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Review

Potential use of chromium to combat thermal stress in animals: A review

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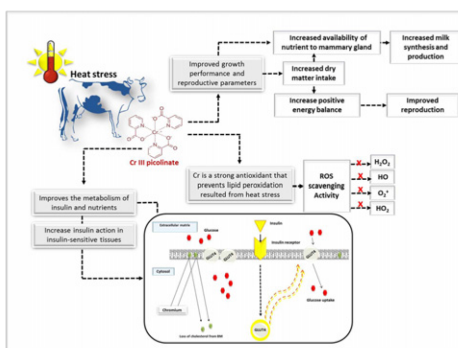
HIGHLIGHTS

- Heat stress influences nutrient digestibility, carcass quality and immune function.
- Chromium (Cr) is a strong antioxidant that prevents HS-induced lipid peroxidation.
- Cr improves nutrient metabolism and cortisol hormone activity.
- Cr promotes insulin action in responsive tissues, thereby increasing farm animal productivity.
- Cr is a promising agent for combating the adverse effects of heat stress in animals.

GRAPHICAL ABSTRACT



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ABSTRACT

Heat stress (HS) has adverse effects on the body: it decreases body weight, feed efficiency, feed intake, carcass quality, and nutrient digestibility. Chromium (Cr) can prevent lipid peroxidation induced by HS through its strong antioxidant activities, especially when it is added to the poultry diet. It improves the action of insulin and nutrient metabolism (of lipids, proteins, nucleic acid, and carbohydrates) through activation of enzymes associated with such pathways. The results of the studies on Cr added to diets with concentrations of 0.05 mg Cr/kg of Cr-methionine led to improved feed efficiency and DM intake by cows and Holstein dairy calves exposed to high environmental temperatures. Moreover, calves that received Cr at levels of 0.05 mg/kg of body weight tended to have higher serum concentrations of glucose and higher ratios of insulin to glucose. In heat-stressed pigs, Cr addition (200 ppb) increased blood neutrophils by about 37%. Several studies have asserted that Cr can inhibit inflammation in lactating cows by promoting the release of Hsp72, assisting production of IL-10 and

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Heat shock proteins

inhibiting degradation of IκBα in HS conditions. In addition, Cr supplementation was observed to possibly have positive impacts on both cell-mediated and humeral immunity in heat-stressed buffalo calves. Studies over the last two decades have shown with certainty that chromium supplementation has an impact on many variables in chickens. Moreover, Cr is believed to increase insulin action in insulin-sensitive tissues (i.e., adipose and muscles), resulting in increased farm animal productivity through the improvement of feed intake, growth rate, carcass quality, reproductive parameters and immune functions.

Contents

1. Introduction

Heat stress (HS) occurs when the heat produced by animals surpasses their capacity to dissipate the extra heat into their surrounding environment (Alagawany et al., 2017; El-Kholy et al., 2018; Farghly et al., 2018). There are two main categories of HS: chronic and acute. Because chronic HS comes from high temperatures over a long period, acclimatization to the environment is possible. Acute HS, on the other hand, comes from rapid increase in the environmental temperature over a short period (Alagawany et al., 2017). HS elicits many physiological consequences. Its impacts include increased body and rectal temperatures, reduced feed consumption, impaired immunity, alteration of blood electrolyte balance and pH, poor feed utilization, depressed cellular energy bioavailability, impaired reproductive functions and impaired endocrine functions (Loyau et al., 2015).

HS alters lipid, protein and carbohydrate metabolism. It also alters homeorhetic adaptations, which are largely caused by increased circulating insulin (Baumgard and Rhoads, 2013). Hence, identification of nutritional approaches to ameliorate the effects of HS on health and production has become of interest recently **(**Khafaga et al., 2019**)**. Alternation in utilization and substrate uptake is also a result of HS, but this phenomenon is not yet fully understood. When temperatures are high, metabolic adaptations occur to increase chances of survival. For example, feed intake in Holstein cattle during summer was found to result in lower insulin concentrations in summer than in winter and spring (Abdelnour et al., 2019). Likewise, plasma insulin was lower in heat-stressed lactating sows compared to a control group, although glucose concentration was the same (de Braganca and Prunier, 1999). In addition, Sevi et al. (2002) reported that plasma non-esterified fatty acids (NEFA) increased in sheep but declined in lactating cows due to heat exposure (Itoh et al., 1998; Shwartz et al., 2009; Wheelock et al., 2010). Under stress conditions, Cr requirements are higher due to increased urinary excretion (Chang and Mowat, 1992; Pechova and Pavlata, 2007; Yari et al., 2010).

Chromium (a low-molecular-weight binding substance) activates insulin receptors and mobilizes the glucose transporter type 4 (GLUT 4) from the inside of the cell to the surface, allowing glucose to enter the cell (Vincent, 2015). Dietary Cr supplementation (0.5 to 1.5 mg/kg of dry matter (DM)) to heat-stressed buffalo calves improved heat tolerance, immune function, and insulin effectiveness. However, it had no effect on feed intake, growth rate, tri-iodothyronine (T3) or thyroxine (T4) concentrations (Kumar et al., 2015a).

The effects of Cr supplementation on production were previously reported for the cases of heat-stressed cows (Soltan, 2010) and normal cows (Sadri et al., 2009). However, the information concerning the influences of Cr on growth rate in heat-stressed calves is not consistent (Kumar et al., 2015a; Sadri et al., 2009; Yari et al., 2010). These inconsistencies could be attributed to the chemical form of Cr used (organic vs inorganic, yeast vs chelated Cr) (Kegley et al., 1997), the environmental conditions (normal vs heat-load conditions), Cr dosage, and method of Cr delivery (starter vs liquid).

