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Effect of Boron Supplemetation on the Overall Health and Productivity of Livestock

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ABSTRACT

Boron having the characteristics between metal and non-metal behaves like a metalloid and is considered as an essential element for plants, while in animals and human the knowledge of its biological effects is not fully explored yet and so it is the mineral of future prospect and interest. Boron is considered as a trace element in periodic table, known to influence various physiological functions specifically the metabolism of vitamins, minerals and hormones along with immunity and antioxidant defense mechanism. It acts as a lewis acid and in its cationic form has high affinity for the hydroxyl group to form borate and boric acid. The chemical properties of boron allow it to form complex with organic molecules containing hydroxyl group and therefore, interact with various metabolites to influence cellular activity. Boron interacts with calcium and phosphorus and its supplementation have direct effect on the bioavailability of Ca and P in the growth and bone development of chickens and other livestock. B plays a role in regulating the enzymatic activity of pathways involved in energy substrate metabolism and insulin release. Antioxidant activities of supplemental B were also elucidated. Boron plays a regulatory role in the metabolism of several micronutrients, such as calcium, phosphorus, aluminum, magnesium and molybdenum along with its effect on serum T3 and T4 concentration in livestock. B supplementation in chicken has shown better feed conversion ratio, bone development and body growth, respectively.

Keywords: Boron, Health, Productivity, Livestock

In recent years, the productivity of broiler and layer chicken has increased considerably, perhaps due to changes in genetic potential of poultry and partly due to improved managemental practices. It is known that the genetic makeup of the bird influences the utilization of Ca (Shafey *et al.* 1990; Hurwitz *et al.* 1995) and thereby its requirement. Excess calcium intake has been shown to reduce growth, feed efficiency and necessitates higher than normal levels of the other required minerals in the diet (Shafey, 1993). Recommended or excess levels of Ca (Nelson and Kirby, 1987) and or P (Qian *et al.* 1994) in diet are known to reduce the utilization of phosphorous in the chicken gut. Conversely, P can be made available to chicken by decreasing the concentrations of Ca and P (Balla *et al.* 1984; Simons *et al.* 1990) below the recommended levels in diets. Boron (B) has been examined and accepted as a possible essential nutrient in the metabolism and utilization of macro and micro-minerals and vitamin D (Kurtoglu *et al.* 2005; Bozkurt *et al.* 2012).

Boron (B) is the fifth element in the periodic table and the only non-metal in Group III A. B having the characteristics between the metal and non-metal (Kılıc *et al.* 2009) and behaves like a metalloid. It acts as a lewis acid and in its cationic form has high affinity for the hydroxyl group to form borate ($B(OH)^{4-}$) and boric acid (H_3BO_3).

This is a weak acid with dissociative constant (pKa) 9.25 and at pH 7.4, B exists mostly as uncharged H_3BO_3 (Naghii, 1999). These distinctive chemical properties of B allow it to form complex with organic molecules containing hydroxyl group and therefore, interact with various metabolites to influence cellular activity (Park *et al.* 2005). Though, the biological importance and dietary essentiality of B as a trace element for livestock and poultry is not absolutely elucidated, limited research conducted worldwide suggests B as a trace element known to influence various physiological functions specifically the metabolism of minerals and hormones (Devirian and Volpe, 2003) along with immunity and antioxidant defense mechanism (Bhasker *et al.* 2016). Armstrong and Spears (2001) studied the interaction among boron, Ca and P on the skeletal development of gilts and suggested that supplementation with boron could improve the bioavailability of Ca and P and the deficiency of this element caused insufficient growth and abnormal bone development (Naghii, 1999) in poultry.

For poultry, B is not considered an essential element. It is recommended in NRC, 1984 at a level of 2 ppm in the feed regardless of the category or type of poultry production and this recommendation has not been made in the latest standards for poultry in NRC, 1994 and ICAR, 2013. In nature, boron is generally present in the form of borate. Plant tissues usually contain 30 - 50 mg boron/kg DM (Argust, 1998), while animal tissues contain 5 - 6 mg boron/kg DM (Okuyan, 1997). Few reports reveal that most of the soils have less than 10 ppm B (Woods, 1994), suggesting its deficiency (Shorrocks, 1997). Fruits, vegetables and legumes are good sources of boron (Sutherland *et al.* 1998), while whole grains contain very little boron (Bhasker *et al.* 2015) and are widely used in poultry diets (WHO, 1998).

The dietary supplementation of boron (B) has become a concern for the poultry industry given its regulatory role in mineral metabolism. Vitamin D, Mg, Ca, P, Mo, F, Al, Se, protein and omega-3 fatty acids are among the nutrients that affect the response to dietary B (Hunt and Nielsen, 1981; Hunt, 1989; 1998; Nielsen *et al.* 1987; 1988; Hegsted *et al.* 1991).

