorption of nitrogen and fiber improved. Amerah *et al.*, 2016 [10] conduct experiments to know the effect of exogenous Xylanases, Amylase and Protease as single or combined activities on nutrient digestibility and growth performance of broilers fed corn-based diets. They reported that Xylanases supplementation improved the FCR compared to the control group during the starter phase and over the entire period (1-42d).

Organic Acids

Organic acids are carboxylic acid with the general structure of R-COOH and hence include fatty acids and amino acids. Organic acids having antibacterial properties which are important to support enteric health and growth performance of poultry. The proposed mode of action of organic acids is related to the reduction of intestinal pH, which might have followed by alterations in the intestinal ecosystem (Canibe *et al.*, 2001) [17]. Organic acids such as lactic, acetic, tannic, fumaric, propionic, caprylic acids, etc. have been exhibit beneficial effects on the intestinal health and performance of birds (Menconi *et al.*, 2014) [55]. Supplementation of organic acids in the diet increased lactic acid bacterial (LAB) counts in the ileum and caecum of broiler chicken. This treatment also significantly decreased Enterobacteriaceae and Salmonella counts in the intestine of birds (Saki *et al*., 2012) [72]. Feeding organic acids resulted in improved body weight gains and FCR (Adil *et al.*, 2010) [4].

Phytobiotics

Phytobiotics are plant-derived natural bioactive compounds that occur naturally in plants and that can be added in feed to improve the growth and performance of chicken. Phytobiotics represent a wide range of bioactive compounds that can be extracted from various plant sources (Windisch *et al.*, 2008) [91]. Antimicrobial activity and immune enhancement are the two major properties of phytobiotics which are essential for the health and well-being of the chicken (Fallah *et al.,* 2013) [30]. The trend in the use of phytobiotics in animal feed has been increased during last two decades. The mechanisms by which the phytobiotics exert their benefits on the gut remain unclear, but possible mechanisms could be proposed as follows: (1) modulating the cellular membrane of microbes leading to membrane disruption of the pathogens, (2) increasing the hydrophobicity of the microbial species which may influence the surface characteristics of microbial cells and thereby affect the virulence properties of the microbes, (3) stimulating the growth of favourable bacteria such as lactobacilli and bifidobacteria in the gut, (4) acting as an immunostimulatory substance and (5) protecting the intestinal tissue from microbial attack (Vidanarachchi *et al.,* 2005; Windisch and Kroismayr, 2007) [88, 90]. Herbs, spices and essential oils contain active compounds (phytochemicals) which can be used as alternatives to antibiotic growth promoters in poultry diets. Phytobiotics feed additives consists of many phytochemicals that can be categories as: phenolics, polyphenols, terpenoids, essential oils, alkaloids, lectins and polypeptides (Hernandez *et al.*, 2006) [35]. Improved growth parameters were detected in birds fed on different kinds of herbs, polysaccharides or essential oils components (Yasodha *et al*., 2019) [93]. The enhancement of the growth performance parameters after supplementation of phytobiotics may be depends on the synergistic mechanism among their active molecular complex (Hussein *et al*., 2020a) [37]. Tabatabaei (2016) [82] reported that phytobiotics could improved the intestinal architecture and villus length and consequently increase the absorptive surface of intestine. Phytobiotics have the ability to stimulate saliva production, secretion of digestible enzymes and bile production resulting in improving the performance and digestibility (Alloui *et al*., 2014) [8]. Phytobiotics decrease the pathogenic bacteria of gut and increase the Lacto*Bacillus* spp count. Several studies reported that supplementation of broiler diet with essential oil mixtures of thymol and cinnamaldehyde (Tiihonen *et al*., 2010) [86], carvacrol (Jamroz *et al*., 2006) [38], clove and cinnamaldehyde (Chalghoumi *et al.*, 2013) [18] etc. improved the feed intake, feed conversion ratio and body weight. Similarly Radwan *et al*., 2008 [67]; Kaya *et al*., 2013 [105] reported that after supplementation of plant extracts and essential oil as improved the egg production, eggshell strength and thickness as well as internal egg quality in layer birds. Phytobiotics acts as antimicrobial substance due to the presence of many bioactive compounds like saponin (bioactive compound) bind with sterol moiety of cell membrane leading to damage of microbial cell membrane (Morrissey and Osbourn, 1999) [60]. It has been speculated that organic acids of some photobiotic feed additives may lower the intestinal pH that leaded to inhibiting the pathogenicity of local pathogens and lowering the level of their toxic products (Manafi *et al*., 2016; Sriranga *et al*., 2021; Singh, 2021) [53, 79, 77]. Elmenawey *et al*. (2019) [28] found that dietary phytobiotics or plant extracts have inhibitory effects on E. coli activity *in vivo*. The efficacy of a mixture of seven essential oils that inhibited the growth of Clostridium perfringens (C. perfringens) *in vitro* has been reported by many studies (Hussein *et al*., 2020b) [36]. Phytogenic compounds have been found to reduce the severity of Eimeria spp. infection in broilers reducing oocyst shedding (Zyan *et al*., 2017) [97]. Some herbs and species like garlic, echinacea and liquoric have immunostimulatory properties due to their composition of vitamin C, carotenoids and flavonoids as well as their abilities to stimulate macrophages, lymphocytes and natural killer cells activities and interferon production (Frankic *et al*., 2009) [32]. The immunostimulant effect of some essential oils may be due to the presence of certain compounds that may bind to Immunoglobulin G (Ig G) receptors which leaded to stimulation of immune response (Ahmed *et al*., 2013). Haemagglutination inhibition antibody titre against avian influenza virus in broiler chicks was significantly increased after giving peppermint oil (Sultan *et al*., 2017) [81]. Abd El-Ghany *et al.* (2020) [1] Concluded that phytobiotics can be used as an alternative to antibiotic growth promoter because they having antimicrobial, antibacterial, anti-parasitic, immunostimulant with improved the poultry performance.

Conclusion

This review manuscript has showed that gut health of chicken depend upon factors including environment, nutrition and genetic makeup of chicken. Chickens' gut health plays a major role in digestion, nutrient utilization and maintenance of proper immunity status of chicken. Nutritional approaches such as supplementation of probiotics, prebiotics, Synbiotics, exogenous enzymes, organic acids and phytobiotics have shown encouraging results in improving gut health of chicken. Hence, the maintenance of proper gut health in chicken may play a vital role in improving and maintenance of health and production of healthy chicken.

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Conflict of Interest

Authors declare that they have no conflict of interest.

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