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Nutrigenomic Application in Poultry

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CHAPTER 1

Introduction

Nutrition is the most important environmental factor affecting the development, health status, growth performance and profitability of poultry production, feeds of poultry constitute up to 70-75% of total production costs. Protein, Energy fat, Minerals, Vitamins, and water are of basic importance for poultry nutrition (Raza et al.,2019).

In recent years there has been an enormous development of molecular genetics techniques allowing the study of genome function on a large scale. These advances have been accompanied by a decrease in costs and greater accessibility, which has contributed to the development of new disciplines that would fall within the generic term "Nutritional Genomics". This nascent area studies the interactions of food and its components with the genome at the molecular, cellular and systemic levels. Nutritional Genomics is currently divided into two different fields of research: "Nutrigenomics" has emerged as a novel and multidisciplinary research field in nutritional science that aims to elucidate how dietary nutrients can interact with genes affecting transcription factors, RNA and protein expression, cellular homeostasis and metabolite production (genome, transcriptome, proteome, metabolome) (Lopez et al., 2003); (Ordovas and Corella, 2003).

Nutrigenomics as the word implies is the study of genomics influence of nutrition on animals. From this perspective, nutrients are dietary signals detected by the cellular sensor which in turn influence gene and protein expression and subsequently metabolite production. Thus patterns of gene expression, protein expression and metabolite production in response to particular nutrients can be viewed as dietary signatures. Nutrigenomics

seeks to examine these dietary signatures in specific cells, tissues and organisms to understand how nutrition influences homeostasis (Benitez and Ovilo, 2017). Through nutrigenomics, we are carefully selecting nutrients for fine-tuning genes and present them in every cell and every tissue of animals (Van,2004).

Nutrigenomics plays an important role in integrating genomic approaches into nutrition research. Well over a decade ago, nutrigenomics diverged from mainstream nutritional science as a specific methodological and conceptual approach (Muller and Kersten, 2003).

The objective of this mini-review is to discuss the basic concepts, and technical terms in nutrigenomics and also discuss the results of some published studies that show how nutrition affects the expression of genes involved in metabolism and how nutritional intervention might change animal products, quality and tissue composition, to improve the Poultry performance and Poultry health.

CHAPTER 2

2. Literature Review

2.1. Nutrigenomics

Nutrigenomics is the study of molecular relationships between nutrition and the response of genes. Nutrigenomics aims to extrapolate how nutrition-induced gene expression changes affect performance traits. Nutrigenomics focuses on the effect of nutrients on the genome, transcriptome, proteome, and metabolome. By determining the mechanism of the effects of nutrients or the effects of a nutritional regime, Nutrigenomics tries to define the relationship between these specific nutrients or specific nutrient regimes (diets) and performance traits. Nutrigenomics is a new science, still in its infancy but isexpanding rapidly. It focuses on the effects that genetic variations have on the binomial diet/disease or the nutritional requirements and recommended intakes for individuals and populations. To achieve its objectives, the methodology used in nutrigenetics includes the identification and characterization of genetic variants that are associated with or are responsible for a different response to certain nutrients or food components (Muller and Kersten, 2003). Nutrigenomics includes investigations into the influence of nutritional constituents on genome functioning in terms of epigenetic modifications and gene expression patterns (Nowacka-Woszuk 2020).

As the demand for broiler chicken is increasing rapidly, feed optimization in chicken farms is a very crucial job in terms of health and production which would not be possible without considering nutrigenomics research. Nutrigenomics play a critical role in poultry production like correlating nutrition and genetics in breeding programs, helps to improve bird performance, increase feed efficiency, deliver better health and

increase meat quality. For the past few years, several nutritional programs have been conducted to explore the effect of diet on neonatal and early-life periods. Researchers have demonstrated that fasting in post-hatch chicken for a period of 24 h has adverse effects which reduce body weight and meat quality in adult broilers. Particularly, nutrigenomics research will lead to the implementation of improved precision feeding strategies by the poultry industry (Chris, 2011).

2.2. Nutrigenomics applications

Nutrigenomics is the study of how different diets, nutrients, and nutritional methods affect the genome. Using DNA microarray technology, we can begin to understand how nutrition influences gene expression and how this modulation relates to animal performance and health. Feed digestion and absorption are dependent on the integrity of avian GIT. Nutrigenomics offers a systems biology perspective on how nutrients interact with gut cells and the microbiota in the intestine to affect intestinal health. Broiler gut health can be improved with different supplements, resulting in increased feed efficiency and growth (Alagawany et al. 2020b; Elnesr et al., 2020).