Nutritional Essentiality and the Mechanism of Action of Boron

The study of the essentiality of B in animal nutrition was limited, until it was reported that supplemental B to cholecalciferol-deficient chicks tended to correct malformations in the marrow sprouts of bone and decreased the number of cases of rickets (Hunt and Nielsen, 1981). In another early work (Rossi *et al.* 1993) B was also shown to alleviate the symptoms of tibial dyschondroplasia. It has been hypothesized that B can enhance the function of other nutrients and hormones acting at the cell membrane level (Nielsen, 2002a). B supplementation has been shown to affect the concentration of steroid hormones in circulation. Nielsen *et al.* (1987) first reported that B supplementation in post-menopausal women increased the serum concentrations of 17β-estradiol and testosterone. Naghii and Samman (1997) found that B supplementation increased plasma estradiol concentrations and tended to increase plasma testosterone concentrations in men. Thus, changes in the status of some nutrients and hormones that act at the cell membrane level can apparently affect the response to various intake levels of B.

Nielsen *et al.* (1988a) suggested that the beneficial effects of B on bone mineralization are related to its parathyroid hormone regulating action, and may have implications on bone growth and bone strength in broiler chickens (Kurtoglu *et al.* 2005; Bozkurt *et al.* 2012) and layer hens (Wilson and Ruszler, 1998; Kucukyılmaz *et al.*

2014). Other results have indicated that B may affect serum thyroid concentration in chickens and pigs (Armstrong *et al.* 2001; Cınar *et al.* 2011). B plays a role in regulating the enzymatic activity of pathways involved in energy substrate metabolism and insulin release, which it modifies by altering the metabolism of Nicotinamide Adenine Dinucleotide (Hunt, 1998). Antioxidant activities of supplemental B were also suggested. The activities of the enzymes superoxide dismutase and glutathione peroxidase destroy reactive oxygen species that cause tissue damage and can be increased by B supplementation (Nielsen, 1994; 1997). However, the mechanism by which B affects the activity of these enzymes is unknown.

Various findings indicate that B may interfere with lipid metabolism in humans and animals. Armstrong *et al.* (2000) reported that pigs supplemented with a 15 mg B/kg diet had increased plasma triglyceride concentrations. Administration of a diet with B caused an increase in the serum triglyceride concentrations of chickens (Hunt and Herbel, 1993) and rats (Hunt and Herbel, 1992) during vitamin D deficiency. The dietary administration of B to rats significantly lowered the serum and plasma low-density lipoprotein, total cholesterol and triglyceride concentrations (Hall *et al.* 1989; Naghii and Samman, 1997). The results from these studies indicate that boron-containing drugs may provide a therapeutic benefit in cases of coronary heart diseases. B has been implicated in immune system function (Hunt and Idso, 1999; Nielsen and Penland, 1999). It has been reported to affect the humoral immune response by increasing antibody production in response to an injected antigen in rats (Bai *et al.* 1997). A decreased inflammatory response was reported when pigs (Armstrong *et al.* 2000) and chicks were fed a diet with added B (Kurtoglu *et al.* 2005).

Effect of B on Performance of Broiler Chicken

It was reported that supplementation of boron has a better feed conversion ratio by 1.9% P<0.05) but did not affect the body weight and feed consumption of chickens grown for 42 days (P>0.05) (Kucukyilmaz *et al.* 2017). B supplementation at levels of 5.6 (Cınar *et al.* 2011), 9.4 (Rossi *et al.* 1993), and 2.6 mg/kg (Bozkurt *et al.* 2012) had no significant effect on the body weight, feed intake, feed conversion ratio or mortality of broiler chickens. Kurtoglu *et al.* (2001) did not find any effect of dietary boron on feed intake and feed conversion ratio in layers up to 300 ppm. Rossi *et al.* (1993) reported that the dietary supplementation of a basal diet with 5 and 40 mg/kg boron improved the growth of male broiler chicks in one experiment. Similarly, Fassani *et al.* (2004) indicated that supplying boron at 30, 60, 90 and 120 ppm provided linear increase in body weight at days 21 and 42 and confirmed a diet of 30 ppm boron exhibiting better feed conversion and without affecting the mortality rates in broilers.

BLOOD BIOCHEMICAL PARAMETERS

Blood Glucose

Supplementation of boron decreased the insulin and blood glucose level in rat supplemented at 10 ppm (Cakir *et al.* 2017). Further Kucukkurt *et al.* (2015) reported the beneficial effect of boron in decreasing the level of blood glucose and insulin when supplemented at 100 ppm in rat. A decrease in glucose and insulin was also detected (Basoglu *et al.* 2000) in dog supplemented with boron.

Serum Cholesterol

Supplementation of boron at 10 ppm reduced the total cholesterol in serum with decreased level of LDL cholesterol and increased the serum HDL (Cakir *et al.* 2017). Kucukkurt *et al.* (2015) also reported the decreased level of total cholesterol in rat supplemented with 100 ppm of boron as borax. Researchers have argued that sodium borate ($Na_2B_4O_7$) plays a protective role against fatty liver disease. In another study carried out on dogs (Basoglu *et al.* 2000), it was proven that sodium borate ($Na_2B_40_710H2O$) was effective in keeping plasma lipid levels low. Administration of boron as sodium borate was reported to decrease the concentrations of total cholesterol, triglyceride, high-density lipoprotein, low-density lipoprotein, very low density lipoprotein, glucose, insulin, and non-esterified fatty acids in blood (Kabu and Civelek 2012).

Serum Protein

Kabu and Civelek (2012) reported no differences in the concentration of total protein (TP), albumin (ALB) and globulin in cattle supplemented with boron as sodium borate ($Na_2B_4O_7$, 30 g/day). Eren *et al.* (2012) suggested a decrease in the level of total protein, albumin and globulin in broiler supplemented with boron at a level of 500, 750 and 1000 ppm.

