Chromium Nutrition in Alleviating the effect of Stressors in Poultry Production: A Review

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Abstract
Trace minerals play an essential role to improve production and nutritional efficiency of livestock products. Each trace mineral can have its own and synergistic metabolic/biologic functions on health and performance of chickens. The relationship between trace minerals supplementation and health of animal has been cohesive, especially on the immune function influenced by chromium, an essential element in poultry. The last two decades have seen a high interest of supplementing Cr³⁺ in poultry diets during stress conditions. This review looks at the nutritional benefits of chromium on the immune function in poultry birds from the aspects of the stressors, histological structure of the immune organs, non-specific immunity, humoral immunity, cellular immunity and cytokines.

Introduction
Chromium supplementation in animal diets is relatively gaining momentum in the livestock industry. There have been several reports before 1950, supplementing chromium on carbohydrate metabolism, insulin action and normal cholesterol/diabetic levels in humans using mice model. The examination of using chromium in food supplement has been extended to lab animals and to farm animals. At present, there are four different forms of organic chromium available in global markets such as Chromium propionate (Cr-prop), chromium picolinate (Cr-Pic), chromium methionate (Cr-meth) and chromium yeast (Cr-yeast). However, regulatory bodies such as FDA (Food and drug administration) and European Union have different set of opinions on the form of chromium source in animal diet and level of inclusion. Chromium picolinate (Cr-Pic) was the first Cr-source approved by USFDA for veterinary medicine in 1996, based on information related to glucose metabolism changes in swine and allowed up to 200 ppb/kg of Dry Matter (DM). Followed this, Cr-prop was approved to use up to 200 ppb in swine diets in 2000. In 2009, USFDA approved to use Chromium propionate (Cr-Prop) in cattle diets up to 500 ppb during stress condition. Later, Other forms of chromium such as Cr-meth is allowed only in swine and Cr-yeast in cattle up to 400 ppb/kg of DM. However, several nutritionist and regulatory bodies understands the importance of Chromium (Cr³⁺) in chickens towards the end of 19th century particularly as a stress regulator. Recently (2016), FDA approves the use of chromium propionate as only organic source in broiler diets (200 ppb Cr). The scope of this review is to focus on the beneficial effect of Cr supplementation in poultry birds during stress condition and impact on performance.

The poultry bird experiences several challenges that lead to both specific and nonspecific stressors each day in production. When an animal first encounters a stressor, the neurogenic system is activated [1]. Failed attempts to combat or flee from the stressor immediately result in the activation of the hypothalamic-pituitary-adrenal cortical system. The activation of this system eventually leads to the proliferation of the adrenal cortical tissue which in turn secretes steroid hormones, adrenocorticotropic [2]. The production symptoms of these corticosteroids include cardiovascular diseases, hypercholesteremia, gastrointestinal lesions and immunity. Previous studies have shown that corticosteroids have a negative impact on broiler growth [3]. Chromium has been shown to reduce the levels of corticosteroids in birds alleviating the negative impact of stress on them [4].

Chromium Metabolism and Beneficial Effects in Livestock
Chromium plays a vital role in glucose metabolism through auto amplification mechanisms of insulin signaling in monogastric animals. Chromodulin, an oligopeptide which is a transporter of chromium in the body. It binds with four equivalents of chromium and interacts with the insulin receptor, by prolonging kinase activity through tyrosine-kinase pathway to improve glucose absorption. Chromodulin is a peptide containing amino acids such as glutamic acid, glycine and cysteine which bind only trivalent (Cr³⁺) form of chromium through ligating effect. Hence,
source of chromium is of importance for better absorption especially in poultry. Chromium has also been shown to improve immune function by immune-stimulatory or immunosuppressive processes as shown by its effects on T and B lymphocytes, macrophages, cytokine production and immune responses that may induce hypersensitivity reactions [1].