2.3. Classical Nutrition Studies and Nutrigenomics

In recent years, the focus of most nutritional research has been on parameters related to animal growth performance, reproduction, intestinal health or the utilization of specific nutrients as a means to reduce excess waste. Classical nutritional studies, which are commonly used, involve a considerable number of individual animals and replication of treatments to establish statistical differences between individual treatments. Depending on the actual hypothesis, nutritional

studies usually take a considerable time to deliver a conclusion. The measured parameters are often closely interrelated; hence it is difficult to demonstrate the effect of a specific dietary ingredient. The key to understanding the relationship between specific nutritional interventions and their impact on health and performance lies in a deeper understanding of the impact of these nutrients on the expression of specific genes or specific metabolic pathways. The development of molecular tools which enable researchers to study the effects of specific nutrients on the whole genome or, in other words, the effect of thousands of genes simultaneously, has opened a completely different avenue for nutritional research. More recently with the development of the field of molecular biology, researchers have been able to study the impact of diet on the organism at the molecular level. The concept of nutritional genomics or specifically the term "nutrigenomics" developed at the turn of the 21st century to describe the trend in human nutrition research towards individualized dietary formulation. In reality, the scope of this field is significantly larger.

Dietary chemicals have been shown to alter gene expression in several ways. For example, they may act as ligands for transcription factor receptors; and be metabolized by primary or secondary metabolic pathways thereby altering concentrations of substrates or intermediates or altering signal transduction pathways (Muller and Kersten, 2003).

2.4. Nutrigenomics: How Does It Work?

Nutrigenomics combines several different sciences to understand the effects of nutrients on physiological responses. In nutrigenomics, nutrients are signals to specific cells in the body, when interpreting the information of such a nutrient, the cell reacts by sending biochemical

information from DNA or genes (the science of genomics) to RNA (the science of transcriptomic) which is in turn translated into specific proteins (the science of proteomics) and ultimately determines the metabolic pathways (the science of metabolomics). All biological processes depend on the flow of information in this sequence. Although these processes are controlled by the basic genetic makeup, external factors such as disease challenges, environmental toxins or specific nutrients can influence these pathways.

The greater understanding of the genome of humans and animals alike is the foundation of nutrigenomics. Although techniques to measure the expression of individual genes have been available for some years, only the development of gene chips (DNA microarrays) has allowed researchers to measure the expression of thousands of genes simultaneously. Gene chips are simply a collection of thousands of microscopic spots of specific DNA sequences. Rather than measuring the effect of a specific nutrient on animal performance or the physiological response at the end of the experiment, researchers can extract specific messenger RNA (mRNA) from tissue at any stage. The amount of mRNA present relates to the relative amount of copies of known genes, measured by using gene chips. Using contrasting colour labels, it can be determined if a gene is up-regulated, down-regulated or unaffected as a result of a specific dietary manipulation (Moody, 2001).

2.5. Effect of Protein on the Gene Expression

Protein-rich diets cause a shortage of mRNA necessary for the expression of the fatty acid synthase gene in the adipocytes, resulting in the moderation of total body fat. Such an effect cannot be observed in the liver tissue. Hepatic fat synthesis, in turn, can be inhibited by providing unsaturated fatty acids in the diet (Clarke, 1993).

2.6. Minerals and Gene Function

Bivalent metals strongly influence gene expression. For instance, both parenteral and oral *zinc or cadmium* applications enhance the transcription rate of the metallothionein (MT) gene in intestinal tissue (Ouellette et al.,1982). *Cadmium* acts also in prolonging the half-life of MT mRNA in hepatocytes. This effect on the half-life prolongation of MT mRNA is metal and tissue-specific: the influence of cadmium is stronger than that of zinc, and the intensity of effect in spermatocytes and spermatids is higher than in hepatocytes and fibroblasts (De et al., 1991). *Zinc* acts as part of the 'zinc- fingers', fixing activator proteins to the active segments of the DNA. Appropriate zinc supply is essential to the balanced regulation of gene expression of pro-inflammatory enzymes like cyclooxygenase- 2 (COX-2). According to (Fong et al. 2005), improvement of zinc status results in a significant reduction of COX mRNA abundance. The dietary supplementation with zinc oxide increases insulin-like growth hormone I (IGF-I) and IGF-I receptor gene expression in the small intestine of weanling piglets (Li et al., 2009). *Iron* influences transferrin and ferritin concentrations by exerting an effect on mRNA stability and the translation rate (Bremner and Beattie, 1990).