Serum Enzyme

Kabu and Civelek (2012) studied the effect of sodium borate ($Na_2B_4O_7$, 30 g/day) orally administrated to 12 pregnant cows on selected hormone levels and serum metabolites. There were no differences in concentration of blood urea nitrogen (BUN), alanine aminotransferase (ALT), total bilirubin, aspartate aminotransferase (AST), and gamma-glutamyltransferase (GGT). Eren *et al.* (2012) suggested an increase in the level of serum ALP, Creatine Kinase and decreased level of AST and ALT in broiler supplemented with 500 ppm of boron. Further, Kucukyilmaz *et al.* (2017) reported an increase in serum ALT activities in broiler supplemented with 20 ppm boron. He did not find any effect of boron supplementation on serum ALP activities at the level 20 ppm.

Serum Thyroxine

Kucukyilmaz *et al.* (2017) did not find any effect of boron supplementation on serum triiodothyronine (T3), thyroxine (T4) in poultry bird supplemented with 20 ppm of boron. Conversely, Kucukkurt *et al.* (2015) reported an increase in plasma T3 level in rat fed a diet supplemented with 100 ppm boron. Armstrong *et al.* (2001) reported that supplementation of boron had no effect on plasma T3 and T4 level in gilts.

Antioxidant Effect

Several researchers suggested an improved antioxidant protective activity of B when supplemented in the diet. Enhanced activities of the enzymes superoxide dismutase and glutathione peroxidase, responsible for destroying reactive oxygen species and preventing tissue damage were suggested with supplementation of Boron (Nielsen, 1994; 1997). Bhasker *et al.* (2016) reported an increasing trend in the SOD activity due to dietary B-supplementation in rat. Several other studies also reported significant ($P < 0.05$) increase in the erythrocytic SOD activity, total antioxidant activity (Turkez *et al.* 2012) and SOD activity in spleen (Hu *et al.* 2014) of rat supplemented with boron. Other studies have also indicated the role of dietary B in ameliorating the toxicity induced by carbon tetrachloride (Ince *et al.* 2014) and malathion (Coban *et al.* 2015), reducing the severity of hepatic cell carcinoma in rats by enhancing the SOD activity in liver and improving the antioxidant defense mechanism under oxidative stress condition.

Boron on Micronutrient Metabolism

Boron plays a regulatory role in the metabolism of several micronutrients, such as calcium, phosphorus, aluminum, magnesium, and molybdenum (Wilson and Ruszler, 1998). The micronutrients of particular interest with regard to bone health are magnesium, vitamin D, phosphorus, and calcium. Supplemental Boron observed to be positively influenced the metabolism of these dietary substances, which

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all play a role in maintaining bone health. As a result, boron may be nutritionally significant in preventing osteoporosis in humans (Nielsen, 1990). The likely role of boron in maintaining the structure and composition of bones were also reported during magnesium deficiency, even in condition when there was an increase in urinary calcium loss (Nielsen, 1990).

Calcium Metabolism

Nielsen (1990) suggested that boron plays a role in calcium metabolism, because higher dietary levels of boron have been shown to decrease calcium excretion and increase plasma ionized calcium levels. There is considerable evidence that large intakes of calcium alone do not prevent bone loss (Gordon and Vaughan, 1986) and based on this evidence, Nielsen *et al.* (1987) researched the influence of certain nutrients on major mineral metabolism other than calcium, vitamin D, and fluoride. He reported supplementation of boron at 3 mg/day significantly lowered urinary calcium and magnesium excretion in postmenopausal women and the differences in excretion were more marked in the women fed inadequate levels of magnesium than in the women fed adequate levels of magnesium. Results indicated that magnesium status significantly influences the action of dietary boron, and that dietary boron caused changes, which favor an increase in plasma calcium levels and bone mineralization (Nielsen *et al.* 1987).

Magnesium Metabolism

Hunt and Nielsen, (1986) studied magnesium-deficient chicks and found that supplemental boron decreased the level of abnormalities caused by inadequate magnesium intake. Subsequent boron supplementation enhanced growth and increased plasma calcium and magnesium concentrations, as well as inhibited the calcification of cartilage (Hunt, 1989). Nielsen *et al.* (1988b) found that in magnesium-deficient rats, inadequate dietary boron led to more severe symptoms of magnesium deficiency, and signs of boron deprivation were of greater significance when the diet was low in both magnesium and methionine (Nielsen *et al.* 1988b).

Vitamin D Metabolism

Hunt and Nielsen (1981) found a possible interaction between boron and vitamin D in chicks. When vitamin D-deficient chicks consumed basal diets containing 1 to 3 mg/kg boron, significantly enhanced growth by 38%, increased plasma ionized calcium concentration, lowered plasma alkaline phosphatase levels, and decreased the number of rickets cases (Hunt and Nielsen, 1981). This study found that boron deprivation depressed growth; the effect was most evident when vitamin D intake was low (Hunt and Nielsen, 1981). When chicks were fed adequate levels of vitamin D, boron supplementation improved growth rate by 11% (Hunt and Nielsen, 1981). Hunt and Nielsen (1986) suggested an indirect effect of boron on vitamin D metabolism through an alteration in calcium, phosphorus, or magnesium metabolism.