Several research papers described the influences of Cr supplementation to heat-stressed dairy calves on feed intake, growth rate, general health status, and blood metabolites. However, the way in which Cr affects the feed intake is not clear. To clarify this mechanism, investigation of ingestion behavior in calves supplemented with Cr is needed.

There are no review articles summarizing the beneficial impacts of Cr on heat-stressed poultry. Therefore, the aim of the present paper is to highlight the consequences of Cr on thermoregulatory responses, growth rate, metabolites of blood, health status, oxidative biomarkers, and immune indices in different heat-stressed ruminants.

2. Heat stress in animals

Heat stress has several direct and indirect effects on dairy animal health: it can disrupt normal metabolism as well as affect the physiological, hormonal, and immune status of animals (Abd El-Hack et al., 2019; Saeed et al., 2019). Incremental increases in environmental temperature exert direct adverse impact on the hypothalamus appetite center, with subsequent reduction in feed intake (Baile and Forbes, 1974). In lactating cows, feed intake starts to decrease at climatic temperatures of 25–26 °C, and it may decline more rapidly at 30 °C and drop by approximately 40% at 40 °C (Rhoads et al., 2013). The purpose of this reduction in feed intake is to decrease production of heat in hot environments (Kadzere et al., 2002). As a result, animals may develop negative energy balance (NEB), with subsequent negative effect on body weight and body condition scores (Lacetera et al., 1996). Additionally, HS may affect the production and composition of milk in dairy animals (Bouraoui et al., 2002; West, 2003; Spiers et al., 2004; Upadhyay et al., 2009; Wheelock et al., 2010). Berman (2005) concluded that the stress-response systems in dairy cattle could be affected negatively in climatic temperatures above 35 °C. Heat-stressed dairy cows developed reduced feed intake and NEB, which is subsequently responsible for milk synthesis decline (Wheelock et al., 2010).

Moreover, HS often alters the physiological mechanisms of the rumen, with resultant increases in health problems and metabolic disorders (Nardone et al., 2010; Soriani et al., 2013). Nonaka et al. (2008) concluded that heat-stressed animal suffer from diminished acetate production and from increased propionate and butyrate production due to alterations in rumen function. As a result, stressed animals consume less roughage and undergo alteration of rumen pH and microbial population (Hall, 2009), diminished rumination and rumen motility (Nardone et al., 2010; Soriani et al., 2013), decreased salivary production, and less dry-matter intake (DMI) (Nardone et al., 2010; Soriani et al., 2013). Also, HS resulted in decreased animal growth, carcass quality and fertility, and in increased mortality rate and care costs (Baumgard and Rhoads, 2013; Mayorga et al., 2019).

It is therefore necessary to develop protocols to overcome the negative impacts of HS. Nutritional intervention is considered to be an economical method for increasing production in summer (Mayorga et al., 2019). Indeed, dietary chromium enhances cellular glucose uptake (Chen et al., 2006) by increasing the binding of insulin to its extracellular receptors (NRC, 1994; Vincent, 2015). In addition, studies showed that average daily feed intake (ADFI), reproduction, immune response and growth performance are improved by Cr supplementation (Burton et al., 1993b; Hayirli et al., 2001; Hung et al., 2014; Lindemann et al., 1995; Sadri et al., 2009; Sales and Jancik, 2011; Yasui et al., 2014). The adverse effect of HS in ruminants and their body reactions against it are summarized in Fig. 1. Similarly, the adverse effect of HS on animal performance, production and reproduction is summarized in Fig. 2.

3. General properties of chromium and sources

Trivalent Cr (Cr^{3+}) has an effect on rodents (rats and mice), raising their sensitivity to insulin (Vincent, 2014). Despite the fact that, according to a report published by the European Food Safety Authority, there is no evidence that Cr is an essential trace element for either animals or humans (Vincent, 2014), Cr has for decades been thought to be an essential nutrient, and current studies show that high pharmacological and nutritional doses should be maintained as a beneficial element (Hua et al., 2012; Vincent, 2001; Vincent, 2017; Ibrahim et al., 2017). Farm animals, humans and laboratory animals have been the subject of studies of Cr as a dietary supplement. These studies showed that stress resulted in Cr deficiency (when Cr is considered essential) (e.g. see Lukaski et al., 1996) and in increased loss of Cr through urinary excretion.

Cr supplementation also overcomes the effects of stress stemming from animal shipping and meat quality improvement. The reviews made by the (NRC, 1994) in the mid-1990s and by Lindemann et al. (1995) are the most comprehensive reviews about the use of Cr supplementation for farm animals. No conclusions about the need for Cr supplementation in the diets of sheep, fish, rats, horses, and rabbits have been drawn or stated by the Animal Research Committee. Nor have any recommendations been made about Cr supplementation for poultry, cattle and swine, even though Cr does have beneficial impacts on heat-stressed cattle and pig leanness and on the effectiveness of reproduction (NRC, 1994).

