

*Review Article***Role of Dietary Zinc in Heat Stressed Dairy Animals: A Review****Brijesh Patel^{1*}, Varsha Jain², Ajitha Kumar, H. M.³, Lokesha, E.⁴, Vaibhav Purwar¹, Arun Prabhakar⁵ and Nishant Kumar⁶**¹Ph.D. Scholar, Division of LPM, ICAR-IVRI, Bareilly, Uttar Pradesh, INDIA²Veterinary Assistant Surgeon, Veterinary Hospital, Bhendri, Dhamtari, Chhattisgarh, INDIA³Ph.D. Scholar, Division of Physiology, ICAR- NDRI, Karnal, Haryana, INDIA⁴Ph.D. Scholar, Division of Nutrition, ICAR-IVRI, Bareilly, Uttar Pradesh, INDIA⁵M.V.Sc. Scholar, Division of LPM, ICAR-IVRI, Bareilly, Uttar Pradesh, INDIA⁶Scientist, ARGO, NDRI, Karnal, Haryana, INDIA***Corresponding author:** romi10888@gmail.com

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Abstract

High ambient temperatures compromise performance and productivity by reducing feed intake and decreasing nutrient utilization, growth rate, feed efficiency and milk production which lead to economic losses in dairy farming. Environmental stress also leads to oxidative stress associated with a reduced antioxidant status in the animals in vivo, as reflected by increased oxidative damage and lowered plasma concentrations of antioxidant vitamins (e.g., vitamins E, A, and C) and minerals (e.g., Zn). Zinc has an important role in numerous biological processes in avian and mammalian species. For instance, Zn is an essential component of many enzymes, and it has both structural and catalytic functions in metalloenzymes. Furthermore, dietary Zn is required for normal immune function as well as proper skeletal development and maintenance. One of the most important functions of Zn is related to its antioxidant role and its participation in the antioxidant defense system. This work compiles past and present information about the role of Zn in heat-stressed dairy animal's health.

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The livestock sector is an integral component of agricultural production system and tool for socioeconomic development and it contributes 4.11% of total gross domestic product (GDP) and 27.25% of agricultural GDP (Jain *et al.*, 2017). India ranks first in the milk production, with 163.7 million tones and per capita availability of 352 g/day (BAHS, 2017). Environmental factors, such as temperature and

light, exert significant effects on the production, health and immunity of animals. Increase in earth atmospheric temperature by 0.8°C since 1880 (NASA, 2015) gives us a red signal about the maintenance of production level in animals. Heat stress during hot summer in tropical countries is a problem of great concern among farmers and livestock producers as it causes great economic loss in dairy farming. Spiers *et al.* (2004) reported that milk yield decreased by 0.41 kg/cow/day for each THI unit increase of above 69. Heat stress in dairy cows is caused by a combination of environmental factors (temperature, relative humidity, solar radiation and air movement). It affects the cellular physiology and systemic metabolism leading to reduction in dry matter intake (DMI) and milk production (Yousef, 1997; Collier *et al.*, 2008). The lactating dairy cows have an increased sensitivity to heat stress compared with non lactating animals, due to milk production elevating metabolism (Purwanto *et al.*, 1990). Moreover, because of the positive relationship between milk yield and heat production, higher yielding cows are more challenged by heat stress than lower yielding animals (Spiers *et al.*, 2004). The upper critical temperature limit in cow may reach up to 25 to 26°C (West, 2003), whereas, comfort zone is between -0.5 to 20°C, however it varies between the breeds. The environmental temperature is not the only factor, relative humidity is also important to describe the cow's comfort zone. The combined effect of temperature and humidity is quantified as Temperature Humidity Index (THI). The normal THI level of 72 is optimal to maintain the milk production of dairy animals (Prasad *et al.*, 2012). Heat stress is one of the wide varieties of factors which causes oxidative stress *in-vivo*. Reactive oxygen species (ROS), the major culprits for causing oxidative stress, are constantly generated *in vivo* as an integral part of metabolism. ROS may cause oxidative stress when their level exceeds the threshold value. They trigger progressive destruction of polyunsaturated fatty acids (PUFA), ultimately leading to membrane destruction. Body employs anti-oxidants to quench these free radicals. The enzymatic antioxidants like superoxide dismutase (SOD), catalase and glutathione peroxidase (GPx) act by scavenging both intracellular and extracellular superoxide radical and preventing lipid peroxidation of plasma membrane. Non-enzymatic antioxidants include vitamins like vitamins C, A and E, minerals like zinc (Zn) and chromium (Cr), proteins like albumin, transferrin, glutathione (GSH) etc. The role of dietary supplements such as vitamins for alleviating the effect of heat stress has been reviewed extensively (Sahin and Kucuk, 2003b). However, effects of Zn on performance, oxidative stress markers, and immunity in heat-stressed animals remain rather limited. The objective of this article was to review studies dealing with the effect of Zn supplementation to heat-stressed animals with respect to its role in metabolic and antioxidant status, immune potency and performance.