Hunt *et al.* (1994) studied day-old cockerel chicks and found that dietary boron decreased the adverse effects of vitamin D deficiency, which included increased plasma glucose, triglyceride, and cholesterol levels. Chicks fed inadequate vitamin D for 26 days displayed decreased food utilization and plasma calcium levels, as well as increased plasma glucose, beta-hydroxybutyrate, triglyceride, triiodothyronine, cholesterol, and plasma alkaline phosphatase concentrations. Boron supplementation at physiological amounts also increased food utilization and growth plate maturation in all chicks. In chicks fed adequate vitamin D, the incidence of rachitic long bones was greater in boron-deficient chicks compared with boron-supplemented chicks (Hunt *et al.* 1994). Thus, it appears that boron plays a significant role in normalizing the disturbed energy substrate utilization caused by vitamin D deficiency, as well as improving the macro mineral content of bone (Hunt *et al.* 1994). Boron supplementation of 3 mg/kg as boric acid tended to increase weight gain in chicks fed insufficient vitamin D (110 IU/ kg) for 16 days (Elliot and Edwards., 1992). Supplementation also tended to decrease weight gain in chicks fed adequate vitamin D (1100 IU/kg) for 16 days (Elliot and Edwards, 1992). Food consumption was not affected by these dietary modifications (Elliot and Edwards., 1992). Hunt and Nielsen (1986) also studied the outcomes of boron, magnesium, and molybdenum interactions on bone structure in vitamin D-deficient chicks. Day-old chicks were fed a basal diet of 125 IU of vitamin D (inadequate), 0.420 µg molybdenum/ kg, 0.465 g boron/kg, and calcium: phosphorus ratio of 1:0.56. Supplementation included boric acid at 0 or 3 mg/kg, magnesium acetate at 300 (inadequate) or 500 mg/kg (adequate), and ammonium molybdate at 0 or 20 mg/kg. After 28 days, dietary boron increased growth in chicks fed inadequate magnesium. These findings indicated a boron-vitamin D interaction, and led to the hypothesis that boron may play a role in either hydroxylating or extending the half-life of vitamin D3, based on its ability to complex with hydroxyl groups of organic compounds (Hunt and Nielsen, 1986). This role would most likely affect bone metabolism and improve bone strength.

The Effect of Boron on the Mineral Composition of Bone

B has an important biological role that affects the mineral metabolism of human and animals by interacting with Ca, Mg, Mn, Mo, K, Cu and vitamin D3. All of these nutrients are important in bone metabolism (Nielsen, 1990; Elliot and Edwards, 1992; Hunt *et al.* 1994; 1997). The impact of dietary B intake on bone abnormalities such as arthritis and osteoporosis has also been observed (Nielsen *et al.* 1987; Travers *et al.* 1990; Newnham, 1994; Bai and Hunt, 1995). This indicates that B can play a vital role in bone development. Mineral composition and ash are the main criteria used for assessing bone density. The bones provide structural support and act as a reservoir for minerals (Mutus *et al.* 2006). Ca and P levels may increase in response to B supplementation, and consequently, the ash level in bones can be assumed to be indicative of the regulatory role of B supplementation on bone mineralization, although in practice this effect can vary.

The effects of dietary B on the bone mineral composition in broilers and layer hens have been investigated by several researchers. Elliot and Edwards (1992) reported that dietary supplementation of poultry with 9.5 mg/kg of B for a period of 1 to 16 days may improve bone ash. A similar tendency was observed in chicks fed 300 mg/kg B for 21 days (Rossi *et al.* 1993). Similarly, Qin and Klandorf (1991) showed in three experiments that the addition 100 mg B/kg of diet increased the bone ash of broiler breeder hens. Supplementation with 50, 100 and 200 mg/kg B during a 16-week growth period increased tibial bone ash in layer pullets, with the greatest increase was observed with supplementation of 50 mg/kg (Wilson and Ruszler, 1997). Likewise, Kurtoglu *et al.* (2005) reported significant increase in the tibial Ca levels, but not ash levels, in broilers supplemented with B.

In this study, B supplementation at 5 and 25 mg/kg reduced the bone Zn concentration and produced a one-fold increase in the bone B concentration but caused no changes in Cu and Fe. Significant increases in the tibia B, Cu and Zn concentrations were observed when 60, 120 and 240 mg/kg of B were added to the laying hen diet; however, the Ca, Mg and P levels remained unchanged (Olgun *et al.* 2012). Negative effects of B supplementation have been observed in other studies on broiler chickens (Fassani *et al.* 2004) and layer hens (Wilson and Ruszler, 1998; Mizrak, 2008; Mizrak *et al.* 2010; Bintas, 2013) whereby there was no change in the Ca or P levels of ash in the femur or tibia in association with dietary B

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supplementation ranging from 30 to 150 mg/kg diet. If B was exerting a specific effect, one would predict there to be some consistent effect on the blood serum mineral profile. However, B either had no effect or inconsistent effects on the concentration of Ca, P, Mg, Fe, Cu and Zn under normal physiological states (Kurtoglu *et al.* 2002; Cinar *et al.* 2011; Bozkurt *et al.* 2012; Olgun *et al.* 2012; Kucukyilmaz *et al.* 2014).