2.7. Vitamins and Gene Expression

Vitamin A exerts its regulatory function in the form of retinol and retinoic acid. The most important target tissues are in the adrenal glands, testes, cerebellum, kidneys, prostate, cerebral cortex, skin and the viscera. After retinoic acid binds to its receptor, it will stimulate the transcription and translation of vitamin A-responsive genes, including some involved in cell differentiation (growth hormone, glycerol phosphate dehydrogenase and leptin production among others. Deficient vitamin A status was found to negatively influence hepatic PEPCK gene expression in mice. By the oral application of retinoic acid that expression could be restored (Scribner et al., 2005). Like those of retinoic acid, the actions of *active vitamin D* are mediated by nuclear hormone receptors. The vitamin D receptor directly binds to DNA at vitamin D-responsive elements as a homodimer or heterodimer to activate gene transcription. Ligand binding to the vitamin D receptor forms a complex of coactivators that modulate gene expression in different cell types (Bohnsack and Hirschi, 2004). A role for *biotin* in gene expression has been recognized by the significant depression of ornithine trans carboxylase gene expression in biotin deficiency. The consequent loss of enzyme activity is the basis for hyperammonaemia (Yuichi et al., 1996).

CHAPTER 3

3. Results and Discussion

3.1. Effect of Amino Acid on Gene Expression

Abdelfatah et al., (2023). experimented with 360, day old male broiler chicks were divided into four groups (90 birds each), then each group was subdivided into three replicated (30 birds each), birds were allocated as follows; G1) served as control which fed on the basal diet only without any dietary treatments, G2) was fed on basal diet fortified with 0.25% glycine from premix, G3) was fed on basal diet fortified with 0.17 % glycine and G4) was fed on basal diet fortified with 0.08 % glycine from premix. During the observation period (35 days), growth performance parameters were recorded. Also, liver samples were collected and subjected to RNA extraction to detect IL6, and IL1B as inflammatory response indicators, Myogenin, Insulin-like Growth Factor 1 (IGF1) as muscular structure indicators and glutathione peroxidase (GSH-PX) as an antioxidant capacity indicator by using (real-time PCR). The result revealed that, at day 35, the BW, BWG, and FI were significantly elevated in G2 (Table 1). G2, G3 and G4 showed better gene expression of Myogenin, IGF1and GSH-Px compared to G1. Moreover, they appeared the lowest gene expression of IL6 and IL1B (Figure 1). These results parallel those reported by Takahashi et al. (2008) who found that the addition of glycine to a broiler chicken diet influences the inflammatory reaction via affecting the production of pro-inflammatory cytokines like IL-1, IL-6, IFN-gamma and TL1A. Also, these results could be explained by those inflammatory diseases may raise the glycine demand of birds during a