The Effects of Heat Stress on Dairy Animals

Changes in physiological parameters give an immediate response to the climatic stress and consequently the level of discomfort to the animals. Rectal temperature (RT) is taken directly inside the body cavity which is typically slightly higher than skin temperature. Change in rectal temperature has been considered as an important measure of physiological status as well as ideal indicator for assessment of stress in animals (Johnson, 1980; West, 2003). Respiration rate is a sensitive indicator of heat stress and the respiration rate increases when environmental temperature increases. Silanikove (2000) reported that measuring respiration rate appears to be the most accessible and easiest approach for evaluating the degree of heat stress in farm animals (low: 40–60 breaths per min, medium high: 60 – 80, high: 80 – 120, and severe stress: above 150 breaths per minute in cattle). Upadhyay *et al.* (2009) reported that there is a significant ($P < 0.01$) increase in pulse rate when the crossbred male calves were given treadmill exercise during hot dry season of the year. Ronchi *et al.* (2001) reported that dry matter intake decreased by 23% in heifers managed at 32°C and 70% relative humidity. Holter *et al.* (1997) established a significant negative correlation between THI and DMI for cows and suggested that the effect of THI is probably mediated through the effects of increasing body temperature of cow. Heat stress affects the productive performance of dairy animals by reducing their dry matter intake (DMI), feed efficiency and milk yield (Gantner *et al.*, 2011; Baumgard *et al.*, 2012). Decreased DMI under heat stress indicates physiological adaptation of animal by decreasing nutrient metabolism and consequent heat increment. The optimum environmental temperature for lactation depends on species, breed and degree of tolerance to heat or cold. The milk yield of Holstein cattle declines at temperature above 21°C, in case of Brown Swiss and Jersey cattle it declines at about 24 to 27°C whereas milk yield of Zebu cattle declines only above 34°C (Hafez, 1968). Therefore high yielding crossbred animals maintained in the tropical countries seems to be under threat of heat stress. Amaral *et al.* (2009) suggested that milk production will be reduced whenever THI exceeds a value of 72. Kadzere *et al.* (2002) observed that at the temperature of 35°C and 40°C there is reduction of milk production by 33% and 50% respectively. The average milk production of Karan Fries and Sahiwal animals at around THI of 72 was 13.4 and 6.6 litre/day (Singh and Upadhyay, 2009). Other than milking period, even cows under dry period experiencing heat stressed has profound effects on milk production in the subsequent lactation in ruminants (Bernabucci *et al.*, 2010). Plasma cortisol level considered as an indicator of heat stress in animals. Increased plasma cortisol indicates the higher heat stress (Patel *et al.*, 2017). Marai and Habeeb, 2010 observed that cortisol values were 9.07 and 12.53 ng/ml during cold and hot season respectively. Similarly other studies also reported the physiological increase in serum cortisol under heat stress conditions (Abilay *et al.*, 1975; Wise *et al.*, 1988; Dhami *et al.*, 2006). Thyroid hormones T₃ and T₄ were decreased from 4.55 ± 0.16 pmol/L and 21 ± 0.08 pmol/L to 3.21 ± 0.08 and 16.70 ± 0.19 pmol/L respectively in goats under heat stress conditions (Sivakumar *et*

al., 2010). Decreased thyroid hormone level seems to be logical as an adaptive mechanism to decrease the metabolic heat production under the stressed conditions (Mader *et al.*, 2010). As a consequence of oxidative metabolism and decreased physiological antioxidants levels results in oxidative stress. Kumar *et al.* (2007) demonstrated the increase in indicator of oxidative stress thiobarbituric acid reactive substances (TBARS) concentration in cattle and buffaloes subjected to thermal stress. Reproductive status of the animals experiences the negative impact of heat stress by modified hormonal and reproductive characteristics. Acute heat stress cows experienced changes in circulating concentrations of progesterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH) and estradiol (Bernabucci *et al.*, 2010), which affect estrous cycle length, estrus expression, and conception rates.

Zinc

Zn is a very important trace element, involved in wide range of metabolic activities and productive performance like growth (Underwood *et al.*, 1999), reproduction and immune system (Abdel *et al.*, 2011; Patel *et al.*, 2017) were influenced. Zn involved in structure and function of many enzymes associated with the carbohydrate, protein metabolism, nucleic acid synthesis, carbon dioxide transport and many other reactions (Pond *et al.*, 1995). Zn is widely distributed throughout the body as a component of metallo-enzymes and metallo-proteins. Zn finger proteins play an integral role in regulating gene expression, consequently impacting a wide variety of body functions including cell division, growth, hormone production, metabolism, appetite control and immune function (Vallee and Falchuk, 1993). Zn deficiency increases oxidative damage of cell membranes caused by free radicals (Oteiza *et al.*, 1996; Salgueiro *et al.*, 2000; Prasad and Kucuk, 2002). Zn plays a critical role in anti-oxidant defense as an integral part of the essential enzymes superoxide dismutase (SOD) (Underwood, 1999). SOD is a major scavenger of free radicals, present in the cytoplasm of many types of cells and in the extracellular space. It converts the superoxide free radical ($O_2^{\cdot-}$) to hydrogen peroxide, which is further decomposed by catalase into water and oxygen (Leung, 1998). The role of Zn as an anti-oxidant has been predicted on its ability to be an intermolecular stabilizer, preventing the formation of disulfide bonds and either displacing or competing with cupric or ferric ions, which trigger the formation of free radicals. Zn increases the synthesis of metallothionein, a cystine-rich protein that acts as free radical scavenger (Oteiza *et al.*, 1996). Zn deficiency has been reported to impair antioxidant functions and an increase in oxidative DNA damage (Jing *et al.*, 2007). The major sources of Zn in the mineral supplements formulated for animal feeding are inorganic salts like Zinc sulphate ($ZnSO_4$), Zn oxide (ZnO), Zn chloride ($ZnCl_2$) etc. Because many natural feed ingredients are marginally Zn-deficient, this micronutrient is commonly supplemented to diets for livestock and poultry (Batal *et al.*, 2001). However, recent research has shown that organic Zn

sources may be more available to the chick than inorganic Zn sources (Kidd *et al.*, 1996; Wedekind *et al.* (1992).