Effect on Arthritis

Since boron can complex with hydroxyl groups of organic compounds, it form corticosteroids, and thus alleviate symptoms of rheumatoid arthritis (Nielsen, 1988). In some parts of Australia where water and soil levels of boron are high; half the cases of musculoskeletal diseases have been reported when compared with areas containing lower boron levels in water and soil (Newnham, 1991). A comparison indicated that the occurrence of arthritis is negatively correlated with the level of boron in the soil, and subsequently in the food supply (Newnham, 1991). In addition, arthritic bones are found to contain less boron than healthy bones. It is possible that boron helps alleviate arthritis by restricting T-cell activity and modifying the levels of serum antibodies (Hunt, 1998).

Interactions of B with Other Minerals in the Diet

Comparison of all published data suggests that B might interact with the metabolism of macro minerals Ca, P and Mg (Hunt, 1989; Hunt *et al.* 1994). Studies with broiler chickens have shown that dietary modifications in the Ca and P levels occasionally influence the action of B. Significant interactions in the dietary Ca-P with supplemental B levels for bone ash, Ca and P levels were reported by Bozkurt *et al.* (2012). B did not increase the tibia Ca and P levels but decreased their faecal excretion when the chicks were fed a Ca-P deficient diet with 30 mg/kg B. In a study by Elliot and Edwards (1992), broiler chickens were fed different concentrations of B (0, 5, 10, 20, 40 and 80 mg/kg diet) and two concentrations of Ca (0.65 and 0.90%). The experiment consisted of six trials, each lasting for 21 days. From these experiments, there was no indication that an interaction between B and calcium existed in cockerels.

It may be that the lower a bird's intake of Ca and P, the more deficient it becomes in these macro minerals and the more positive the effect of B on the absorption and utilization of Ca and P. Another hypothesis to explain the increase in bodily organs and bones may be a reaction of the borate anion with the molybdate assay, which may result an apparent increase in P (Armstrong and Spears, 2001). Conversely, experiments with B supplementation or deprivation have shown that birds had markedly improved bone mineral composition when cholecalciferol or Mg was deficient. Kurtoglu *et al.* (2005) studied the effects of 5 and 25 mg/kg B supplementation in diets with inadequate (6.25 mg/kg) or adequate (50 mg/kg) cholecalciferol content on characteristics of the tibia of 45 day old chicks. B supplementation affected the tibial B, Zn and Ca concentrations but did not have any effect on the tibial Fe or Cu concentrations or the tibia ash. The authors argued that B might be beneficial when the chicks were fed a diet inadequate in vitamin D3. This appears to support the hypothesis by Nielsen (1990) that B may have a pronounced influence on mineral metabolism only when animals are subjected to nutritional or other stresses.

CONCLUSION

Boron compounds have been shown to exert potent anti-osteoporotic, anti-inflammatory, hypolipemic or hyperlipemic, anticoagulant, antioxidant, and antineoplastic effects. Other than this boron supplementation has effects on bone mineralization, mineral and energy metabolism, enzyme and hormone activities as well as effect on feed conversion ratio and body growth rate. So boron seems to make positive contributions to the overall health and productive performance of livestock.

REFERENCES

Argust, P. 1998. Distribution of boron in the environment. *Biological Trace Element Research,* 66(1): 131-143.

Armstrong, T.A. and Spears, J.W. 2001. Effect of dietary boron on growth performance, calcium and phosphorus metabolism, and bone mechanical properties in growing barrows. *Journal of animal science*, **79**(12): 3120-3127.

Armstrong, T.A., Spears, J.W. and Lloyd, K.E. (2001). Inflammatory response, growth, and thyroid hormone concentrations are affected by long-term boron supplementation in gilts. *Journal of animal science*, **79**(6): 1549-1556.

Armstrong, T.A., Spears, J.W., Crenshaw, T.D. and Nielsen, F.H. 2000. Boron supplementation of a semi purified diet for weanling pigs improves feed efficiency and bone strength characteristics and alters plasma lipid metabolites. *The Journal of Nutrition,* **130**(10): 2575-2581.

Bai, Y. and Hunt, C.D. 1995. Dietary boron alleviates adjuvant-induced arthritis (AIA) in rats. *Journal of Fedration of American Society of Experimental Biology*, **9**(3): 576-576.

Balla, G.C., Nelson, T.S. and Kirby, L.K. 1984. Effect of different dietary levels of calicum and phosphorus on phytate hydrolysis by chicks. *Nutrition Reports International*, **32**: 909–913.

Basoglu, A., Sevinc, M., Guzelbektas, H. and Civelek, T. 2000. Effect of borax on serum lipid profile in dogs. *Journal of Veterinary Research*, **4**: 153-156.

Bhasker, T.V., Gowda, N.K.S., Mondal, S., Krishnamoorthy, P., Pal, D.T., Mor, A. and Pattanaik, A.K. 2016. Boron influences immune and antioxidant responses by modulating hepatic superoxide dismutase activity under calcium deficit abiotic stress in Wistar rats. *Journal of Trace Elements in Medicine and Biology*, **36**: 73-79.

Bhasker, T.V., Gowda, N.K.S., Pal, D.T., Bhat, S.K. and Pattanaik, A.K. 2015. Boron profile in common feedstuffs used in tropical livestock systems. *Animal Feed Science and Technology*, **209**: 280-285.