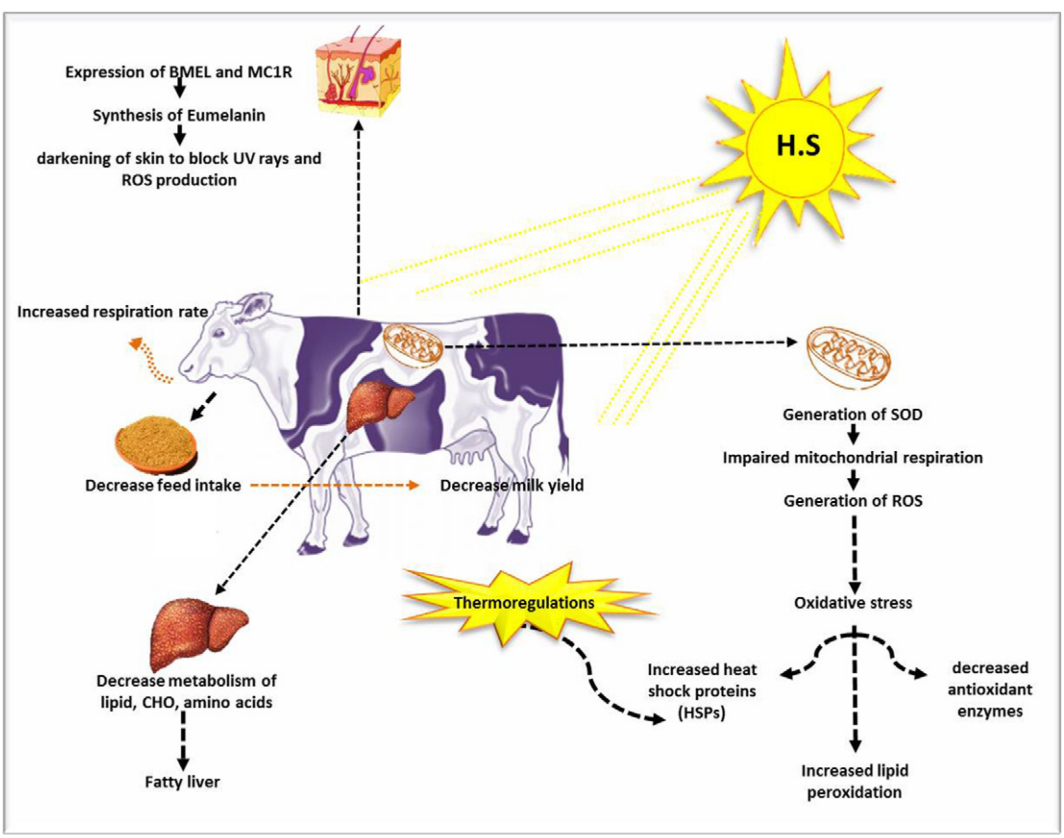

Fig. 1. Summary of heat stress adverse impacts and body reactions in ruminants.

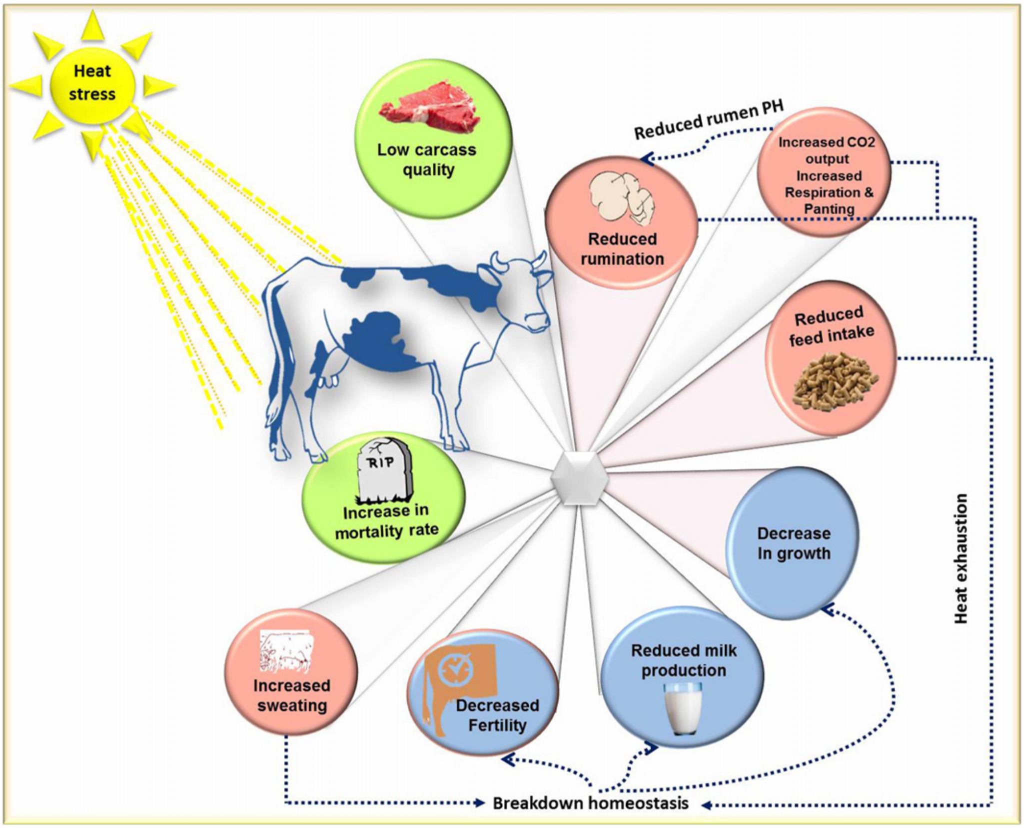

Fig. 2. Effect of heat stress on animal performance, production and reproduction.

