www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277-7695
ISSN (P): 2349-8242
NAAS Rating: 5.23
TPI 2022; SP-11(11): 1435-1440

www.thepharmajournal.com
Received: 26-09-2022
Accepted: 28-10-2022

Kaushalendra Kumar
Department of Animal Nutrition, Bihar Veterinary College, Bihar Animal Sciences University, Patna, Bihar, India

Ravi Ranjan Kumar Sinha
Department of Livestock Production Management, Bihar Veterinary College, Bihar Animal Sciences University, Patna, Bihar, India

Sanjay Kumar
Department of Animal Nutrition, Bihar Veterinary College, Bihar Animal Sciences University, Patna, Bihar, India

RK Nirala
Department of Livestock Production Management, Bihar Veterinary College, Bihar Animal Sciences University, Patna, Bihar, India

Savita Kumari
Department of Veterinary Microbiology, Bihar Veterinary College, Bihar Animal Sciences University, Patna, Bihar, India

SP Sahu
Department of Livestock Production Management, Bihar Veterinary College, Bihar Animal Sciences University, Patna, Bihar, India

Corresponding Author:
Ravi Ranjan Kumar Sinha
Department of Livestock Production Management, Bihar Veterinary College, Bihar Animal Sciences University, Patna, Bihar, India

Significance of tannins as an alternative to antibiotic growth promoters in poultry production

Kaushalendra Kumar, Ravi Ranjan Kumar Sinha, Sanjay Kumar, RK Nirala, Savita Kumari and SP Sahu

Abstract
The world's supplies of protein are significantly influenced by the poultry sector, and each year, the number of poultry produced globally grows larger. However, the poultry business is dealing with a variety of problems, such as bacterial infection, coccidiosis, oxidative stress, food pad dermatitis (FPD), and environmental pollution, which affect food safety, poultry production efficiency, animal welfare, and the environment. In addition, limitations on the use of antibiotic growth promoters (AGP) have made a number of these adverse consequences worse. Since high doses of tannins can reduce feed intake and negatively impact nutrient digestibility and absorption, they have historically been viewed as antinutritional factors. However, recent research has shown that some tannins, when used in the right way, can improve the intestinal microbial ecosystem, enhance gut health, and consequently increase productive performance. Tannins, on the other hand, have been found to possess antibacterial, antioxidant, anti-parasitic, immunomodulatory, and anti-inflammatory characteristics; as a result, they have attracted attention as prospective bioactive substances to aid in easing the difficulties of AGP removal in the chicken sector. In order to diminish the need for AGP and otherwise increase poultry production efficiency, tannin supplementation, either alone or in combination with the other measures, may be a successful strategy.

Keywords: Tannin, antibiotic growth promotors, performance, gut health, poultry

Introduction

Since many years ago, antibiotics have been utilized to promote growth, and they have been successful in boosting the productivity of chickens. A major portion of the world's food supply is made up of poultry products, including meat and eggs, which are a staple source of protein everywhere (Mottet and Tempio, 2017) [30]. AGP usage in poultry farming is now prohibited or limited in several nations (Hu and Cowling, 2020) [20] due to growing public concern over the spread of antibiotic-resistant microorganisms from poultry products. Finding AGP substitutes is crucial because they must be economical, environmentally benign, and have antibacterial and growth-promoting properties without having negative effects on humans or animals (Yang *et al.*, 2015) [51].

Tannins are secondary metabolites that are found in plants, seeds, bark, wood leaves, and fruit skins. They act as a plant's defense system against predators since they are polyphenolic compounds that have the ability to precipitate proteins (Redondo *et al.*, 2014) [35]. Because tannins can reduce feed intake, nutrient digestibility, and chicken development performance, high quantities of tannins have been demonstrated to have antinutritional effects in monogastric animals. However, tannins have recently received a lot of interest in the poultry industry as an alternative to AGP due to their antibacterial, antioxidant, and anti-inflammatory characteristics (Daglia, 2012) [12]. Because they come from waste products of plant-based agriculture and industry, many tannins are also regarded as sustainable feed additives. Tannins have a variety of effects on chicken growth and the gut environment, but it is still unclear how they work and how consistently they affect these factors. To make the best use of supplementary tannins in hens, it is crucial to comprehend the chemical characteristics and biological consequences of tannins. This article primarily focuses on how tannins can help poultry producers overcome obstacles and improve the ways in which tannins are used.