Zn Supplementation in Heat-Stressed Dairy Animals

Performance and Productivity

Zn deficiency in animals is characterized by decreased feed intake, growth, low circulating levels of growth hormone (GH) its receptor, insulin-like growth factor-I and GH binding protein (MacDonald, 2000). Jia *et al.* (2008) identified an increase in ADG and feed efficiency when 15-45 mg Zn/kg DM was supplemented to a basal diet containing 22 mg Zn/kg DM in Liaoning Cashmere goats. However, Mandal *et al.* (2007) and Salama *et al.* (2003) did not find any significant change in DMI of bulls and goats respectively. Anton (2013) reported that group of cows supplemented with ZnSO₄ had higher milk production compared to that in the cows of the groups that have not received this mineral. This gain in milk yield was positively correlated with increase in the plasma zinc level. Cope *et al.* (2009) supplemented 60 ppm ZnO to lactating Holstein Friesen cows and observed increased milk yield and no changes in milk composition. However, Griffiths *et al.* (2007) reported an increase in milk production in cows fed a combination of organic sources of Zn, Mn, Cu and Co. Similarly, Habeeb *et al.* (2013) reported that supplemental Zn resulted in increased milk yield in goat. Nayeri *et al.* (2014) supplemented 75 ppm ZnSO₄ to HF cow and reported an increase in milk yield. Chandra *et al.* (2013) and Patel *et al.* (2017) also reported significant increase in milk yield at 60 and 120ppm zinc respectively in dairy cows.

Somatic Cell Count (SCC)

Zn is also important for maintenance of proper immunity, udder health and reproduction in cows. Zn is involved in the catalytic, structural and regulatory processes of keratinization (Sordillo *et al.*, 1997). Zn is important for synthesis of keratin which lines the inside of teat duct. Keratin lining helps to maintain a protective barrier on the surface epithelium of teat and keep out the microorganism that can cause mastitis (Boland, 2003).

Different breeds of cow's viz. Friesian (40 ppm, Shakweer *et al.* 2010), Sahiwal (80 ppm, De *et al.*, 2014) and in Karan Fries cow's (80 and 120 ppm) supplemented with Zn significantly reduced the SCC in milk. Whereas, Cope *et al.* (2009) reported supplementation of 600 mg Zn/day as ZnO to lactating cows reduced milk SCC in treated groups. Indicating that fortification of diet with extra Zn in milking animals had added benefit on udder health and clean milk production. However, dose required for reduction in SCC is not specific. It varies between the breeds and it may also depend on the management conditions of the cows.

Antioxidant Status

An increased free radical production lowers the concentrations of antioxidant vitamins and minerals such as E, C, A, and Zn in serum (Halliwell and Gutteridge, 1989; Sahin *et al.*, 2005). Studies shown that concentrations of malondialdehyde (MDA), an indicator of lipid peroxidation, in serum decreases with dietary Zn picolinate supplementation in heat stressed animals. Similarly, Nagalakshmi *et al.* (2012) supplemented zinc carbonate in female rats also found significantly ($P < 0.01$) lower lipid peroxidation in supplemented groups as compared to control. Sahin and Kucuk (2003b) and Kucuk *et al.* (2003) reported that 30 or 60 mg/kg of Zn decreased serum and liver MDA levels in heat-stressed birds. Whereas, Patel *et al.* (2017) reported similar decreasing trend of MDA in postpartum heat stressed cows at 80 and 120 ppm of dietary Zn. Onderci *et al.* (2003) also reported that 30 mg/kg of ZnSO₄ and 400 µg/kg of Cr supplementation decreased serum MDA concentrations and increased the concentrations of vitamins C, E, and A in cold-stressed laying hens. In addition to decreased MDA concentration Sahin *et al.* (2005) also reported linear increase in serum antioxidant vitamin C and E as dietary 30 or 60 mg/kg of ZnSO₄ and Zn picolinate supplementation increased. Decreased MDA concentration in above said studies indicates the antioxidant role of Zn. Since Zn acts as a cofactor of the antioxidative enzyme Cu-Zn SOD speculated that increased scavenging of free radical and prevention of peroxidation. SOD also inhibits the NADPH-dependent lipid peroxidation (Prasad and Kucuk, 2002) and also via inhibiting glutathione depletion as well (Prasad, 1997). Due to the ability to replace Fe and Cu from binding sites, Zn can compete with these transition metals to bind to the cell membrane and decrease the production of free radicals and thus exert a direct antioxidant action (Kucuk, 2003). Zn also induces production of metallothionein, which is an effective scavenger for hydroxyl radical. It has been suggested that Zn-metallothionein complexes in the islet cells provide protection against immune-mediated free radical attack (Salgueiro *et al.*, 2000; Prasad and Kucuk, 2002). Another mode of action proposed for Zn as an antioxidant is its interaction with vitamin E. During Zn deficiency, probably due to defective formation of chylomicrons in the enterocyte, absorption of lipid-soluble vitamins such as E and A is impaired. Thus, some of the oxidative damage in Zn-deficient animals may be linked to the impaired vitamin E status during Zn deficiency (Kim *et al.*, 1998). Heat-stressed quail, shown that serum vitamin C, vitamin E, and Zn concentrations linearly increased, whereas MDA concentrations linearly decreased as dietary vitamin E (0, 250, and 500 mg/kg) and Zn picolinate (0, 30, and 60 mg/kg) supplementation increased (Sahin *et al.*, 2006b). Heat shock proteins (HSP) are thought to play a role in cellular protection under high ambient temperature, with a proposed relationship between the development of thermo tolerance and HSP synthesis, especially HSP70 (Lindquist and Craig, 1988). A lower HSP70 expression was observed in animals receiving therapeutic levels of Zn picolinate (30 and 60 mg/kg) and in quails reared under TN conditions (Sahin *et al.*, 2009).