Several researchers started exploring the effect of chromium in laying hens, breeder chicks and broilers for different requirements. Pronounced effects have been observed in layer birds especially on egg production, egg quality and egg cholesterol levels. Chromium has also been shown to play a key role in lipid, protein and nucleic acid metabolism in livestock [5]. Though, chromium propionate is the only organic form of chromium approved by FDA, researchers started exploring other sources of chromium for better bio-availability such as Chromium picolinate, chromium nicotinate, Cr-yeast and Chromium chloride.

Intensive poultry production whether it is broiler, layer or breeder the expectation is very high to deliver the maximum possible animal protein in a shortest possible period with minimum possible expenses. To get the maximum profit from poultry farming, it is not only essential to provide the best possible nutrition and housing but also to eliminate the potential stressors (Figure 1) affecting the performance of birds. Due to deficiency of Cr levels in diets, external supplementation of chromium has been critical to minimize the negative effects due to stress by improving the performance and immunity of birds.

**Stress in Birds**

Despite “Stress” being the familiar term to understand, there is no universal definition for stress. One definition states that “Stress is any biological response elicited when an animal perceives threat to its homeostasis” and another describes, “Anything causing a negative impact or well-being of the animal” [6]. Often some of them could be termed as “Physiological Limits to Growth”, like ascites and associated metabolic defects in broilers, leg problems in layers etc., [7]. One of the challenges the poultry producer must overcome in the pursuit of this goal is potential stressors that the broiler may experience during the life cycle [8].

**What Causes Stress to Birds?**

Among the stressors, most of them could be maneuvered well except the environmental stress. The environmental stress has a larger level of impact from nature, which is quite puzzling to achieve comprehensively otherwise leads to unfavorable conditions (For example minimizing cold air entry and ammonia elimination in winter). The environmental stress has the highest impact on the production and economicsignificance of commercial poultry. In tropical geographies like South Asian countries, it is nearly impossible to deliver the ideal atmospheric temperature of 18-22OC.

**Impact of Cold Conditions**

Lowered atmospheric temperatures can cause adverse effects including increased feed intake, reduced egg production, and impaired egg quality in layers. In breeders, poor feed efficiency [9] and reduced nutrient digestibility [10] lead to improper chick quality. During environmental stress, elevation of corticosterone level accelerates the generation of free radicals and suppresses the immune function [11]. Those radicals like peroxides, superoxides and hydroxides neutralize specific co-factor enzyme and anti-oxidants leads to a weaker immune system. Such ambient temperatures also result in more mineral excretion and poor growth [12].

**What Happens in the Birds during Stress?**

When the bird or any animal undergoes stress, the nervous system gets activated and creates a “fight or flight” response [13]. Failed attempts to overcome of move away from the stressor results in the activation of hormonal system and secretion of corticosteroids (corticosterone) in to the blood stream [1,14]. Munck et al., [15] reported that stress-induced glucocorticoid levels do not protect against the source of stress itself but rather against the body’s normal reactions to stress, preventing those reactions from overshooting and themselves threatening homeostasis. In case of climatic conditions, temperatures above or below the thermally neutral zone (18-22°C), corticosteroid secretion increases as a response to stress [16].

A stressful condition (Figure 2) leads to the excessive production of free radicals, which results in oxidative stress and an imbalance in the oxidant / antioxidant system [17]. If corticosteroids remain at an elevated level in the circulation, there are many possible effects, including, but not limited to, changes in nutrients especially glucose and mineral metabolism, alteration in immune functions [8,18].
Stress and Immune Functions

Elevated corticosterone tends to inhibit the immune system functions, reducing the lymphocyte proliferation, immunoglobulin production, cytokine production and anti-inflammatory agents [15]. Prolonged periods of stress [19] like environmentally (heat or cold) induced stress [10], leads to regression of lymphoid tissues, thymus, bursa and spleen [20]. Chronic exposure reduces the antibody response to the antigens i.e. vaccines [13].