Classification and occurrence of tannins

Plant tannins are classified into hydrolysable tannins (HT) with tannin derivatives (e.g., gallic acid and ellagic acid) and condensed tannins (CT).

A third family of tannin that is specific to brown algae is called phlorotannins (PT). Different tannins have different bio availabilities (absorbabilities), and the degree of bioavailability varies depending on a number of factors, including the derivatives of each tannin (for example, gallic acid and ellagic acid), their affinity for protein, their molecular structure, and their molecular weight. To address several problems in the production of poultry, tannins' bioavailability should be taken into account. In contrast, highly accessible tannins would be more advantageous as anti-inflammatory and antioxidant compounds. Tannins with poor bioavailability may have greater antibacterial properties in chickens.

The HT, which primarily consists of gallotannins and ellagitannins (molecular weight 500–3000 Da), has a central polyol (often glucose) that is esterified with phenolic groups (e.g., gallic acid and ellagic acid). The CT is present in forage legumes like lentils, black-eyed peas, chickpeas, and red kidney beans as well as in fruits like berries, pears, and apples, as well as in almonds, red and green grapes (and their juice and wine). The CT is more complicated structurally and has a higher molecular weight (1000–20,000 Da) than the HT (Huang *et al.*, 2018) [21]. Contrary to HT, CT are not susceptible to hydrolysis, which would indicate low bioavailability in the hens' gastrointestinal tract (GIT). Epithelial cells in the large intestine have the ability to digest and absorb CT. When compared to HT, the CT has a lower bioavailability and can reach the chicken's large intestine. The majority of the PT, polyphenols generated from algae, are between 10 and 100 kDa in size (Bawadi *et al.*, 2005) [6]. Their molecular weights range from 126 Da to 650 kDa. As a result of their low molecular weights, PT can be readily digested and absorbed in the GIT tracts. Prior to using tannins in chicken diets, it is crucial to understand the precise chemical characteristics of each tannin.

Potential of tannins to mitigate the challenges in poultry production

Bacterial infection

Salmonella, Escherichia, Campylobacter, Clostridium, Listeria, Mycobacterium, and Aeromonas are major pathogenic bacteria found in poultry products (meat and eggs). These bacteria not only negatively affect chickens' gut health and growth rate, but they also pose a threat to the public's health by infecting people with foodborne illnesses (Thung *et al.*, 2016) [45]. Salmonellosis is one of the major illnesses that humans contract by eating poultry products and is brought on by S. Typhimurium and S. Enteritis (Thung *et al.*, 2016) [45]. Studies conducted in vitro revealed that Salmonella spp. and other pathogens were susceptible to the bacteriostatic (inhibiting bacterial growth) and bactericidal (killing bacteria) actions of tannins and their derivatives. Potential mechanisms of tannins' antibacterial effects include their direct interactions with cell wall components, which can change the structure of the cell wall and make bacteria's membranes more permeable, as well as their suppression of microbial enzyme activities and deprivation of essential nutrients like proteins and minerals (like iron) for pathogenic bacteria (Tan, 2019) [43]. In addition to having antibacterial properties, tannins can prevent Salmonella spp. from spreading throughout the body by advantageously modifying the components of the gut ecology.

Table 1: Application of tannin in broiler chickens.

Sources	Type of tannins	Animals	Dose rates	Effects	References
Tannic acid	HT	Broiler chicken	0.50%	Increased growth performance; reduced blood glucose level; reduced cholesterol content in liver	Starcevic *et al.* (2015) [42]
Tannic acid	HT	Broiler chicken	1%	Decreased body weight gain and feed intake; improved the fatty acid profile of breast muscle of broilers under heat stress by decreasing monounsaturated fatty acids	Ebrahim *et al.* (2015) [14, 15]
Chestnut	HT	Broiler chicken	0.15% to 1.2%	Reduced *Clostridium perfringens* (*Eimeria tenella, Eimeria acervulina, Eimeria maxima*) in the gut	Tosi *et al.* (2013) [47]
Chestnut	HT	Laying hens (50 weeks)	0.20%	No effect on egg weights, cell thickness or yolk color; reduced cholesterol content; increased monounsaturated fatty acid	Antongiovanni *et al.* (2015) [4]
Grape seed extract	CT	Eimeria tenella challenged broiler chickens	5, 10, 20, 40, and 80 mg/ kg diet	Decreased mortality and increased weight gain after the *E. tenella* infection in dose-dependent manner with 10 to 20 mg/kg yielded the best results; increased antioxidant status and improved growth performance of infected birds	Wang *et al.* (2008) [50]
Grape seed extract	CT	Broiler chickens (0 to 42 days)	125, 250, 500, 1,000, and 2,000 mg/kg	No effect on growth performance, mortality, total lipid, reduced total cholesterol and low-density lipoprotein cholesterol; increased antibody titer against Newcastle disease virus vaccines	Farahat *et al.* (2017) [17]
Grape pomace	CT and other phenolic compounds	Broiler chickens	6%	No effect on growth performance; increased Lactobacillus, Enterococcus and decreased the counts of Clostridium in the ileal content; increased populations of E. coli, Lactobacillus, Enterococcus, and Clostridium in the cecal digesta	Viveros *et al.* (2011) [49]