Hormone Status

Dang *et al.* (2013) supplemented 80 ppm ZnSO₄ in Karan Fries cows and found reduced cortisol values under oxidative stress conditions in supplemented group compared to control (7.44 ± 0.62 vs. 9.95 ± 1.47). Patel *et al.* (2017) at 120ppm and Purwar *et al.* (2017) at 40 ppm along with the other feed additives in crossbred cows reported decreased serum cortisol level under heat stress conditions. Decreasing thyrotropin-releasing hormone (TRH) and target T₃ and T₄ levels under heat stress was considered to be due adaptive mechanism of animals for reducing heat production. However, Habeeb *et al.* (2013) and Patel *et al.* (2017) supplemented 30 ppm and 120 ppm respectively in goat and cows found increased T₃ and T₄ levels. It may be due to role of Zn in synthesis of T₃ which in turn converted to T₄ (Freake *et al.* 2001).

Immunity

Numerous studies have evaluated the effects of heat stress on the immune responses in animals and chickens. The heterophil-to-lymphocyte ratio has been used as a sensitive indicator of heat stress, among chicken populations (Gross and Siegel, 1983; Mashaly *et al.*, 2004). An increased heterophil-to-lymphocyte ratio was observed under high ambient temperature, which indicates a relationship between heat stress and nonspecific immune reactive cells (McFarlane and Curtis, 1989; Mashaly *et al.*, 2004). Zn is an important element for all aspects of immunity (Chandra and Dayton, 1982; Sherman, 1992) and is critical for the integrity of the cells involved in the immune response (Dardenne *et al.*, 1985). Zn deficiency causes a decrease in cellular immunity (Prasad and Kucuk, 2002) and adversely affects thymus (Fraker *et al.*, 1977), spleen (Luecke *et al.*, 1978), and interleukin production (Dowd *et al.*, 1986). Abnormal T-lymphocyte development is thought to be the primary consequence of Zn deficiency (Dardenne and Bach, 1993). Zinc deficiency causes an imbalance in functions of T helper-1 and T helper-2 cells (Shankar and Prasad, 1998). Heat stress condition mainly affects the epithelial barrier function, results in impairment in nutrient absorption and endotoxemia (Fernandez *et al.*, 2014). Supplementing dietary Zn may aid in repair and maintenance of epithelial integrity in digestive tract.

Reproduction

The patterns of reproductive behavior of farm animals vary with the variation in climatic conditions. Pronounced variations observed in the signs of estrus, rates of conception and frequency of calving are generally attributed to climatic factors. Roth *et al.* (2001) reported that heat stress caused an immediate as well as a delayed effect on ovarian follicular growth in Holstein cows. However, Wolfenson *et al.* (1995) reported that there was no immediate effect of heat stress on the population of small, medium, and large follicles in Gir cows. Rabiee *et al.* (2010) reported that secretion of gonadotropin-releasing hormone from

the hypothalamus and the gonadotropins, luteinizing hormone (LH) and follicle stimulating hormone (FSH) from the anterior pituitary gland affected by heat stress. Habeeb *et al.* (2013) supplemented zinc in diet of goat during transition period and found that days from weaning to estrous, duration of estrus and days of kidding interval were significantly lower in supplemented group compared to control. Kundu *et al.* (2014) evaluate the effect of dietary ZnO on post-partum reproductive performance of Teresa goat and found favorable result in terms of incidence of estrus, conception rate and kidding rate. Patel *et al.* (2017) also reported that supplementation of 80 and 120 ppm Zinc in feed during peripartum period to Karan fries cows is effective in improving post partum reproductive performance.

Conclusion

Heat stress in dairy animals results in compromised performance. This effect can be subsidized by supplementing dietary Zn. Based on few available research studies in animals under heat stress and Zn supplementation, it can be concluded that, expected increase in oxidative damage, decreased DMI, elevated cortisol, decreased thyroid hormones, reproductive performance and immunosuppression in heat stress can be reversed by supplementing Zn. The role of dietary Zn supplementation for alleviating the effect of heat stress has been reviewed extensively in poultry, however, in animals it is scanty. Hence further studies are needed in animals to confirm the role of dietary Zn on heat stress alleviation.