Stress and Nutrient Metabolism

Stress induced alterations leads to mobilization or production of glucose for energy needs to maintain the homeostasis [8] and the skeletal muscle are more susceptible in this catabolic condition. In addition to this, this corticosterone reduces the muscular protein synthesis [21] and stimulates the protein synthesis in liver leads to hypertrophy. The increase in liver weight could be due to increase in liver fat because lipids shown to increase in liver in broiler under corticosterone stress condition [22]. In addition, it minimizes the lipolysis and increases the rate of fat deposition [23] especially abdominal fat accretion in broilers.

Corticosterone induced by stress also has impact on mineral metabolism through inducing osteoporosis and interfering the mineral absorption from intestine by inhibiting the mineral binding protein synthesis [24]. Mineral binding proteins are the carriers which transports the metal elements across from intestinal lumen to circulation. Several reports confirmed that the birds under stress have significantly lower protein and carbohydrate digestibility, might be due to increased feed passage time leads to higher excretion and increased catabolic activity.

Stress and Tissue Depletion

Stressed animals divert or utilize the nutrients according to the need in tissues, in order from greatest to least: neural, visceral, skeletal and adipose [25]. Activation of nervous system leads to production of more amount of corticosterone which promotes the gluconeogenesis via liberation of substrates from body tissues for endogenous glucose production [26]. From meat production point of view, the most detrimental effect is the catabolism of muscle protein becoming free amino acids for glucose production. Despite providing best possible nutrients, the relatively poor gain and growth could be due to parallel wastage under stress induced corticosterone. Else, minimizing the impact of corticosterone might increase the gain and live performance.

How it Impacts the Performance?

Probably the most recognizable effect of corticosterone which is induced by stress is on live performance, a sharp reduction in weight gain [27], increased feed intake [28] and elevated feed conversions. Broilers typically increases the display in abdominal fat deposition reduction in muscle accretion.

Methods to Overcome

Several ways to overcome the stress factors in broiler birds has been suggested by different nutritionist through feed formulation. Increasing glycogenic amino acids in the diets and sufficient essential amino acid availability is the best solution to overcome the stress conditions. Other approaches such as improving mineral availability through organic source, glucose and electrolyte balancing, a higher percent of unsaturated fatty acids profile and better hygienic environmental conditions.

Nutritional Additive that Supports

There is no single step solution for the multi-causative, stress related impact on animal production. Though the stress might have multiple origins, but the path of impact is through the stress hormone "cortisol". In the current scenario of animal production, the performance requirement itself is a bigger stress factor. Under such circumstances, anything aimed to improve the stress tolerance and animal performance should target the control of cortisol level. Although there are no specifications for chromium in poultry, it is recommended by NRC [29] for animals undergoing environmental stress. Deficiency of chromium under summer conditions causes disorders of carbohydrate and protein metabolism, reduction in insulin sensitivity in the peripheral tissues as well as a decrease in growth rate [30].

Chromium on Nutrient Metabolism

Chromium is an essential trace element required for carbohydrate, protein, and fat metabolism [31,32]. Several studies confirmed that the association between chromium and stress metabolism [33] through decreased sensitivity to stress and reduced concentration of cortisol in blood [34]. It is very evident from the study conducted by Bahrami et al., [35] that supplementation of Cr decreases cortisol levels in serum (Figure 3).

Several researchers confirmed that Chromium supplementation proven to increase the amino acid and glucose uptake by skeletal muscles in chickens. Supplementation of chromium increases the glucose utilization (Cupo and Donaldson, 1987) carcass quality and decreases the body fat content [36]. Moony and Cromwell [37] observed an increased proportion of muscle tissue in response to chromium supplementation under stress condition. Although, Cr helps to increase the muscle content and reduce steroid secretion which minimizes fat deposition in liver. Being the active component of the Glucose Tolerance Factor (GTF), Cr3+ stimulates and regulates the action of insulin [38]; thus, it is involved in anabolic and catabolic processes [39]. Also, chromium involves in several enzymatic
reactions for stabilization of proteins and nucleic acids [40-42]. Cr interferes in insulin metabolism to minimize lipid peroxidation in chickens [43] (Figure 4).