Coccidiosis

One of the most pervasive and damaging enteric diseases in the production of chicken is coccidiosis, a parasitic disease brought on by protozoa of the family Eimeridae. There are currently nine Eimeria species known to exist in chickens, including *E. acervulina, E. brunetti, E. maxima, E. necatrix, E. praecox, E. mitis, E. tenella, E. mivati,* and *E. hagani* (Clark *et al.*, 2016). Through the fecal-oral pathway, Eimeria spp. infect and spread throughout the mucosal epithelial layers in the various sections of the GIT (Li *et al.*, 2019) [23]. The effectiveness of poultry production and welfare can be significantly impacted by coccidian infection, which can impair growth rate and gut barrier integrity as well as cause inflammation, diarrhoea, haemorrhaging, and even mortality in broiler chickens (Teng *et al.*, 2020) [44]. Additionally, necrotic enteritis, an enteric infectious disease mostly caused by *C. perfringens* when Eimeria spp. are present, is intimately linked to coccidiosis. Prophylactic coccidiostats and anticoccidial medications have been added to poultry feeds to combat coccidiosis in the poultry business. It is crucial to find novel treatment options that cause very minimal resistance and efficiently control coccidiosis in broiler chickens because resistance to all currently available medications has been observed (Noack *et al.*, 2019) [32]. Prebiotics, plant extracts, organic acids, essential oils, and lipids are examples of bioactive substances that have been examined in chickens as potential preventive coccidiostat and anticoccidial medication substitutes.

Tannins are known to have anticoccidial effects due to their capacity to form complexes with parasite enzymes and metal ions, both of which are necessary for Eimeria spp. and can stimulate the chickens' immune systems (Chung *et al.*, 1998) [10]. According to Tonda *et al.* (2018) [46], feeding broilers with Eimeria spp. infections 500 mg/kg of gallnut tannic acid extract reduced the total number of oocysts found in their excretions and the severity of their intestinal lesions. The scientists also demonstrated that the feed conversion ratio of cocci-vaccinated birds was improved by gallnut tannic acid extract, which may indicate that the extract strengthened protective immunity after coccidiosis vaccination. The antioxidant characteristics of tannins, which can repair an Eimeria-damaged gastrointestinal tract, are strongly related to tannins' positive effects on the gut health of fowl infected with Eimeria spp. (Mishra and Jha, 2019) [29]. Contrarily, Mansoori and Modirsanei (2012) [26] demonstrated that supplemental tannic acid (10 g/kg) numerically increased D-xylose absorption in chickens that had been vaccinated against coccidiosis followed by challenges with Eimeria spp. However, supplemental tannic acid increased the total number of oocysts in excreta, indicating that high dosages of tannins can attenuate the Different tannin sources and amounts as well as various testing circumstances could be to blame for the disparity (e.g., challenge dosages of Eimeria spp.). More thorough studies are needed to understand the mechanisms underlying the anticoccidial effects of tannins in chickens and to identify the proper concentrations and types of tannins to prevent coccidiosis in chickens, even though many studies have suggested that supplementing with tannins may benefit broiler chickens infected with Eimeria spp.

Oxidative stress

One of the main challenges facing the poultry business is heat stress, which has a detrimental influence on chicken welfare, intestinal health, meat quality, and growth performance. The increased production of ROS caused by faster metabolic processes brought on by mitochondrial respiration is thought to be a possible factor in the harmful effects of heat stress on poultry (Lin *et al.*, 2006) [24]. Enzymatic and non-enzymatic antioxidants have the ability to counteract ROS and keep the ratio of oxidants to antioxidants in check under normal circumstances. However, if there is an imbalance between oxidants and antioxidants in chickens, overly created ROS might harm gut health and cause inflammation, which lowers chicken development performance (Nawab *et al.*, 2018) [31].