References

1. Abdel Monem, U. M. and El-Shahat, K. H. 2011. Effect of different dietary levels of inorganic zinc oxide on ovarian activities, Reproductive performance of Egyptian Baladi ewes and growth of their lambs. *Bulgarian. J Vet Med.*, 14 (2):116–123.
2. Abilay, T. A., Mitra, R. and Johnson, H. D. 1975. Plasma cortisol and total progesterin levels in Holstein steers during acute exposure to high environmental temperature (42 C) conditions. *J. anim. sci.*, 41 (1): 113-117.
3. Anton, A., Solcan, G. and Solcan, C. 2013. The impact of copper and zinc deficiency on milk production performances of intensively grazed dairy cows on the North-East of Romania. In *Proceedings of World Academy of Science, Engineering and Technology* (No. 80, p. 478). *W. Acad. Sci., Engineering and Technology (WASET)*.
4. Batal, A. B., T. M. Parr, and D. H. Baker. 2001. Zinc bioavailability in tetrabasic zinc chloride and the dietary zinc requirement of young chicks fed a soy concentrate diet. *Poult. Sci.* 80:87–90
5. BAHS, 2017. Basic Animal Husbandry statistics. Department of Animal Husbandry, Dairying and Fisheries, Ministry of Agriculture, Government of India, New Delhi.
6. Baumgard, L. H., and R. P. Rhoads. 2012. Ruminant nutrition symposium: Ruminant production and metabolic responses to heat stress. *J. Anim. Sci.* 90(6): 1855-1865.
7. Bernabucci, U., Lacetera, N., Baumgard, L. H., Rhoads, R. P., Ronchi, B. and Nardone, A. 2010. Metabolic and hormonal acclimation to heat stress in domesticated ruminants. *J. Anim. Sci.*, 4(07): 1167-1183.
8. Bernabucci, U., Ronchi, B., Lacetera, N. and Nardone, A. 2005. Influence of body condition score on relationships between metabolic status and oxidative stress in periparturient dairy cows. *J. Dairy Sci.*, 88(6): 2017-2026.

9. Boland, M.P. 2003. Trace minerals in production and reproduction in dairy cattle. *Advances in Dairy technology*, 15: 319-330.
10. Chandra, G. and Aggarwal, A. 2013. Effect of DL-Tocopherol Acetate on Calving Induced Oxidative Stress in Periparturient Crossbred Cows during summer and Winter Seasons. *Ind. J. Anim. Nut.*, 26(3): 204-210.
11. Chandra, R. K., and D. H. Dayton. 1982. Trace element regulation of immunity and infection. *Nutr. Res.* 2:721-733
12. Collier, R. J., Collier, J. L., Rhoads, R. P. and Baumgard, L. H. 2008. Invited review: genes involved in the bovine heat stress response. *J. Dairy Sci.*, 91(2): 445-454.
13. Cope, C. M., Mackenzie, A. M., Wilde, D. and Sinclair, L. A. (2009). Effects of level and form of dietary zinc on dairy cow performance and health. *J. Dairy Sci.*, 92:2128-2135.
14. Dang, A. K., Jamwal, M., Kaur, M., Kimothi, S. P., Pal, S., De, K. and Kapila, R. 2013. Effect of micronutrient supplementation around calving on the plasma cortisol levels of Murrah buffaloes and Sahiwal and Karan Fries cows. *Trop. Anim. Health Prod.*, 45(4): 1047-1050.
15. Dardenne, M., and J. M. Bach. 1993. Rationale for the mechanism of zinc interaction in the immune system. Pages 501-509 in *Nutrient Modulation of the Immune Response*. S. Cunningham-Rundles, ed. Marcel Dekker, New York, NY.
16. Dardenne, M., W. Savino, S. Borrih, and J. F. Bach. 1985. A zinc dependent epitope of the molecule of thymulin, a thymic hormone. *Proc. Natl. Acad. Sci. USA* 82:7035-7038.
17. De, Kalyan., Pal, Shashi., Prasad, Shiv and Dang, A. K. 2014. Effect of micronutrient supplementation on the immune function of crossbred dairy cows under semi-arid tropical environment. *Trop Anim Health Prod.*, 46:203-211.
18. Dharni, A. J., Parmar, B. C., Raval, R. J., Gupta, R. S. and Trivedi, M. M. 2006. Effect of challenge feeding during summer on the productive and reproductive performance and blood biochemical, metabolic and hormonal profile of crossbred lactating cows. *Int. J. Cow Sci.*, 2:52-59.
19. Do Amaral, B. C., Connor, E. E., Tao, S., Hayen, J., Bubolz, J. and Dahl, G. E. 2009. Heat-stress abatement during the dry period: Does cooling improve transition into lactation *J. Dairy Sci.*, 92(12): 5988-5999.
20. Dowd, P. S., J. Kelleher, and P. J. Guillou. 1986. T-lymphocyte subsets and interleukin-2 production in zinc-deficient rats. *Br. J. Nutr.* 55:59-69.
21. Fernandez, M. V. S., Pearce, S. C., Gabler N. K., Patience, J. F., Wilson, M. E., Socha, M. T., Torrison, J. L., Rhoads, R. P., and Baumgard, L. H. 2014. Effects of supplemental zinc amino acid complex on gut integrity in heat-stressed growing pigs. *Animal*, 8:1.
22. Fraker, P. J., S. M. Haas, and R. W. Leucke. 1977. Effect of zinc deficiency on the immune response of the young adult A/J mouse. *J. Nutr.* 107:1889-1895.
23. Freake, H. C., Govoni, K. E., Guda, K., Huang, C. and Zinn, S. A. 2001. Actions and interactions of thyroid hormone and zinc status in growing rats. *J. Nutr.*, 131(4): 1135-1141.
24. Gantner, V., Mijic, P., Kuterovac, K., Solic, D. and Gantner, R. 2011. Temperature-humidity index values and their significance on the daily production of dairy cattle. *Mljekarstvo*, 61:56-63.
25. Griffiths, L.M., Loeffler, S.H. and Socha, M.T. 2007. Effects of supplementing complexed zinc, manganese, copper and cobalt on lactation and reproductive performance of intensively grazed lactating dairy cattle on the South Island of New Zealand. *Anim. F. Sci. Tech.*, 137: 69-83.
26. Gross, W. B. and H. S. Siegel. 1983. Evaluation of the heterophil/ lymphocyte ratio as a measure of stress in chickens. *Avian Dis.* 27:972-978.
27. Habeeb, A.A.M., *EL-Tarabany, A.A. and Gad, A.E.* 2013. Effect of Zinc Levels in Diet of Goats on Reproductive Efficiency, Hormonal Levels, Milk Yield and Growth Aspects of Their Kids, *Global Veterinaria*, 10 (5): 556-564.
28. Hafez, E.S.E. 1968. *Adaptation of domestic animals*. Edition, illustrated. Publisher, Lea & Febiger.
29. Halliwell, B. E., and J. M. C. Gutteridge. 1989. Lipid peroxidation: A radical chain reaction. Pages 188-218 in *Free Radicals in Biology and Medicine*. 2nd ed. Oxford University Press, New York, NY