4. Mode of action of chromium in animal nutrition

Chromium chloride, chromium polynicotinate, and chromium picolinate (CrP, Fig. 3) are considered to be nutritional supplements and micronutrients. Several investigations concluded that chromodulin is a naturally occurring biomolecule that binds to trivalent Cr and could explain the action of Cr in metabolism of lipids and carbohydrates (Davis and Vincent, 1997). Chromodulin is able to stimulate insulin-dependent glucose metabolism in adipocytes (Yamamoto et al., 1988).

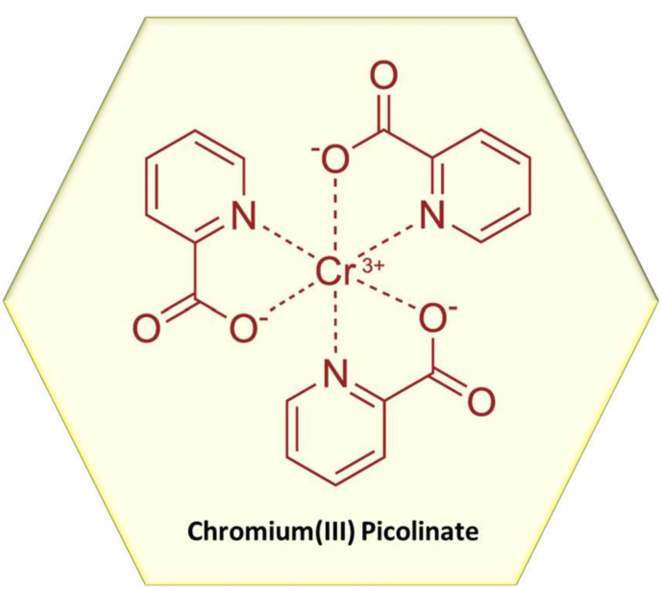

Fig. 3. Chemical formula of Cr III picolinate.

Moreover, it could activate the membrane phosphotyrosine phosphatase in adipocyte membranes (Davis et al., 1996).

Supplemented levels of Cr are expected to induce little alteration on body weight and body composition. However, the administration of high levels of Cr could potentially lead to altered Cr status, with subsequent alteration in metabolisms (John, 2004).

In addition, CrP has the potential to control levels of blood sugar in diabetes, control blood pressure levels, and reduce cholesterol. Cr acts as a cofactor for insulin; therefore, it activates insulin receptor kinase and increases the number of insulin receptors. CrP attenuates weight gain, but the mechanism for this is unknown (Anton et al., 2008). It may have an action through its influence on the balance of energy to either decrease feed intake or increase energy expenditure.

Cr affects reproduction by enlarging the seminal vesicles, increasing prostate weight and reducing testis weight (Marouani et al., 2012). It also affects weight loss by decreasing fat percentage and increasing lean body mass (Anderson, 1998).

Stress stimulates the hypothalamus to produce corticotropin, which stimulates the pituitary to produce the adrenocorticotropic hormone, which in turn stimulates the adrenal cortex to release corticosterone. Corticoids depress the immune system and reduce the concentration of serum protein. They also raise blood glucose levels and decrease the utilization of glucose, thus functioning as antagonists to Cr, which influence the release of corticosteroids. The role of Cr^{3+} against cellular glucose uptake is summarized in Fig. 4.

5. Impacts of chromium in heat-stressed animals

The potential beneficial impact for dietary supplementation of Cr during HS could be obtained through several pathways. The main findings related to Cr supplementation in heat-stressed animals are summarized in Table 1 and discussed in the following sections.