Bintas, E. 2013. The Dietary Supplemental effect of boron and zeolite, either alone or in combination on aged laying hens (Doctoral dissertation, Msc. Thesis. Adnan Menderes University, Fen Bilimleri Enstitüsü, Aydın-Turkey.

Bozkurt, M., Kucukyılmaz, K., Catlı, A.U., Cınar, M., Cabuk, M. and Bintas, E. 2012. Effects of boron supplementation to diets deficient in calcium and phosphorus on performance with some serum, bone and fecal characteristics of broiler chickens. *Asian-Australasian Journal of Animal Sciences*, **25**(2): 248-255.

Cakir, S., Eren, M., Senturk, M. and Sarica, Z.S. 2017. The effect of boron on some biochemical parameters in experimental diabetic rats. Biological trace element research, 1-8.

Cinar, M., Kucukyilmaz, K., Bozkurt, M., Catli, A., Bintaş, E., Seyrek, K. and Konak, R. 2011. Farklı bor düzeyleri ve bor ile fitaz enziminin birlikte kullanımının etlik piliçlerde performans ile bazı kan, kemik ve dışkı parametreleri üzerine etkilerinin belirlenmesi. Final Project report. Project number. TAGEM/HAYSÜD/09/13/04/03. Aydın, Turkey.

Coban, F.K., Ince, S., Kucukkurt, I., Demirel, H.H. and Hazman, O. 2015. Boron attenuates malathion-induced oxidative stress and acetylcholinesterase inhibition in rats. *Drug and Chemical Toxicology*, **38**(4): 391-399.

Devirian, T.A. and Volpe, S.L. 2003. The physiological effects of dietary boron. *Critical Reviews in Food Science and Nutrition*, **43**: 219-231.

Elliot, M.A. and Edwards Jr, H.M. 1992. Studies to determine whether an interaction exists among boron, calcium, and cholecalciferol on the skeletal development of broiler chickens. *Poultry Science*, **71**(4): 677-690.

Eren, M., Uyanik, F., Guclu, B.K. and Atasever, A. 2012. The influence of dietary boron supplementation on performance, some biochemical parameters and organs in broilers. *Asian Journal of Animal and Veterinary Advances*, **7**(11): 1079-1089.

Fassani, E.J., Bertechini, A.G., Brito, J.A.G., Kato, R.K., Fialho, E.T. and Geraldo, A. 2004. Boron supplementation in broiler diets. *Brazilian Journal of Poultry Science,* **4**: 213-217.

Gordan, G.S. and Vaughan, C. 1986. Calcium and osteoporosis. *The Journal of nutrition*, **116**(2): 319-322.

Hall, I.H., Spielvogel, B.F., Griffin, T.S., Docks, E.L. and Brotherton, R.J. 1989. The effects of boron hypolipidemic agents on LDL and HDL receptor binding and related enzyme activities of rat hepatocytes, aorta cells and human fibroblasts. *Research Communications in Chemical Pathology and Pharmacology*, **65**(3): 297-317.

Hegsted, M., Keenan, M.J., Siver, F. and Wozniak, P. 1991. Effect of boron on vitamin D deficient rats. *Biological Trace Element Research*, **28**(3): 243-255.

Hu, Q., Li, S., Qiao, E., Tang, Z., Jin, E., Jin, G. and Gu, Y. 2014. Effects of boron on structure and antioxidative activities of spleen in rats. *Biological Trace Element Research*, **158**(1): 73-80.

Hunt, C.D. 1989. Dietary boron modified the effects of magnesium and molybdenum on mineral metabolism in the cholecalciferol-deficient chick. *Biological Trace Element Research*, **22**(2): 201-220.

Hunt, C.D. 1994. The biochemical effects of physiologic amounts of dietary boron in animal nutrition models. *Environmental Health Perspectives*, **102**(7): 35-42.

Hunt, C.D. 1998. One possible role of dietary boron in higher animals and humans. *Biological Trace Element Research*, **66**: 205–225.

Hunt, C.D. 1998. Regulation of enzymatic activity. *Biological Trace Element Research*, **66**(1): 205-225.

Hunt, C.D. and Herbel, J.L. 1993. Physiological amounts of dietary boron improve growth indicators of physiological status over a 20-fold range in vitamin D3 deficient chick. Proceedings of the symposium on trace elements in man and animals. Verlag Media Touristik, Gersdof, Germany: 714-718.

Hunt, C.D. and Herbel, J.L. 1992. Boron effects energy metabolism in the streptozotocin-injected, vitamin D3 deprived rat. *Magnesium and Trace Elements,* **10**: 374-386.

Hunt, C.D. and Idso, J.P. 1999. Dietary boron as a physiological regulator of the normal inflammatory response: a review and current research progress. *Journal of Trace Elements in Experimental Medicine*, **12**(3): 221-234.

Hunt, C.D. and Nielsen, F.H. 1981. Interaction between boron and cholecalciferol in the chick. In Proceedings. symposium on trace element metabolism in man and animals. *Australian Academy of Science*, **4**: 597–600.