30. Holter, J. B., West, J. W., and McGilliard, M. L. 1997. Predicting ad libitum dry matter intake and yield of Holstein cows. *J. Dairy Sci.*, 80(9): 2188-2199.
31. Jain V., Patel B., Umar F.P., Ajithakumar H.M., Gurjar S.K., Gupta ID and Verma A 2017. Identification of single nucleotide polymorphism in protein phosphatase 1 regulatory subunit 11 gene in Murrah bulls, *Vet. World*, 10(2): 244-248.
32. Jia, W. B., Jia, Z. H., Zhang, W., Wang, R. L., Zhang, S. W. and Zhu, X. P. 2008. Effects of dietary zinc on performance, nutrient digestibility and plasma zinc status in Cashmere goats. *Small Rumin. Res.*, 80:68-72.
33. Jing, M. Y., Sun, J. Y., Zi, N. T., Sun, W., Qian, L. C., and Weng, X. Y. 2007. Effects of zinc on hepatic antioxidant systems and the mRNA expression levels assayed by cDNA microarrays in rats. *Ani. Nutr. Metab.*, 51(4): 345-351.
34. Johnson, H.D. 1980. Depressed chemical thermogenesis and hormonal functions in heat. In: Environmental Physiology Aging, Heat, and Altitude. Elsevier /North Holland, New York. 3-9.
35. Kadzere, C. T., M. R. Murphy, N. Silanikove, and E. Maltz. (2002). Heat stress in lactating dairy cows: A review. *Livest. Prod. Sci.*, 77(1): 59-91.
36. Kidd, M. T., P. R. Ferket, and M. A. Qureshi. 1996. Zinc metabolism with special reference to its role in immunity. *World's Poult. Sci. J.* 52:309-323.
37. Kim, E. S., S. K. Noh, and S. I. Koo. 1998. Marginal zinc deficiency lowers the lymphatic absorption of α -tocopherol in rats. *J. Nutr.* 128:265-270.
38. Kucuk, O., N. Sahin, and K. Sahin. 2003. Supplemental zinc and vitamin A can alleviate negative effects of heat stress in broiler chickens. *Biol. Trace Elem. Res.* 94:225-235.
39. Kumar, A., Kumar, P. and Singh, S. V. 2007. Oxidative stress marker's profile in erythrocytes of natural and heat exposed cattle and buffaloes. *J. Dairy Sci.*, 60(2): 114-118.
40. Kundu, M. S., De, A. K., Jeyakumar, S., Sunder, J., Kundu, A., and Sujatha, T. 2014. Effect of zinc supplementation on reproductive performance of Teressa goat. *Veterinary World*, 7: 380-383.
41. Leung, F. Y. 1998. Trace elements that act as antioxidants in parenteral micronutrition. *J. Nutr. Bioch.*, 9(6): 304-307.
42. Lindquist, S. and E. A. Craig. 1988. The heat shock proteins. *Annu. Rev. Genet.* 22:631-637.
43. Luecke, R. W., C. E. Siminol, and P. J. Fraker. 1978. The effect of restricted dietary intake on the antibody mediated response of the zinc deficient A/J mouse. *J. Nutr.* 108:881-887
44. MacDonald, R.S. 2000. The role of zinc in growth and cell proliferation. *J. Nutr.* 130 (5S Suppl.):1500S-1508S
45. Mader, T. L., Gaughan, J. B., Johnson, L. J., and Hahn, G. L. 2010. Tympanic temperature in confined beef cattle exposed to excessive heat load. *Int. J. Biometeorol.*, 54(6): 629-635.
46. Mandal, G. P., Dass, R. S., Isore, D. P., Garg, A. K., and Ram, G. C. 2007. Effect of zinc supplementation from two sources on growth, nutrient utilization and immune response in male crossbred cattle (*Bos indicus* \times *Bos taurus*) bulls. *Anim. F. Sci. Tech.*, 138(1): 1-12.
47. Marai, I. F. M., and Haebe, A. A. M. (2010). Buffalo's biological functions as affected by heat stress— A review. *Livest. Sci.*, 127 (2), 89-109.
48. Mashaly, M. M., G. L. Hendricks., M. A. Kalama., A. E. Gehad., A. O. Abbas., and P. H. Patterson. 2004. Effect of heat stress on production parameters and immune responses of commercial laying hens. *Poult. Sci.* 83:889-894.
49. McFarlane, J. M., and S. E. Curtis. 1989. Multiple concurrent stressors in chicks. 3. Effects on plasma corticosterone and the heterophil:lymphocyte ratio. *Poult. Sci.* 68:522-527.
50. Nagalakshmi, D., Parashu Ramulu, S. and Usha Rani, M. 2012. Effect of graded levels of zinc supplementation on growth performance and oxidative defense mechanism in rats. *J. Pharm.* 2: 2319-4219.
51. NASA (2015) National Aeronautics and Space Administration. Goddard Institute for Space Studies available <http://earthobservatory.nasa.gov/Features/WorldOfChange/decadaltemp.php> access on 25th April, 2017.