By scavenging ROS and controlling enzymatic antioxidants in animals, tannins are thought to alleviate or lessen the consequences of oxidative stress particularly that brought on by heat stress (Yang *et al.*, 2019) [36]. According to Ramnath and Rekha (2009) [34], supplementing Brahma Rasayana, which contains a variety of tannins, increased the activity of enzymatic antioxidants like superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione reductase (GR), and reduced glutathione (GSH) in the blood of chickens raised in cold temperatures. Additionally, the addition of grape (*Vitis vinifera*) pomace, high in CT, improved intestinal shape, antioxidant enzyme activities (GPx and SOD), and relative weight of the bursa of Fabricius and thymus in heat-stressed broiler chickens (Hosseini-Vashan *et al.*, 2020) [19]. In order to reduce oxidative stress in heat-stressed birds, feeding with the right amounts of tannins may be a successful tactic.

Food pad dermatitis

Growing chicken with foot pad dermatitis (FPD) develop lesions on the plantar area of their footpads. Paws are the third most important economic component of broiler chickens, and FPD can harm the chickens' growth rate, gut health, and welfare, which results in significant economic losses in the poultry industry. Among a variety of parameters, including bedding materials and depth, drinkers, and nutrient shortages, the two most significant characteristics that contribute to FPD are litter moisture and quality. By improving faecal consistency (for example, faecal dry matter contents) and litter quality, tannins can reduce the incidence and severity of FPD (Redondo *et al.*, 2014) [35,]. Tannic acid treatment at a dose of 2000 mg/kg decreased the frequency and severity of FPD in broiler chickens without having any negative effects on the hens' ability to grow or produce high-quality litter or have viscous intestines, according to Cengiz *et al.* (2017) [8]. In addition, chickens' faeces had more dry matter when treated with 700 mg/kg and 2000 mg/kg of sweet chestnut wood extract, which is high in tannins (Rezar and Salobir, 2014) [37]. Additionally, tannins' antibacterial, antioxidant, and anti-inflammatory capabilities likely contributed to the reduction of FPD incidence and severity in broiler hens, as oxidative stress and inflammation might worsen the severity and effects of FPD in chickens (Mayne *et al.*, 2007) [27]. By improving faecal consistency and litter quality, supplementation of tannins has the potential to lessen the severity and incidence of FPD in broiler chickens.

Environment pollution associated with poultry farming

In poultry production facilities, reactive nitrogen species like ammonia, nitrous oxide, and other oxides of nitrogen, as well as sulfur-containing compounds like hydrogen sulphide and sulphur dioxide, are produced. These pollutants include greenhouse gases like carbon monoxide, carbon dioxide, and methane. Types of feeds, manure conditions, and housing accessories are some factors influencing the generation of nitrogen compounds and harmful gases (bedding and heating materials). Although the production of poultry is not a significant source of noxious or greenhouse gases, the continued expansion of poultry production coupled with higher intensity of excretion and emission per unit compared to other species calls for more attention to be paid to the need to develop strategies to reduce the production of nitrogen excretion and emissions of noxious and greenhouse gases (Malomo *et al.*, 2018) [25]. Tannins are known to increase nitrogen (N) uptake and reduce methane generation in ruminant animals (Aboagye *et al.*, 2019) [1]. Despite the fact that chickens (monogastric animals) have a different GIT from ruminants, tannins may affect the gut health and microbiota as well as the way that chickens use nitrogen, which could reduce the amount of nitrogen and methane released into the atmosphere. According to Ahmed and Yang (2017) [3], supplementing with ellagitannins, punicalagin, punicalin, and pedunculagin, among other HT-containing byproducts of the Punica granatum (fruit), lowers the emission of ammonia and methanethiol from broiler chicken excrement. Additionally, a study by Bostami *et al.* (2015) [7] found that supplementing broiler chicks with fermented pomegranate leftovers that contain ellagitannins reduced gas emission (ammonia and hydrogen sulphide) from excreta, perhaps by lowering microbial activity and pH of excreta. Further investigation is required to establish the most effective tannin types and dosages for lowering nitrogen excretion and greenhouse gas emissions during the production of poultry.