Hunt, C.D. and Nielsen, F.H. 1986. Dietary boron affects bone calcification in magnesium- and cholecalciferol deficient chick, in: Underwood, E.J. (Ed) *Trace Elements in Human and Animal Nutrition* (5^{th} ed.): 275-277.

Hurwitz, S., Plavnik, I., Shapiro, A., Wax, E. and BAR, H.T.A. 1995. Calcium metabolism and requirements of chickens are affected by growth. *Journal of Nutrition*, **125**: 2679–2686.

ICAR 2013. Indian Council of Agricultural Research. Nutrients requirements of animals-poultry, (3^{rd} ed.): 15.

Ince, S., Kucukkurt, I., Demirel, H.H., Acaroz, D.A., Akbel, E. and Cigerci, I.H. 2014. Protective effects of boron on cyclophosphamide induced lipid peroxidation and genotoxicity in rats. *Chemosphere*, **108**: 197-204.

Kabu, M. and Civelek, T. 2012. Effects of propylene glycol, methionine and sodium borate on metabolic profile in dairy cattle during periparturient period. *Revue de Medecine Veterinaire*, **163**(8): 419-430.

Kilic, A.M., Kilic, O., Andac, I. and Celik, A.G. 2009. Boron mining in Turkey, the marketing situation and the economical importance of Boron in the World IV. *In International boron symposium,* Eskisehir-TURKEY, **1**: 15-17.

Kucukkurt, I., Akbel, E., Karabag, F. and Ince, S. (2015). The effects of dietary boron compounds in supplemented diet on hormonal activity and some biochemical parameters in rats. *Toxicology and Industrial Health*, **31**(3): 255-260

Kucukyilmaz, K., Bozkurt, M., Cinar, M. and Tuzun, A.E. 2017. Evaluation of the boron and phytase, alone or in combination, in broiler diets. *The Journal of Poultry Science*, **54**(1): 26-33.

Kucukyilmaz, K., Erkek, R. and Bozkurt, M. 2014. The effects of boron supplementation to layer diet varying in calcium-phosphorus on performance, egg quality, bone strength and mineral constituents of serum, bone and feces. *British Poultry Science,* **55**: 804-816.

Kurtoglu, F., Kurtoglu, V., Celik, I., Kececi, T. and Nizamlioglu, M. 2005. Effects of dietary boron supplementation on some biochemical parameters, peripheral blood lymphocyte, splenic plasma cell counts and bone characteristics of broiler chicks fed with adequate or inadequate vitamin D3 containing diet. *British Poultry Science*, **46**: 87-96.

Kurtoglu, V., Kurtoglu, F. and Coskun, B. 2001. Effects of boron supplementation of adequate and inadequate vitamin D3-containing diet on performance and serum biochemical characters of broiler chickens. *Research in Veterinary Science,* **71**: 183-187.

Kurtoglu, V., Kurtoglu, F., Coskun, B., Seker, E., Balevi, T. and Cetingul, I.S. 2002. Effects of boron supplementation on performance and some serum biochemical parameters in laying hens. *Revue de Medecine Veterinaire*, **153**: 823-828.

Mizrak, C. 2008. Damızlık Yumurta Tavugu Yemlerine Farklı Seviye ve Formda Bor Ilavesinin Performans, Kemik Gelisimi, Yumurta Kalitesi ve Bazı Kan Parametreleri Uzerine Etkisi. Doktora Tezi. Ankara Universitesi. Fen Bilimleri Enstitusu, Zootekni Anabilim Dalı, Ankara, Turkey (in Turkish).

Mizrak, C., Yenice, E., Can, M., Yildırım, U. and Atik, Z. 2010. Effects of dietary boron on performance, egg production, egg quality and some bone parameters in layer hens. *South African Journal of Animal Science*, **40**(3): 257-264.

Mutus, R., Kocabagli, N., Alp, M., Acar, N., Eren, M. and Gezen, S.S. 2006. The effect of dietary probiotic supplementation on tibial bone characteristics and strength in broilers. *Poultry Science*, **85**(9): 1621-1625.

Naghii, M.R. 1999. The significance of dietary boron, with particular reference to athletes. *Nutrition and Health*, **13**(1): 31-37.

Naghii, M.R. and Samman, S. 1997. The effect of boron supplementation on its urinary excretion and selected cardiovascular risk factors in healthy male subjects. *Biological Trace Element Research,* **56**(3): 273-286.

Nielsen, T.S. and Kirby, L.K. 1987. The calcium binding properties of natural phytate in chick diets. *Nutrition Reports International*, **35:** 949–956.

Newnham, R.E. 1991. Essentiality of boron for healthy bones and joints. *Environmental Health Perspectives*, **102**(7): 83-85.

Nielsen, F.H. 1990. Studies on the relationship between boron and magnesium which possibly affects the formation and maintenance of bones. *Magnesium and Trace Elements*, **9**(2): 61-69.

Nielsen, F.H. 1994. Biochemical and physiologic consequences of boron deprivation in humans. *Environmental Health Perspectives*, **102**(7): 59-73.

Nielsen, F.H. 1997. Boron in human and animal nutrition. *Plant and Soil*, **193**(1): 199-208.

Nielsen, F.H., Hunt, C.D., Mullen, L.M. and Hunt, J.R. 1987. Effect of dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women. *Journal of Fedration of American Society of Experimental Biology*, **1**(5): 394-397.