52. Nayri, A., Upah, N. C., Sucu, E., Defrain, J. M. and Baumgard, L. H. 2014. Effect of the ratio of zinc amino acid complex to zinc sulfate on the performance of Holstein cows. *J. Dairy Sci.*, 97:4392–4404.
53. Onderci, M., N. Sahin., K. Sahin, and N. Kilic. 2003. The antioxidant properties of chromium and zinc: In vivo effects on digestibility, lipid peroxidation, antioxidant vitamins and some minerals under a low ambient temperature. *Biol. Trace Elem. Res.* 92:139–150.
54. Oteiza, P. L., Olin, K. L., Fraga, C. G., and Keen, C. L. 1996. Oxidant defense systems in testes from zinc-deficient rats. *Proc. Soc. Exp. Biol. Med.*, 213(1): 85-91.
55. Patel, B., Kumar, N., Jain, V., Ajithakumar, H.M., Kumar, S., Raheja, N., Lathwal, SS., Datt C. and Singh. SV. 2017. Zinc Supplementation Improves Reproductive Performance Of Karan-Fries Cattle. *I. J. Ani. Repro.* 38 (1): 20-22.
56. Patel, B., Kumar N., Jain V., Raheja N., Yadav SK., Kumar N., Lathwal SS. and Singh SV. 2017. Effect of zinc supplementation on hormonal and lipid peroxidation status of peri-parturient Karan Fries cows during heat stress conditions. DOI:10.18805/ijar.v0iOF.9139.
57. Ptale B., Kumar N, Jain V., Dang, A. K., Sharma, R., Lathwal, SS and Singh SV. 2017. Effect of zinc supplementation on production performance and udder health of periparturient Karan Fries cows during heat stress. *Indian J. Dairy. Sci.* 70(4):379-385.
58. Patel B., Kumar N., Jain V., Raheja N. and Lathwal SS. 2017. Effect of Zinc Supplementation on Uterine Involution Status and Ovarian Follicular Size in Karan Fries cows. *Intas Polivet (2017) Vol. 18 (1): 31-33.*
59. Pond, W.C., Church, D.C. and Pond, K.R 1995. Zinc in basic animal nutrition and feeding, 4th edn. John Wiley and Sons, New York, pp 190–193.
60. Prasad, A. S. 1997. The role of zinc in brain and nerve functions. Pages 95–111 in *Metals and Oxidative Damage in Neurological Disorders*. A. Connor, ed. Plenum Press, New York, NY.
61. Prasad, A. S., and Kucuk, O. 2002. Zinc in cancer prevention. *Cancer and metastasis Reviews*, 21(3-4): 291-295.
62. Prasad, A., Muhammed, E., Kannan, A. and Aravindakshan, T. 2012. Thermal stress in dairy cattle. *J. Veter. Asso.*, 10: 45-51.
63. Purwanto, B.P., Abo, Y., Sakamoto, R., Furumoto, F. and Yamamoto, S. 1990. Diurnal patterns of heat production and heart rate under thermoneutral conditions in Holstein Friesian cows differing in milk production. *J. Agric. Sci.*, 114 (1990):139.
64. Purwar, V., Oberoi, P.S. and Dang, A.K. 2017. Effect of feed supplement and additives on stress mitigation in Karan Fries heifers. *Vet. World*, 10(12): 1407-1412.
65. Rabiee, A. R., Lean, I. J., Stevenson, M. A., and Socha, M. T. 2010. Effects of feeding organic trace minerals on milk production and reproductive performance in lactating dairy cows: A meta-analysis. *J. Dairy Sci.*, 93(9): 4239-4251.
66. Ronchi, B., Stradaoli, G., Supplizi, A. V., Bernabucci, U., Lacetera, N., Accorsi, P. A. and Seren, E. 2001. Influence of heat stress or feed restriction on plasma progesterone, oestradiol-17 β , LH, FSH, prolactin and cortisol in Holstein heifers. *Livest. prod. Sci.*, 68(2): 231-241.
67. Roth, Z., Arav, A., Bor, A., Zeron, Y., Braw-Tal, R. and Wolfenson, D. 2001. Improvement of quality of oocytes collected in the autumn by enhanced removal of impaired follicles from previously heat-stressed cows. *Reproduction*, 122(5): 737-744.
68. Sahin K & Kucuk O. 2003b. Zinc supplementation alleviates heat stress in laying Japanese quail. *Journal of Nutrition*, 133: 2808-2811.
69. Sahin, K., M. O. Smith, M. Onderci, N. Sahin, M. F. Gursu, and O. Kucuk. 2005. Supplementation of zinc from organic or inorganic 2182.
70. Sahin, K., M. Onderci, N. Sahin, F. Gulcu, N. Yildiz, M. Avcı, and O. Kucuk. 2006b. Responses to dietary vitamin E and zinc picolinate at different environmental temperatures. *Anim. Feed Sci. Technol.* 129:39–48.
71. Sahin, N., M. Tuzcu, I. Ozercan, K. Sahin, A. S. Prasad, and O. Kucuk. 2009. Zinc picolinate in the prevention of leiomyoma in Japanese quail. *J. Med. Food*.