Productive performance of poultry

Currently, the majority of studies have shown that, when used properly in monogastric diets, certain tannins can boost gut health, the intestinal microbial environment, and, ultimately, productivity. The principal effects of tannins on monogastric animals relate to their ability to bind to proteins and the lowering of protein, starch, and energy digestibility (Agus *et al.*, 2017) [2]. When chickens were fed diets with tannins, according to Goliomytis *et al.* (2015) [18], dry matter intake, bodyweight, feed efficiency, and nutrient digestibility were reduced, but Ebrahim *et al.* (2015) [14, 15] found a reduction in feed intake and body weight increase. However, Chamorro *et al.* (2015) [9] observed that there were no effect on growth performance, egg weight, cell thickness, or layer yolk colour. While some researchers found that supplementing different sources of tannins at modest dosages (0.5 to 5 g/kg) had no effect on growth performance and even had negative effects on the birds' ability to grow, other researchers found the opposite. These variations could be the result of various tannin sources, a longer supplementation time, or particular testing settings (e.g., genetics of chickens, temperature and abundance of pathogens in the living conditions).

The immune system, gastrointestinal environment, and gut microbiota of chickens reared under standard conditions can be enhanced by supplementary tannins when used in the right amounts. According to a study by Karaffová *et al.* (2019) [22], the upregulation of immunoglobulin A and mucin 2 by tannins helped hens maintain certain mucosal immune components. In addition, Erlejman *et al.* (2008) [16] showed that CT can interact with tumour necrosis factor- receptors (pro-inflammatory cytokines) to reduce inflammation, which suggests that tannins directly influence the immune system without producing antimicrobial and antioxidant effects.

By tracking variables like as feed conversion ratio (FCR), body weight gain (BWG), apparent metabolizable energy (AME), residual feed intake (RFI), and time to reach desired weight, one may estimate the performance of poultry. Due to its critical involvement in feed digestion and nutrient absorption, the makeup of the gut microbiota can have an impact on FCR. Due to an elevated FCR, Campylobacter has been associated with poor productivity (Awad *et al.*, 2015) [5]. Different bacterial populations associated with FCR have been found in research using the cecum. Most research found that higher FCR was associated with Lactobacilli, while lower FCR was shown to be related to Faecalibacterium genera. In a study, neither higher nor decreased FCR in the jejunum has been associated to any microbial colonies (Stanley *et al.*, 2012) [41]. While Leptotrichia, Pediococcus, Rohdococcus, and Escherichia coli were associated with low FCR in the jejunum, another investigation connected Lactobacillus, Fructobacillus, and Paralactobacillus with high FCR (Shah *et al.*, 2019) [38]. Shigella, Enterobacteria, and E. coli were associated with decreased BWG, whereas Clostridium coccoides was associated with higher BWG. A few bacterial species in the ileum have been found to be associated with chicken productivity. The majority of the time, increased performance and better health have been linked to Lactobacillus species (Ocejo *et al.*, 2019) [33]. Contrarily, two investigations found that low productivity was linked to Lactobacillus species in the ileum (Metzler-Zebeli *et al.*, 2019) [28]. The faecal bacteria Lactobacillus and Bacteroides have been linked to research that found that they improve productivity (Singh *et al.*, 2012) [40]. As a result, the chicken's ability to produce can be impacted by the gut microbiota's makeup. Yet more research is needed to properly understand the connection between chicken productivity and the composition of their gut microbiome. High feed efficiency has been related with less diversified gut microbiota in chickens, according to some authors, whereas others have found a correlation between higher bacterial community complexity and richness and improved feed efficiency.

According to Diaz Carrasco *et al.* (2018) [13], a mixture of chestnut (HT) and quebracho tannins (CT) altered the diversity of the cecal microbiota in chickens, decreased the number of members of the genus Bacteroides, and increased the number of individuals from the order Clostridiales, mostly from the families Ruminococcaceae and Lachnospiraceae. According to Viveros *et al.* (2011) [49], tannins may potentially have prebiotic effects by promoting the growth of beneficial microorganisms. Because the microbiota of chickens is strongly related to the gut ecology of chickens, tannins' ability to modulate the microbiome may help to partially explain the gut health-promoting benefits of chickens (Shang *et al.*, 2018) [39]. Even in the absence of challenge models, supplementary tannins may help broiler chickens grow more quickly and have healthier gut microbes and ecosystems.