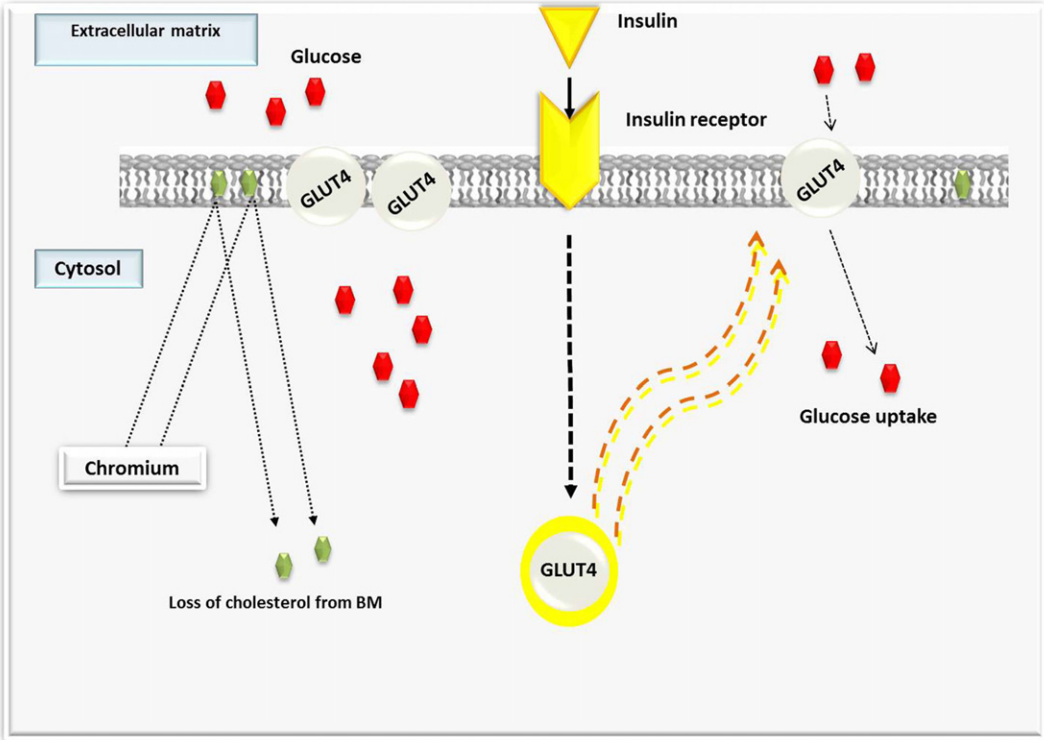

Fig. 4. The role of Chromium (III) against cellular glucose uptake (insulin binds to its receptor, which in turn initiates several protein-signaling cascades, including a signal that causes the translocation of the GLUT4 into the plasma membrane (PM). Cr (III) induces a loss of PM cholesterol. Accumulation of GLUT4 at the PM has been shown to be dependent on the Cr (III)-induced cholesterol loss and leads to an increase in cellular glucose uptake.

5.1. Thermoregulatory responses

Thermoregulatory response is considered to be the first indicator of HS. HS is associated with increased respiration, pulse rate and body temperature in homothermic animals. A dietary supplement of 0.05 mg of Cr-methionine/kg of body weight significantly reduced the respiration rate (RR) in heat-stressed dairy calves (Mousavi et al., 2019b). Cr (0.05 mg/kg of body weight) had the same effect but had no effect on RT (Kargar et al., 2018b). In heat-stressed calves, Cr-methionine at 0.05 mg/kg of body weight reduced diarrhea to −0.9 d, pneumonia to −0.7 d and medication to −1.5 d before weaning (Kargar et al., 2018b; Mousavi et al., 2019a).

Most studies indicated that Cr decreases RT to overcome the effects of HS (Kargar et al., 2018b). Mousavi et al. (2019a) found no effect of Cr-methionine on diarrhea, pneumonia, medication days or RT in heat-stressed calves. Also, Kumar et al. (2015a) found no effect of 0.5, 1 or 1.5 mg of inorganic Cr/kg on pulse rate (PR), RR or RT in heat-stressed buffalo calves. An-Qiang et al. (2009) measured the values of RR and RT for cows undergoing Cr supplementation (3.6, 7.2 or 10.8-milligram chromium/head per day) and cows without any supplementation and found no differences. According to the previous results, Cr has no impact on somatic cell count and or on RT, PR or RR in lactating cows (Qi et al., 2018b). A separate study indicated that Cr propionate (200 ppb) has no effect on RR, skin temperature (ST) or body temperature (BT) in heat-stressed pigs (Mayorga et al., 2019).

5.2. Growth performance

Thermal stress has been reported to decrease feed intake, weight gain and effectiveness of feed intake (Abdelnour et al., 2019). Separate studies corroborated that heat-load results in decreased feed intake and growth performance and that indicated that, in turn, it results in decreased energy expenditure for tissue synthesis (Johnson et al., 2015; Kerr et al., 2003; Le Bellego et al., 2002; Mayorga et al., 2019). To counter this, Cr supplementation can result in increased feed intake in heat-stressed animals and hence growth performance, as shown by several studies (Hayirli et al., 2001; Hung et al., 2014; Mayorga et al., 2019; Sahin et al., 2002). Likewise, Cr yeast increased feed intake in heat-stressed lactating dairy cows compared with a control group (21.24 and 19.56 kg/day, respectively) (Alsaiady et al., 2004; Hayirli et al., 2001).

Feed efficiency and average daily gain increased in the case of calves in their growth stage fed Cr at a level of 4 mg/head (Chang and Mowat, 1992). This result is due to the increase in total levels of immunoglobulins in serum (Burton, 1995; Burton et al., 1996; Chang and Mowat, 1992). Moreover, the supplementation of 0.05 mg Cr/kg of body weight of Cr-methionine in cows' diets increased feed efficiency and DMI (Arthington et al., 1997). Supplementation of 3.6, 7.2 and 10.8 mg chromium/head/day to heat-stressed dairy cows resulted in a significant increase in DMI ($p < 0.05$) according to An-Qiang et al. (2009). Mousavi et al. (2019a) reported that supplementation of Cr to dairy calves under HS resulted in increases in DMI ($p = 0.002$) and in average daily gain (ADG) ($p = 0.02$) but had no effect on effectiveness of feed ($p = 0.93$) or on body weight ($p = 0.14$). On the other hand, Kargar et al. (2018b) found that dietary supplementation of chromium improved the intake of feed and growth rate in dairy Holstein calves exposed to high environmental temperature (83.3 units). Also, the addition of Cr at a level of 0.05 mg/kg of body weight to a milk substitute or to diets for cattle during the pre- and post-weaning periods led to increases, at the end of the experiment, in feed intake, DM intake and average body weight gain, by 16.4%, 11.85% and 7.07% respectively. Cr supplementation improves growth rate and body weight by enhancing the absorption and digestion of nutrients (Ghorbani et al., 2012; Kargar et al., 2018a). Moreover, in finisher gilts exposed to high temperatures, the application of nano-chromium tripicolinate (400 ppb) resulted in a reduction in cortisol level by 25% and an increase in feed intake by 6% (Hung et al., 2014). Mayorga et al. (2019) discovered that final body

Table 1
The main findings related to Cr supplementation in heat stressed-animals.