72. Salama, A. A., Caja, G., Albanell, E., Such, X., Casals, R., and Plaixats, J. 2003. Effects of dietary supplements of zinc-methionine on milk production, udder health and zinc metabolism in dairy goats. *J. Dairy Sci.*, 70(01): 9-17.
73. Salgueiro, M. J., Zubillaga, M., Lysionek, A., Sarabia, M. I., Caro, R., De Paoli, T. and Boccio, J. 2000. Zinc as an essential micronutrient: a review. *Nutrition Research*. 20(5): 737-755.
74. Singh, S.V. and Upadhyay, R.C. 2009. Impact of temperature rise on physiological function, thermal balance and milk production of lactating Karan fries and Sahiwal cows. *Indian Vet. J.* 86: 141-144.
75. Shakweer, I. M. E., EL-Mekass, A. A. M., and EL-Nahas, H. M. 2010. Effect of two different sources of zinc supplementation on productive performance of friesian dairy cows. *Egyptian J. Anim. Prod.*, 47(1): 11-22.
76. Shankar, A. H. and A. S. Prasad. 1998. Zinc and immune function: The biological basis of altered resistance to infection. *Am. J. Clin. Nutr.* 68:447-463.
77. Sherman, A. R. 1992. Zinc, copper and iron nutrition and immunity. *J. Nutr.* 122:604-609.
78. Silanikove, N. 2000. Effects of heat stress on the welfare of extensively managed domestic ruminants. *Liv. Prod. Sci.*, 67(1): 1-18.
79. Singh, S.V. and Upadhyay, R.C. (2009). Impact of temperature rise on physiological function, thermal balance and milk production of lactating Karan fries and Sahiwal cows. *Indian Vet. J.* 86: 141-144.
80. Sivakumar, A. V. N., Singh, G. and Varshney, V. P. 2010. Antioxidants supplementation on acid base balance during heat stress in goats. *Asian Aust. J. Anim. Sci.*, 23(11): 1462-1468.
81. Sordillo, L. M., Shafer-Weaver, K. and DeRosa, D. 1997. Immunobiology of the mammary gland. *J. Dairy Sci.*, 80(8):1851-1865.
82. Spiers D.E, Spain J.N, Sampson J.D and Rhoads R.P. 2004. Use of physiological parameters to predict milk yield and feed intake in heat-stressed dairy cows. *J. Therm. Biol.* 29(7-8):759-764.
83. Underwood, E. J. and Suttle, N. F. 1999. In *The mineral nutrition of livestock*, 3rd ed. CABI Publishing, CAB International, Wallingford, Oxon, UK. Technology 93: 193-203.
84. Upadhyay, R. C., Ashutosh, R. V., Singh, S. V. and Aggarwal, P. K. 2009. Impact of Climate Change on reproductive functions of cattle and buffaloes. *Global Climate Change and Indian Agriculture (Edited by PK Aggarwal)*. Published by ICAR, New Delhi, 107-110.
85. Vallee, B. L. and Falchuk, K.H. 1993. The biochemical basis of zinc physiology. *Physiol. Rev.* 73: 79-118.
86. Wedekind, K. J., A. E. Hortin, and D. H. Baker. 1992. Methodology for assessing zinc bioavailability: Efficacy estimates for zinc-methionine, zinc sulfate, and zinc oxide. *J. Anim. Sci.* 70:178-187.
87. West, J. W. 2003. Effects of heat-stress on production in dairy cattle. *J. Dairy Sci.*, 86(6): 2131-2144.
88. Wise, M. E., Armstrong, D. V., Huber, J. T., Hunter, R. and Wiersma, F. 1988. Hormonal alterations in the lactating dairy cow in response to thermal stress. *J. Dairy Sci.*, 71(9): 2480-2485.
89. Wolfenson, D., Thatcher, W. W., Badinga, L., Savio, J. D., Meidan, R., Lew, B. J. and Berman, A. 1995. Effect of heat stress on follicular development during the estrous cycle in lactating dairy cattle. *Biol. Reprod.*, 52(5): 1106-1113.
90. Yousef, J. L. M., Habeeb, A. A. and El-Kousey, H. 1997. Body weight gain and some physiological changes in Friesian calves protected with wood or reinforced concrete sheds during hot summer season of Egypt. *Egypt. J. Anim. Prod.*, 34: 89-101.