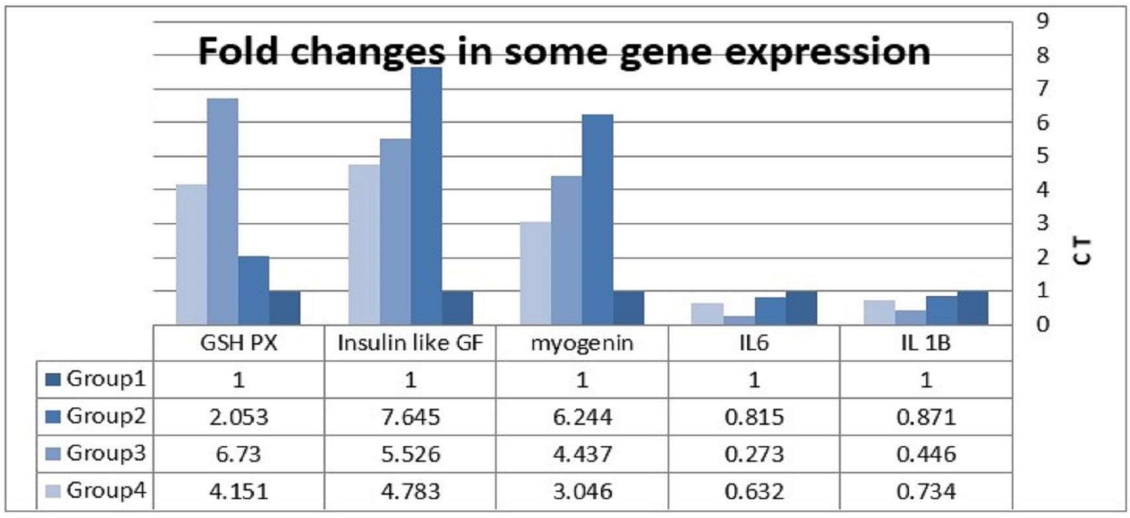
point in life when they have an innate need for this nutrient, it's also thought that adding glycine to broiler ration could aid counteract the catabolic alterations that come with immune activation (Takahashi et al., 2008). In addition, the lowered inflammatory reaction in broiler chickens reared on a glycine-supplemented diet could be explained by the modulation of TNF-α, IL-1β and IL-10 secretion in mammals (You et al., 2006). Furthermore, birds' final weight was shown to be highly connected with the gene expression related to growth. The expression of the jejunal mucin 2 gene (MUC2, essential for the maintenance of the mucus layer on the surface of the intestinal lumen) was increased (3.8-fold) with increasing lysine in the low crude protein diet of broilers when compared to the control diet (Lee et al. 2020), Also, in ovo injection of methionine led to the upregulation of genes related to growth and metabolism (somatostatin R5 and thyroid stimulating hormones) and antioxidants (SOD, GSTa and GSH-px) in the liver tissues of newly hatched broiler chicks compared with the control group (Elwan et al. 2021).

In conclusion, the highest concentration of glycine fortification (0.25%) reveals the best body performance. All glycine-treated groups have proper gene expression of Myogenin and IGF1, a significant increase in the gene expression of GSH-Px, and the lowest genes expression of IL6 and IL1BFurther studies are rec- ommended to investigate the role of glycine in the improvement of the immune response during microbial experimental infection with correlation to its impact on gut microbiota.

Table 1. Effect of dietary glycine fortification on growth performance of broiler chickens.

	G1	G2	G3	G4
Initial weight	45±1.5	45±1.0	46.6± 0.66	46.6±0.88
Body weight (g) 35 days	1840.50±29.58[b]	1962.61±17.18[a]	1817.11±18.40[b]	1777.16±17.26[b]
BWG (g) Days 1-35	1795.50±80.75[b]	1917.61±11.75[a]	1770.44±89.6 [b]	1753.61±18.92[b]
FI (g) Days 1-35	3505.18±13.33[b]	3587.61±28.7[a]	3461±19.24 [b]	3447.5±22.9[b]
FCR Days 1-35	1.96±0.09	1.87±0.02	1.96±0.1	1.96±0.02

Data are expressed as Mean±Standard error. G1: Control - basal diet; G2 basal diet +0.25% glycine; G3: basal diet + 0.17% glycine; G4 basal diet +0.08% glycine.
[a,b,c] Different superscripts in the same row indicate significant difference ($p \leq 0.05$).



	GSH PX	Insulin like GF	myogenin	IL6	IL 1B
Group1	1	1	1	1	1
Group2	2.053	7.645	6.244	0.815	0.871
Group3	6.73	5.526	4.437	0.273	0.446
Group4	4.151	4.783	3.046	0.632	0.734

Fig. 1. Effect of glycine fortification on changes in some gene expression.
G1: Control - basal diet; G2 basal diet +0.25% glycine; G3: basal diet + 0.17% glycine; G4 basal diet + 0.08% glycine

3.2. Effect of Minerals on Gene Expression

Ibrahim et al., (2017) showed that different sources of Zinc (Zn) were compared to assess their possible effects on performance, nutrients retention, mineral distribution and some serum parameters of broiler chickens. A total of 200 one-day old Ross 308 chicks were divided into in equal four dietary treatments groups with five replicates each of ten chicks. The experimental groups were given the basal diet (inorganic ZnO), basal diet supplemented with organic Zn (Zn methionine), nano-ZnO and Zn- mix (organic Zn and nano-ZnO) at a concentration of 50 mg/kg of diet. After 42 days of the feeding trial, the group supplemented with nano-ZnO exhibited the best final body weight and feed conversion ratio (2380 g/bird and 1.69, respectively) Table 3. Dietary Zn-mix and nano-ZnO positively affected mRNA expression of insulin, like growth factor-1 and growth hormone genes in broilers when compared to the inorganic ZnO source (Figure 2). Similarly, Zn augmented the growth factor synthesis, as IGF-1 and influenced the action of calcium-regulating hormones (Lowe et al., 2002). Also, Zn plays an important role in the formation of insulin through its enzyme systems (Brody, 1994). Compared with the inorganic Zn, Zn-supplemented group, the serum level of IGF-1 was increased in the organic Zn group (Tomaszewska et al., 2017).