Parameter	Species	Form & dosage	Findings	References
1-Thermoregulatory responses	Dairy calves.	• Cr-methionine (0.05 mg /kg BW0.75). • Cr (0.05 mg/kg BW0.75). • Cr-methionine at 0.05 mg/kg BW0.75–	• Significantly reduced the Respiration rate (RR). • Reduced the RR but has no effect on rectal temperature (RT). • Reduced the days with diarrhea (−0.9 d), pneumonia (−0.7 d) and total medication days (−1.5 d) before weaning in heat stressed calves. • No effect of Cr methionine on diarrhea, pneumonia, medication days and RT in heat stressed calves.	• (Mousavi et al., 2019b) • (Kargar et al., 2018b) • (Mousavi et al., 2019a) • (Mousavi et al., 2019a)
	Buffalo calves.	• Cr (0.5, 1 or 1.5 mg inorganic Cr/kg	• No effect on PR, RR and RT in heated buffalo calves.	• (Kumar et al., 2015a, 2015b)
	Cows.	• (3.6, 7.2 or 10.8 milligram chromium/head per day)	• Values of RR and RT for cows take Cr supplement and cows without any supplement were with no differences • According to the previous results Cr has no impact on somatic cell count and (RT, PR, RR) in lactating cows.	• (An-Qiang et al., 2009) • (Qi et al., 2018a, 2018b)
	Pigs.	• Cr propionate (200 ppb).	• No effect on RR, ST and BT in heat stressed pigs.	• (Mayorga et al., 2019)
2-Growth performance	Cows.	• Cr yeast. • Cr–methionine at 0.05 mg Cr/kg. • Cr (3.6, 7.2 and 10.8 mg chromium/head/day)	• Increased feed intake in heat stressed lactating dairy cows compared with control group (21.24 and 19.56 kg/day, respectively 21.24 and 19.56 kg/day, respectively. • Increases feed efficiency and dry matter intake. • Significant increase ($p < 0.05$) as reported in the DMI.	• (Alsaiady et al., 2004) • (Arthington et al., 1997) • (An-Qiang et al., 2009)
	Calves.	–• 0.05 mg/kg BW0.75 Cr.– • 4 mg/head.–– • 0.5 mg/kg of supplemental Cr as Cr propionate.	• The supplement of Cr to heat stressed dairy calves resulted in increasing total DMI ($p = 0.002$), ADG ($p = 0.02$) but has no effect on feed efficiency ($p = 0.93$) or final body weight ($p = 0.14$). • Dietary supplementation of Chromium improved feed intake and growth rate in Holstein dairy calves exposed to high environmental temperature (THI = 83.3 units), Also, the addition of Cr to a milk substitute or diets during pre and post-weaning cattle increases the feed intake, dry matter intake and average body weight gain at the end of the experiment of 16.4%, 11.85 and 7.07% respectively. • Cr supplement improves growth rate and body weight through enhancing the absorption and digestion of nutrients. Under a variety of stress conditions, Cr requirement of calves is increased. • Feed efficiency and average daily gain increased in case of growing calves fed Cr. • This result is due to increase the total levels of immunoglobulins in serum. • Cr supplementation to Murrah buffalo calves showed no significant effect on feed conversion ratio (FCR) over a period of 120 days, average daily gain (ADG) and dry matter intake. • Under normal conditions, Cr has no influence on feed intake or total DMI.	• (Mousavi et al., 2019a) • (Kargar et al., 2018a) • (Ghorbani et al., 2012) • (Chang and Mowat, 1992) • (Burton et al., 1996) • (Kumar et al., 2015a, 2015b) • (Bunting et al., 2000)
	Pigs	• 200 ppb of Chromium propionate.	• Final body weight has increased in heat stressed finishing pigs.	• (Mayorga et al., 2019)
3-Milk yield and composition	Dairy cows.	• (4 g/head/day) of Dietary chelated chromium. • Cr at 0.05 mg Cr/kg). • Moderate levels of Cr. • 10 mg/day Cr from 21 days pre-partum to 35 postpartum. • Chromium picolinate.	• Adding to the diet of heat loaded dairy cows has no effect on milk fats, protein, lactose, and solids non-fat percentage. • A significant rise ($p < 0.05$) in milk protein, fat and lactose levels by 1.043,1.066,1.02%, respectively is recorded when heat stressed dairy cows are supplied with Cr. • Increase in feed intake, dry matter efficiency and a decline in the insulin levels leading to a significant increase in milk secretion as a result of increasing the mammary nutrient flow. • The activity of Insulin growth factor (IGF) that has functional and structural homology to insulin receptors are supported through the improvement of milk production which also mimic the action of bovine somatotropin (bST). • An increase in milk production which was associated with decrease lipolysis and increase glucose uptake that will result in DMI rise. • The milk yield has increased ($p = 0.013$), dietary Cr has no significant on milk components (protein, fat and lactose) in dairy cows under high temperature (THI = 79.61).	• (Alsaiady et al., 2004) • (Nikkhah, 2012) • (Winkelman and Overton, 2012) • (Alsaiady et al., 2004) • (McNamara and Valdez, 2005) • (An-Qiang et al., 2009)
4-Blood variables	Cows.	• Chromium yeast (6 mg/head /day). • 0.05 mg of supplemental Cr/kg of BW 0.75 • Chromium picolinate (3.5 mg of Cr/cow daily). • 3.5 m g/kg of Cr/cow.	• Failed to show any effect on blood serum level of hemagglutination test (HA), cholesterol, triglycerides, urea, IGF-1, BHBA, albumen, and glucose while there is a drop in total blood and protein concentration. • Serum, insulin and NEFA reduced significantly. • No changes in glucose, blood urea nitrogen (BUN), creatinine, and cholesterol of lactating cows under heat stress conditions. • Significantly increased Hsp72 (11.68 μg/L) compared to those did not receive Cr (6.21 μg/L), Cr may play an anti-inflammatory role in lactating cows by promoting the release of Hsp72, increasing the production of IL-10, and inhibiting the degradation of IκBα under summer hot situation.	• (Soltan, 2010). • (Yari et al., 2010) • (Jin et al., 2017) • (Qi et al., 2018a, 2018b)
	Calves.	• Cr-methionine (0.05 mg /kg BW 0.75). • Chromium at level 0.05 mg/kg BW 0.75 • 1 and 1.5 mg/kg of DMI. • 0.5 mg of Cr/kg of DMI. • Cr-methionine (0.05 mg /kg BW0.75). • 0.04 mg Cr/kg of BW0.75. • 0.5, 1, and 1.5 mg of Cr/kg • (0.03 mg of Cr/kg of	• Dairy farm calves suffering from heat stress had no significant influence on glucose, albumin, and A/G ratio, triglyceridecholesterol, βHBA and BUN. Nevertheless, the serum concentration of globulin tended to be higher in Cr + calves during the experimental period. • Higher serum concentrations of glucose and a higher ratio of insulin to glucose measured at the end of the experiment. • Chromium supplementation had small effects on blood glucose and insulin in calves under normal or heat-stress conditions. • Blood insulin concentration reduced in heat-stressed buffalo calves but not at 0.5 mg/kg of DMI. • Blood concentrations of glucose and insulin decreased and increased,	• (Mousavi et al., 2019a) • (Kargar et al., 2018b; Yari et al., 2010) • (Ghorbani et al., 2012) • (Kumar et al., 2015a, 2015b) • (Bunting et al., 2000) • (Mousavi et al., 2019a) • (Kargar et al., 2018b) • (Kumar et al., 2015a, 2015b)