**Chromium on Immunity**

Reduced loss of certain trace minerals (Zn, Fe, Cu and Mn) during stress has been observed after the supplementation of chromium [44]. Chromium supplementation supports the immune function by enhancement of the cell mediated and humoral immune responses [45,46]. Rajalekshmi et al., [47] studied the influence of chromium supplementation in broiler chicks on cell mediated immunity and humoral immunity. Significant improvement in antibody
titre (Figure 5) value was observed at 400 ppb of Cr-propionate supplementation against Newcastle disease. Also, significant improvement in lymphocyte proliferation ratio from 400 ppb dosage over control diet (Figure 6).

**Chromium on Environmental Stress**

Supplementation of organic chromium and vitamin C under low temperatures, could increase the production, and feed efficiency. Both have a synergistic effect on glucose tolerance and reduction of cortisol generation in blood. Vitamin C, is also acts an anti-oxidant to scavenge free radicals generated under stress condition. A linear relationship was observed in the digestibility of dry matter; crude protein and ether extract by 5.30%, 6.30% and 6.52% respectively. Sahin et al., [48] observed that, supplementation of organic chromium (400 ppb) to laying hens reared under low ambient temperatures had shown increase in egg production and improved feed efficiency. Low ambient temperature (6.9°C) induced effects on nutrient utilization could be alleviated by the supplementation of chromium.

**Chromium on Bird Performance**

The benefits of including Cr at recommended dosage in poultry diets can be observed more efficiently under environmental, dietary, and hormonal stresses [49]. Dietary chromium supplementation could increase the growth rate in stressed broilers [50], increase the feed intake and live weight gain. Chromium supplementation is reported to reduce the corticosteroid levels and improve carcass quality and less fat deposition in broilers under stress condition [51]. There have been reports on improved carcass quality with chromium supplementation, even in the absence of any specific stress factors. Chromium supplementation and its effect on reduction in corticosteroid levels helps to improvement in carcass quality [52] in broiler chickens because corticosteroids are known to affect muscle protein synthesis [53]. Rajalekshmi et al., [47] observed significant improvement in dressing percentage and breast meat over control above 400 ppb of Cr (Figure 7).

Increased supplemental chromium linearly increased the primary or secondary antibody titers against SRBCs, serum total protein,
gobulin, calcium and insulin concentrations, whereas, total lipids, cholesterol, glucose and corticosterone levels significantly decreased [54]. Chromium supplementation is observed to enhance the immune response, either through a direct effect on the cytokines [55] or through the indirect effect of reducing the gluco-corticosteroid levels [56]. There was improvement in the antibody response to NDV with chromium supplementation beyond 200 ppb levels. Similarly, LPR improved quadratically with increase in dosage of chromium supplementation through organic source over control diet.

**Chromium on Reproduction**

Supplementation of chromium significantly increased egg production and egg weight in environmental stress conditions. Significant improvements in semen physical properties and seminal malondialdehyde concentration were observed in birds reared under low ambient temperatures due to chromium supplementation [54]. The improvement in semen physical properties might be due to the action of antioxidants of chromium which reduced the oxidants damage and maintained the integrity of cell membrane. Dietary Cr supplementation significantly increased the fertility and hatchability percentages.

**Conclusion**

- Exposure to various stressors resulting in the production of the stress hormone corticosterone. Corticosterone causes impaired immune system function and regression of the lymphoid tissues.
- Stress results in alterations in carbohydrate, protein, lipid, and mineral metabolism, which in turn causes the depletion of structural protein and the deposition of abdominal fat.
- Controlling the stress hormone corticosterone could be an ideal option to minimize the negative effects of stress on animal performance, Immune functions and carcass quality.
- Regulatory bodies approved organic Chromium Propionate help in overcoming the stress related issues caused through cortisol and improves the immune functions, nutrient metabolism and animal performance.

**References**

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