Table 2. Effects of dietary different forms of Zn on performance (1-42 days) nutrient retention of broiler chickens (means ± standard error)

Items	Control[1]	Organic-Zn[2]	Nano-ZnO[3]	Zn-mix[4]
Body weight (g)	2018±19.20[d]	2106± 9.54[c]	2380±12.66[a]	2302± 4.16[b]
Body weight gain, g/bird	1972 ± 32.35[d]	2061±16.86[c]	2335 ±22.91[a]	2256 ± 7.57[b]
Feed intake (g)	4043±86.02	3938± 58.59	3954±83.64	3948±12.90
Feed conversion ratio	2.05± 0.02[a]	1.91± 0.02[b]	1.69±0.03[d]	1.75± 0.01[c]
Zn (mg/kg)	250.32±0.04[b]	265.3±0.04[a]	265.36±0.06[a]	260.32±0.04[a]
Fe (mg/kg)	12.50±0.06	13.34±0.01	13.61±0.03	14.10±0.02
Cu (mg/kg)	11.10±0.09	11.50±0.1	12.54±0.04	12.35±0.08

[1]Control: group supplemented with inorganic zinc oxide; [2]Organic-Zn: group supplemented with Zn methionine; [3]Nano-ZnO: group supplemented with nano Zn-oxide and [4]Zn-mix: group supplemented with both Zn methionine and nano Zn-oxide.

[a-b-c-d]Means in a row with different superscripts were significantly different (P<0.05).

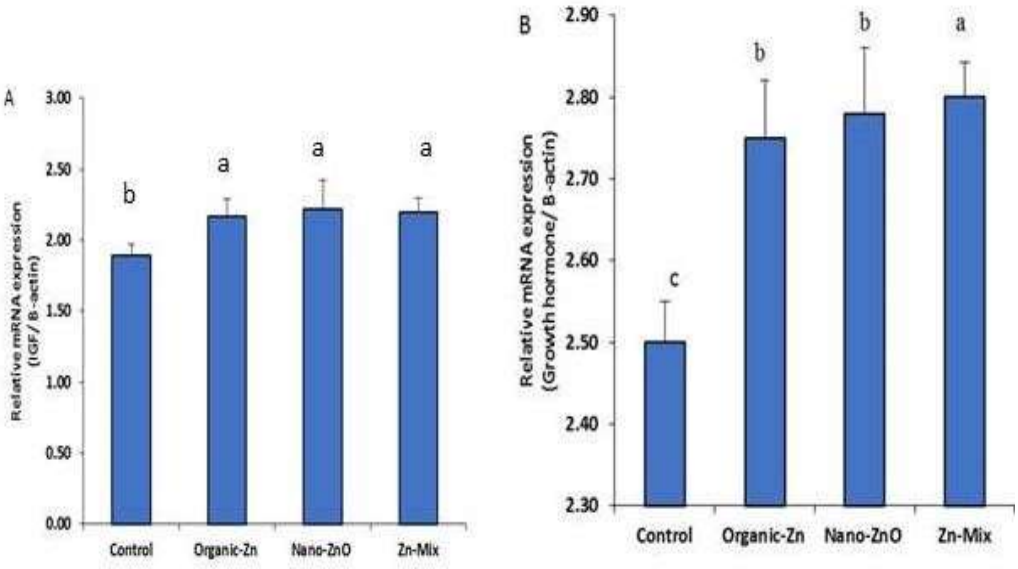
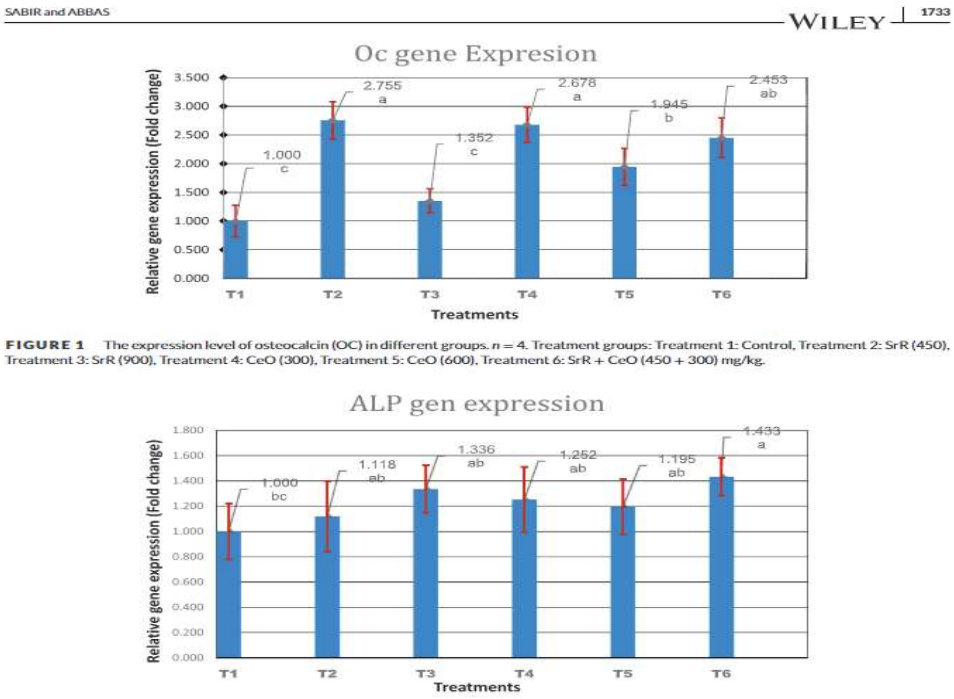