Conclusions

The effects of tannins have shown to be useful in the search for an antibiotic-free growth stimulant for chicken production. Tannins are useful as a feed addition and as an important component in animal health. The evaluation of the literature on the advantages and effects of tannins in poultry production is vast. Although tannins can be used as feed additives and their inclusion in feed has the potential to reduce issues, replace antibiotic growth promoters, and increase the effectiveness of poultry production with healthy poultry produce, their level of inclusion will vary depending on the source, chemical composition, age, and species of poultry.

References

1. Aboagye IA, Oba M, Koenig KM, Zhao GY, Beauchemin KA. Use of gallic acid and hydrolyzable tannins to reduce methane emission and nitrogen excretion in beef cattle fed a diet containing alfalfa silage. J Anim. Sci. 2019;97:2230-2244.
2. Agus S, Achmadi SS, Mubarik NR. Antibacterial activity of naringenin-rich fraction of pigeon pea leaves toward Salmonella thypi. Asian Pac. J Trop. Biomed. 2017;7:725-728.
3. Ahmed ST, Yang CJ. Effects of dietary Punica granatum L. by-products on performance, immunity, intestinal and fecal microbiology, and odorous gas emissions from excreta in broilers. J Poult. Sci. 2017;54(2):157-166.
4. Antongiovanni M, Minieri S, Buccioni A, Galigani I. Effect of a tannin from chestnut wood (*Castanea sativa* Miller) on cholesterol and fatty acids of eggs; c2015.

http://www.wpsa.com/index.php/wpsa-proceedings/2015/xxii-europeansymposium-on-the-quality-of-poultry-meat-and-the-xvi-europeansymposium-on-the-quality-of-eggs-and-egg-products/2150-effect-of-a-tanninfrom-chestnut-wood-castanea-sativa-miller-on-cholesterol-and-fatty-acids-ofeggs/file.