Table 1 (*continued*)

Parameter	Species	Form & dosage	Findings	References
		BW0.75). • Raising Cr doses (from 0 to 0.02 and 0.04 mg Cr/kg of BW0.75).	respectively, when dairy calves were supplemented with cr. - Hormones: • No notable effect on the T3, T4, T3/T4 ratio, and cortisol hormones activities However, they also reported that calves fed with Cr, recorded higher blood insulin level and insulin to glucose ratio as compared to those in the control group. • No influences on serum levels of T3, T4 and cortisol measured at pre and post weaning. • Similar findings were observed in buffalo calves that received 0.5, 1, and 1.5 mg of Cr/kg of DMI. • Increased blood T4 concentration and reduced T3 to T4 ratio in dairy calves. • Quadratic decline in serum T4, whereas blood T3 decreased only with the higher Cr dose supplementation in dairy calves.	• (Ghorbani et al., 2012) • (Yari et al., 2010)
	Cows	• (Cr-Yeast, 8 mg/d).	- Antioxidants: • Significant reduction of creatine kinase as a response to yeast-chromium dietary supplementation to lactating heat-stressed cows, which may be attributed to the use of different animal models, proper dose gradients of Cr, and chemical forms of Cr.	• (Mousavi et al., 2019a)
	Calves.	• 1.0 mg Cr/kg DM and above. • High Cr-yeast. • 4 mg of supplemental Cr/kg of DM and Cr nicotinate. • 1.5 mg of Cr/kg.	• Positive impacts in improving both humeral and cell-mediated immunity in heat-stressed buffalo calves. -Increased serum total Ig and IgM levels in high Cr-yeast supplemented calves following transport stress. • No change in total IgM in both high-Cr yeast and Cr nicotinate supplemented transport stressed calves. • To heat stressed buffalo calves, decreased significantly Hsp70.	• (Kumar et al., 2015a, 2015b) • (Burton et al., 1993a, 1993b) • (Kegley and Spears, 1995). • (Kumar et al., 2015a, 2015b), (Qi et al., 2018a, 2018b)
	Pigs.	• Chromium propionate supplementation (200 ppb). • Chromium tripicolinate nanoparticles (400 ppb). • 200 μg/kg Cr as Cr-Nano.	• Increase in blood neutrophils by 37% corresponded to the control group. • Plasma glucose, insulin and NEFA levels in serum were not changed in chromium tripicolinate nanoparticles-treated pigs (400 ppb) compared to those in the control group. • 13.2 and 20.6% higher serum concentration of IgM and IgG.	• (Mayorga et al., 2019) • (Hung et al., 2014) • (Wang et al., 2007)

weight increased in heat-stressed finishing pigs when fed with 200 ppb of chromium propionate.

Rumination activity was reported to decrease as a result of environmental heat load (Soriani et al., 2013). Decreased rumen motility as a result of a slowing in the fractional digesta passage rate has led to a decrease in feed intake (Nikkhah, 2012). Although the mechanism by which Cr affects rumination patterns is unclear, the insulin-potentiating pathway may be involved. In contrast with previous results, Cr supplementation given over 120 days to Murrah buffalo calves had no significant effect on feed conversion ratio (FCR), ADG or intake of DM (Kumar et al., 2015a). Similar results recorded by Qi et al. (2018a), Subiyatno et al. (1996) showed that Cr has no influence on DM intake. Also, the results of tests performed under normal conditions by Bunting et al. (2000) and Ghorbani et al. (2012) showed that Cr has no influence on feed intake or total DMI. The timing of supplementation of Cr to the diet (pre-partum or immediately post-partum) had an impact on the response.