Figure 2. Effect of different dietary forms of zinc on the relative mRNA expression of A) insulin-like growth factor-1 and B) growth hormone genes of broilers chicken.

Sabir and Abbas, (2023). In a study was conducted to investigate the effect of SrR, CeO, and their combinations on tibia quality in broilers. A total of 384 one-day-old Ross chicks were divided into six treatments, with four replicates per treatment (16 birds per replicate). The control group was fed a standard diet, and other groups were fed SrR at levels 450, 900 mg/kg feed, CeO at levels 300 and 600 mg/kg feed and a combination of 450 SrR + 300 CeO mg/kg feed, showed higher gene expression of OC significantly was noticed in all treated groups compared to the control, except the group fed 900 mg/kg SrR. ALP gene expression was increased significantly in the combination group (450 SrR + 300 CeO mg/kg feed) compared to the control group. The SrR and CeO can be used as beneficial additives in the feed to improve the tibia quality of broilers.

Figure 3. The expression level of Osteocalcin(OC) and Alkalinephosphatase (ALP).



3.3. Effect of Vitamins on Gene Expression

Niu and Liu, (2018) approved a study on 240 one-day-old broiler chicks were divided into 3 treatments with 4 replicates of 20 birds. The birds were fed a corn-soybean meal diet supplemented with 0, 100, and 200 mg/kg of vitamin E (Vit.E), respectively. The results indicated that Vit.E supplementation led to the mRNA expression of Total superoxide dismutase (T-SOD) and glutathione peroxidase (GSH-Px) in the liver was linearly increased with the increase in dietary Vit. E ($P < .05$). The results showed that under these experimental conditions, the efficacy of improving the meat quality and antioxidant capacity in broiler chickens fed with 200 mg/kg Vit.E diet is greater compared to that of those fed with 100 mg/kg Vit.E diet supplementation, significantly upregulates the expression of total anti-oxidative capabilities (AOE) genes that improving meat quality in broilers by upregulating the expression of antioxidant enzyme genes in broilers (Table 4), These findings suggest that dietary Vit. E could increase meat quality by upregulating the expression of antioxidant enzyme genes in broilers. Also Jena et al., (2012) showed that Administration of Vit E to hypothyroid rats resulted in elevated catalase (CAT) mRNA levels. Hsiao et al. (2018) revealed that vitamin D3 metabolites significantly upregulated calcium homoeostasis-related genes, including glucuronidase, TRPV6, and calbindin mRNA levels, improving calcium metabolism.