5. Awad WA, Smorodchenko A, Hess C, Aschenbach JR, Molnar A, Dublecz K, *et al.* Increased intracellular calcium level and impaired nutrient absorption are important pathogenicity traits in the chicken intestinal epithelium during Campylobacter jejuni colonization. Appl. Microbiol. Biotechnol. 2015;99:6431-6441.
6. Bawadi H, Bansode R, Trappey A, Truax R, Losso J. Inhibition of Caco-2 colon, MCF-7 and Hs578T breast, and DU 145 prostatic cancer cell proliferation by water-soluble black bean condensed tannins. Cancer Lett. 2005;218:153-162.
7. Bostami A, Ahmed S, Islam M, Mun H, Ko S, Kim S, *et al.* Growth performance, fecal noxious gas emission and economic efficacy in broilers fed fermented pomegranate byproducts as residue of fruit industry. Int. J. Adv. Res. 2015;3:102-114.
8. Cengiz O, Koksal BH, Tatli O, Sevim O, Ahsan U, Bilgili SF, *et al.* Effect of dietary tannic acid supplementation in corn-or barley-based diets on growth performance, intestinal viscosity, litter quality, and incidence and severity of footpad dermatitis in broiler chickens. Livest. Sci. 2017;202:52-57.
9. Chamorro S, Viveros A, Rebol´e A, Rica BD, Arija I, Brenes A. Influence of dietary enzyme addition on polyphenol utilization and meat lipid oxidation of chicks fed grape pomace. Food Res. Int. 2015;73:197-203.
10. Chung KT, Lu Z, Chou M. Mechanism of inhibition of tannic acid and related compounds on the growth of intestinal bacteria. Food Chem. Toxicol. 1998;36:1053-1060.
11. Clark EL, Macdonald SE, Thenmozhi V, Kundu K, Garg R, Kumar S, *et al.* Cryptic Eimeria genotypes are common across the southern but not northern hemisphere. Int. J. Parasitol. 2016;46:537-544.
12. Daglia M. Polyphenols as antimicrobial agents. Curr. Opin. Biotechnol. 2012;23:174-181.
13. Diaz Carrasco JM, Redondo EA, Pin Viso ND, Redondo LM, Farber MD, Fernandez Miyakawa ME. Tannins and bacitracin differentially modulate gut microbiota of broiler chickens. Biomed. Res. Int; c2018.
14. Ebrahim R, Liang JB, Jahromi MF, Shokryazdan P, Ebrahimi M, Chen WL. Effects of tannic acid on performance and fatty acid composition of breast muscle in broiler chickens under heat stress. Ital. J Anim. Sci. 2015;4(4):572-7.
15. Ebrahim R, Liang JB, Jahromi MF, Shokryazdan P, Ebrahimi M, Li CW, *et al.* Effects of tannic acid on performance and fatty acid composition of breast muscle in broiler chickens under heat stress. Ital. J Anim. Sci. 2015;14:3956.
16. Erlejman AG, Jaggers G, Fraga CG, Oteiza PI. TNFα-induced NF-κB activation and cell oxidant production are modulated by hexameric procyanidins in Caco-2 cells. Arch. Biochem. Biophys. 2008;476:186-195.
17. Farahat MH, Abdallah FM, Ali HA, Hernandez-Santana A. Effect of dietary supplementation of grape seed extract on the growth performance, lipid profile, antioxidant status and immune response of broiler chickens. Animal. 2017;11(5):771e7.
18. Goliomytis M, Kartsonas N, Charismiadou MA, Symeon GK, Simitzis PE, Deligeorgis SG. The Influence of Naringin or Hesperidin Dietary Supplementation on Broiler Meat Quality and Oxidative Stability. PLoS ONE. 2015;10:e0141652.
19. Hosseini-Vashan SJ, Safdari-Rostamabad M, Piray AH, Sarir H. The growth performance, plasma biochemistry indices, immune system, antioxidant status, and intestinal morphology of heat-stressed broiler chickens fed grape (*Vitis vinifera*) pomace. Anim. Feed Sci. Technol. 2020;259:114343.
20. Hu YJ, Cowling BJ. Reducing antibiotic use in livestock, China. Bull. World Health Organ. 2020;98:360.
21. Huang Q, Liu X, Zhao G, Hu T, Wang Y. Potential and challenges of tannins as an alternative to in-feed antibiotics for farm animal production. Anim. Nutr. 2018;4:137-150.
22. Karaffova V, Bobikova K, Levkut M, Revajova V, Sevcikova Z, Levkut M. The influence of Farmatan® and Flimabend® on the mucosal immunity of broiler chicken. Poult. Sci. 2019;98:1161-1166.
23. Li C, Yan X, Lillehoj HS, Oh S, Liu L, Sun Z, *et al.* Eimeria maxima-induced transcriptional changes in the cecal mucosa of broiler chickens. Parasites Vectors. 2019;12:285.
24. Lin H, Decuypere E, Buyse J. Acute heat stress induces oxidative stress in broiler chickens. Comp. Biochem. Physiol. Part A Mol. Integr. Physiol. 2006;144:11-17.
25. Malomo GA, Bolu SA, Madugu AS, Usman ZS. Nitrogen Emissions and Mitigation Strategies in Chicken Production. Anim. Husband. Nutrit. 2018;43:43-62.
26. Mansoori B, Modirsanei M. Effects of dietary tannic acid and vaccination on the course of coccidiosis in experimentally challenged broiler chicken. Vet. Parasitol. 2012;187:119-122.
27. Mayne R, Powell F, Else R, Kaiser P, Hocking P. Foot pad dermatitis in growing turkeys is associated with cytokine and cellular changes indicative of an inflammatory immune response. Avian Dis. 2007;36:453-459.
28. Metzler-Zebeli BU, Siegerstetter SC, Magowan E, Lawlor PG, Petri RM, NE OC, Zebeli Q. Feed Restriction modifies intestinal Microbiota-host mucosal networking in Chickens Divergent in Residual Feed Intake. M-Systems; c2019. p. 4.
29. Mishra B, Jha R. Oxidative stress in the poultry gut: Potential challenges and interventions. Front. Vet. Sci. 2019;6:60.
30. Mottet A, Tempio G. Global poultry production: Current state and future outlook and challenges. World. Poult. Sci. J. 2017;73:245-256.
31. Nawab A, Ibtisham F, Li G, Kieser B, Wu J, Liu W, *et al.* Heat stress in poultry production: Mitigation strategies to overcome the future challenges facing the global poultry industry. J Therm. Biol. 2018;78:131-139.
32. Noack S, Chapman HD, Selzer PM. Anticoccidial drugs of the livestock industry. Parasitol. Res. 2019;118:2009-2026.
33. Ocejo M, Oporto B, Hurtado A. 16S rRNA amplicon sequencing characterization of caecal micro biome composition of broilers and free-range slow-growing chickens throughout their productive lifespan. Sci. Rep.