Nielsen, F. H., Shuler, T. R., Zimmerman, T. J. and Uthus, E. O. (1988). Magnesium and methionine deprivation affect the response of rats to boron deprivation. *Biological Trace Element Research*, **17**(1), 91-107.

Nielsen, F.H. 2002a. The nutritional importance and pharmacological potential of boron for higher animals and human, in: Goldbach, H.E., Rerkasem, B.M., Wimmer, A., Brown, P.H., Thellier, M. and Bell, R.W. (Eds) *Boron in Plant and Animal Nutrition*, pp: 37-49

Nielsen, F.H. and Penland, J.G. 1999. Boron supplementation of perimenopausal women affects boron metabolism and indices associated with macrominerals metabolism, hormonal status and immune function. *Journal of Trace Elements in Experimental Medicine,* **12**: 251-261.

Nielsen, F.H., Hunt, C.D., Mullen, L.M. and Hunt, J.R. 1987. Effect of dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women *Journal of Fedration of American Society of Experimental Biology,* **87**: 394-397.

Nielsen, F.H., Shuler, T.R., Zimmerman, T.J. and Uthus, E.O. 1988a. Dietary magnesium, manganese and boron affect the response of rats to high dietary aluminium. *Magnesium,* **7**(3): 133-147.

Nielsen, F.H., Shuler, T.R., Zimmerman, T.J. and Uthus, E.O. 1988b. Magnesium and methionine deprivation affect the response of rats to boron deprivation, *Biological Trace Element Research*, **17**: 91-107.

NRC 1984. National Research Council. Nutrients requirements of poultry, 8th ed. National Academic Press, Washington, DC, pp. 71.

NRC 1994. National Research Council. Nutrients requirements of poultry, 9th ed. National Academic Press, Washington, DC, pp 155.

Okuyan, M.R. 1997. Biochemistry of animal nutrition. Ankara Universitesi Ziraat Fakültesi Yayinlari, Yayin no: 1491, Ders kitabi: 450, Ankara, pp. 350 (in Turkish).

Olgun, O., Yazgan, O. and Cufadar, Y. 2012. Effects of boron and copper dietary supplementation in laying hens on egg shell quality, plasma and tibia mineral concentrations and bone biomechanical properties. *Revue de Médecine Vétérinaire,* **163**: 335-342.

Park, M., Li, Q., Shcheynikov, N., Muallem, S. and Zeng, W. 2005. Borate transport and cell growth and proliferation: not only in plants. *Cell Cycle*, **4**(1): 24-26.

Qian, H., Kornegay, E. T., Veit, H. P., Denbow, D. M. and Ravindran, V. 1994. Effect of supplemental Natuphos® phytase on tibial traits of turkeys fed soybean meal-based semi-purified diets. *Poultry Science*, **73**: 89-95.

Qin, X., and Klandorf, H. 1991. Effect of dietary boron supplementation on egg production, shell quality, and calcium metabolism in aged broiler breeder hens. *Poultry Science*, **70**(10): 2131-2138.

Rossi, A. F., Miles, R. D., Damron, B. L. and Flunker, L. K. 1993. Effects of dietary boron supplementation on broilers. Poultry science, **72**(11): 2124-2130.

Shafey, T. M., McDonald, M. W. and Pym, R. A. E. 1990. Effects of dietary calcium, available phosphorus and vitamin D on growth rate, food utilisation, plasma and bone constituents and calcium and phosphorus retention of commercial broiler strains. *British Poultry Science*, **31**(3): 587-602.

Shorrocks, V.M. 1997. The occurrence and correction of boron deficiency. *Plant and Soil*, **193**(1-2): 121-148.

Simons, P.C.M., Versteegh, H.A.J., Jongbloed, A.W., Kemme, P.A., Slump, P., Bos, K.D., Wolters, M.G.E., Beudeker, R.F. and Verschoor, G.J. 1990. Improvement of phosphorus availability by microbial phytase in broilers and pigs. *British Journal of Nutrition*, **64**(2): 525-540.

Sutherland, B., Strong, P. and King, J.C. 1998. Determining human dietary requirements for boron. *Biological Trace Element Research*, **66**(1): 193-204.

Travers, R.L., Rennie, G.C. and Newnham, R.E. 1990. Boron and arthritis: the result of a double-blind pilot study. *Journal of Nutritional and Environmental Medicine,* **1**: 127-132.

Turkez, H., Geyikoglu, F., Tatar, A., Keles, M.S., & Kaplan, I. 2012. The effects of some boron compounds against heavy metal toxicity in human blood. *Experimental and Toxicologic Pathology*, **64**(1-2), 93-101.

WHO (World Health Organization) 1998. Environmental health criteria 204: boron. International programme on chemical safety, Geneva, Switzerland. ISBN 9241572043, pp. 105–106

Wilson, J.H. and Ruszler, P.L. 1997. Effects of boron on growing pullets. *Biological Trace Element Research*, **56**(3): 287-294.

Wilson, J.H. and Ruszler, P.L. 1998. Long term effects of boron on layer bone strength and production parameters. *British Poultry Science*, **39**(1): 11-15.

Woods, W.G. 1994. An introduction to boron: history, sources, uses, and chemistry. *Environmental Health Perspectives*, **102**(7): 5-11.