Table 3. Effects of VE on mRNA expression of SOD and GSH-Px in broilers.

Items	0 mg/kg vitamin E	100 mg/kg vitamin E	200 mg/kg vitamin E
T-SOD	0.36 ± 0.05^{c}	0.71 ± 0.02^{b}	0.92 ± 0.03^{a}
GSH-Px	0.25 ± 0.008^{b}	0.82 ± 0.006^{a}	0.89 ± 0.00048^{a}

In the same row, values with different small letter superscripts indicate a significant difference ($P< .05$), values with different capital letter superscripts represent highly significant differences ($P< .01$), whereas with no letter superscripts show no significant differences ($P > .05$).

3.4. Herbal plants and their derivatives

Phytogenic compounds can adjust the gene expression profles of intestinal mucosa (Liu et al. 2014) and encourage digestive secretions to induce nutrient digestibility (Abo Ghanima et al. 2020; Alagawany et al. 2020a). The gene expression of Occludin was signifcantly augmented in the diets supplemented with a plant extract blend (PEB, derived from liquorice, camomile, curcuma and olive leaf) at levels of 500–1000 mg/kg, improving broiler performance and gut health (Farahat et al. 2021). Naji et al. (2014) elucidated that myogenin expression is higher in the group supplemented with phytosterol polyhydroxyphytosterol (Castastesrone) at a level of 20 g/kg than in the control group, whereas myostatin expression is lower. Application of herbs as feed additives could stimulate mucin 2 gene expression, making it useful for poultry. Kamali and Masoudi (2014) showed that supplementation of cinnamon, thyme, and turmeric in broiler diets could boost expression of mucin 2 genes in the small intestine, and this could induce intestinal digestive function and defence. In 2019, Paraskeuas and Mountzouris (2019) stated a signifcant increase in the expression of zonula occludens 2, claudins 5 and mucin owing to the dietary supplementation of 100 mg phytogenic additive/kg.

Ahmadipour and Khajali (2019) stated that feeding Urtica dioica at 1% and 1.5% led to an upregulation of hepatic antioxidant genes catalase (CAT) and superoxide dismutase 1 (SOD1) of broiler chickens. Xiao et al. (2021) found that mRNAs for genes encoding factors involved in adipogenesis and fat storage, CCAAT/enhancer-binding protein b,1-acylglycerol-3-phosphate-O-acyltransferase 2, perilipin-1, and sterol regulatory element-binding transcription factor 1, were more greatly expressed in the adipose tissues of broiler chickens supplemented.

Quercetin supplementation alleviates oxidative injuries by augmenting Nrf2 signalling pathway and increase heme oxygenase-1 (HO-1) gene

expression of. The authors concluded that quercetin could relieve oxidative injuries in the intestines of broiler chickens through the MAPK/Nrf2 signalling pathway (Sun et al. 2020). Furthermore, quercetin enhances mitochondrial function by boosting the translocation of Nrf2 from the cytoplasm to the nucleus and activating the Nrf2 signalling pathway (Li et al. 2016). Also, dietary quercetin with 400 ppm strengthens the intestinal barrier as indicated by increasing the expression and secretion of mucin 2 (MUC2) and promoting Lactobacillus growth in the caecum and restore redox balance after oxidative condition (Dong, Lei, and Zhang 2020).

The protective role of quercetin could be directly via activating antioxidant enzymes or through stimulation of other transcription factors that lead to enhancing the antioxidant defence status especially during challenging conditions. In conclusion, the inclusion of herbal plants and their extracts in poultry diets can regulate the expression of metabolism, immunity, and antioxidant genes Alagawany et al. 2022).

CHAPTER 4

Conclusion

In conclusion, the results of the available experiments allow us to emphasize the importance of the influence of genetic nutrition interactions on different physiological and metabolic processes with transcendence in poultry production and health.

Molecular nutrition in terms of nutrigenomics will serve as a new tool for nutritional research in mitigating the problems related to bird health and production. In the coming year innovations in nutrition research with the use of various molecular technologies will indubitably update our basic understanding of nutrient gene interrelationship and help to define new methods for managing poultry production. Finally, by targeting the specific gene through nutritional manipulation, it may be possible to get the desired performance in terms of health as well as production.

In the future knowledge obtained by nutrigenomics approaches may be applied to specifically modulate performance traits by nutrition and to develop new (more knowledge-based) Poultry feeds/nutrientregimes

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