2019;9:2506.
34. Ramnath V, Rekha P. Brahma Rasayana enhances in vivo antioxidant status in cold-stressed chickens (*Gallus gallus domesticus*). Indian J Pharmacol. 2009;41:115.
35. Redondo LM, Chacana PA, Dominguez JE, Miyakawa MEDF. Perspectives in the use of tannins as alternative to antimicrobial growth promoter factors in poultry. Front. Microbiol; c2014. p. 5.
36. Yang R, Hui Q, Jiang Q, Liu S, Zhang H, Wu J, *et al.* Effect of Manitoba-grown red-osier dogwood extracts on recovering Caco-2 cells from H2O2-induced oxidative damage. Antioxidants. 2019;8:250
37. Rezar V, Salobir J. Effects of tannin-rich sweet chestnut (*Castanea sativa* mill.) wood extract supplementation on nutrient utilisation and excreta dry matter content in broiler chickens. Eur. Poult. Sci. 2014;78:1-10.
38. Shah TM, Patel JG, Gohil TP, Blake DP, Joshi CG. Host transcriptome and micro biome interaction modulates physiology of full-sibs broilers with divergent feed conversion ratio. NPJ Biofilms Micro biomes, 2019;5:1-13.
39. Shang Y, Kumar S, Oakley B, Kim WK. Chicken gut microbiota: Importance and detection technology. Front. Vet. Sci. 2018;5:254.
40. Singh KM, Shah T, Deshpande S, Jakhesara SJ, Koringa PG, Rank DN, *et al.* High through put 16S rRNA gene-based pyrosequencing analysis of the fecal micro biota of high FCR and low FCR broiler growers. Mol. Biol. Rep. 2012;39:10595-10602.
41. Stanley D, Denman SE, Hughes RJ, Geier MS, Crowley TM, Chen H, et al. Intestinal micro biota associated with differential feed conversion efficiency in chickens. Appl. Microbiol. Biotechnol. 2012;96:1361-1369.
42. Starcevic K, Krstulovic L, Brozic D, Mauric M, Stojevic Z, Mikulec Z. Production performance, meat composition and oxidative susceptibility in broiler chicken fed with different phenolic compounds. J Sci. Food Agri. 2015;95(6):1172e8.
43. Tan Z. Roles of Iron Uptake in the Survival, Colonization and Virulence of Salmonella in Animal Guts. Master’s Thesis, University of Manitoba, Winnipeg, MB, Canada; c2019.
44. Teng PY, Yadav S, De Souza Castro FL, Tompkins YH, Fuller AL, Kim WK. Graded Eimeria challenge linearly regulated growth performance, dynamic change of gastrointestinal permeability, apparent ileal digestibility, intestinal morphology, and tight junctions of broiler chickens. Poult. Sci. 2020;99:4203-4216.
45. Thung T, Mahyudin N, Basri D, Radzi CWM, Nakaguchi Y, Nishibuchi M, *et al.* Prevalence and antibiotic resistance of Salmonella Enteritidis and Salmonella Typhimurium in raw chicken meat at retail markets in Malaysia. Poult. Sci. 2016;95:1888-1893.
46. Tonda R, Rubach J, Lumpkins B, Mathis G, Poss M. Effects of tannic acid extract on performance and intestinal health of broiler chickens following coccidiosis vaccination and/or a mixed-species Eimeria challenge. Poult. Sci. 2018;97:3031-3042.
47. Tosi G, Massi P, Antongiovanni M, Buccioni A, Minieri S, Marenchino L. Efficacy test of a hydrolysable tannin extract against necrotic enteritis in challenged broiler chickens. Ital. J Anim. Sci. 2013;12:123e32.
48. Viveros A, Chamorro S, Pizarro M, Arija I, Centeno C. Brenes A. Effects of dietary polyphenol-rich grape products on intestinal micro flora and gut morphology in broiler chicks. Poult. Sci. 2011;90:566-578.
49. Viveros A, Chamorro S, Pizarro M, Arija I, Centeno C, Brenes A. Effects of dietary polyphenol-rich grape products on intestinal micro flora and gut morphology in broiler chicks. Poult. Sci. 2011;90(3):566e78.
50. Wang ML, Suo X, Gu JH, Zhang WW, Fang Q, Wang X. Influence of grape seed proanthocyanidin extract in broiler chickens: effect on chicken coccidiosis and antioxidant status. Poult. Sci. 2008;87(11):2273e80.
51. Yang C, Chowdhury MAK, Hou Y, Gong J. Phytogenic Compounds as Alternatives to In-Feed Antibiotics: Potentials and Challenges in Application. Pathogens. 2015;4:137-156.