Overall, the addition of Cr yeast to the diet has been observed to attenuate the negative impacts of high environmental temperatures and result in a reduction in feed intake and efficiency. Cr requirements for calves increase under a variety of stress conditions (Chang and Mowat, 1992; Pechova and Pavlata, 2007). Such variations are due to changes in the concentration of supplementation and the method of adding Cr to milk only or colostrum plus milk. Cr requirements as a whole rise during thermal heat load; this is a result of increased Cr urinary excretion, which in turn results in diminished feed intake (Kargar et al., 2018b; Pantelic et al., 2018; Yari et al., 2010). In short, to attenuate the impacts of HS, dietary Cr should be used to improve both the performance of animals and their welfare (Kargar et al., 2018b).

5.3. Milk yield and composition

Adding (4 g/head/day) of dietary chelated chromium to the diet of heat-stressed dairy cows has no effect on milk fats, protein, lactose, or the non-fat percentage of solids (Alsaiady et al., 2004). A significant rise ($p < 0.05$) in milk protein, fat and lactose levels by 1.043%, 1.066% and 1.020% respectively was recorded by Nikkhah (2012) when heat-stressed dairy cows were supplied with 0.05 mg Cr/kg. Moderate levels of Cr resulted in an increase in the ingestion of feed, DM effectiveness and a decline in insulin levels, leading to a significant augmentation in milk secretion as a result of increased mammary nutrient flow (Winkelman and Overton, 2012).

Insulin growth factor (IGF) activity, which has functional and structural homology with insulin receptors, is supported through the improvement of milk production, which also mimics the action of bovine somatotropin (bST) (Alsaiady et al., 2004). Likewise, milk production increased, resulting in a decline in lipolysis. In a separate study, increase in glucose uptake, which leads to a rise in DMI (NRC, 1994), resulted from receiving 10 mg/day of Cr from 21 days pre-partum to 35 postpartum (McNamara and Valdez, 2005). Additionally, milk yield was found to increase ($p = 0.013$) after the supplementation of chromium picolinate to the diet of heat-stressed cows (An-Qiang et al., 2009). On the other hand, An-Qiang et al. (2009) reported that dietary Cr had no significant effect on milk components (protein, fat and lactose) in dairy cows under high temperature (79.61). The beneficial effect of chromium on glucose and NEFA metabolism in dairy cattle is illustrated in Fig. 5.

5.4. Blood variables

Cr yeast (4 mg/day) fed to lactating cows failed to show any effect on the blood serum levels of hemagglutination (HA), cholesterol, triglycerides, urea, IGF-1, BHBA, albumen, and glucose (Mirzaei et al., 2011; Soltan, 2010) but did show a drop in total blood and protein concentration (Soltan, 2010). Serum, insulin and NEFA reduced significantly when 0.05 mg Cr/kg of body weight of Cr yeast was supplemented (Yari et al., 2010). Recently, in dairy farm calves suffering from HS, dietary supplementation with 0.05 mg of Cr-methionine/kg of body weight had no significant influence on glucose, albumin, A/G ratio, triglyceride cholesterol, β- Hydroxybutyrate (βHBA) or blood urea nitrogen (BUN). Nevertheless, the serum concentration of globulin tended to be higher in calves supplemented with Cr^{+3} during the experimentation period (Mousavi et al., 2019a).

Calves supplied with chromium at a level of 0.05 mg/kg body weight tended to have higher serum concentrations of glucose and higher ratios of insulin to glucose measured at the end of the experiment (Kargar et al., 2018b). The same results were recorded by Yari et al. (2010) and Ghorbani et al. (2012). Similarly, Jin et al. (2017) suggested that dietary supplementation of chromium picolinate (3.5 mg of Cr/cow daily) to lactating cows under HS conditions did not exhibit any changes in glucose, BUN, cholesterol or creatinine.

Mayorga et al. (2019) reported similar results as he demonstrated that heat-stressed finishing pigs supplied with 200 ppb of chromium propionate did not show any shift in most of the blood parameters except for neutrophils. Heat-stressed pigs treated with chromium propionate supplementation (200 ppb) showed an increase in blood neutrophils by 37% compared to the control group (Mayorga et al., 2019). Adding chromium ($p < 0.01$) was found to raise albumin/globulin ratio as well as cholesterol level (Soltan, 2010). Enhanced insulin action allows glucose to enter the cell and can repress lipolysis. Reduced mobilization of fats was reported to decrease dependence on body storage and lessen NEFA (Yang et al., 1996). Reduced NEFA raises DMI through the reversed lipostatic mechanism: as the levels of NEFA increase, the intake of food will decrease (Forbes, 2007; McNamara and Valdez, 2005). Milk production was found to increase when insulin action is improved as a result of the reduction in NEFA and insulin levels despite fixed glucose levels (Hayirli et al., 2001). Yari et al. (2010) and Ghorbani et al. (2012) reported similar results. Similarity, Jin et al. (2017) suggested that dietary supplementation of 3.5 mg of chromium picolinate daily to lactating cows under heat-stress conditions did not exhibit any changes in cholesterol, glucose, BUN or creatinine levels. In finisher gilts reared under summer conditions, plasma glucose, insulin and NEFA levels in serum did not change in chromium tripicolinate nanoparticles-treated pigs (400 ppb) compared to those in the control group (Hung et al., 2014).

Bareille and Faverdin (1996) found evidence indicating that insulin can affect rumination by increasing the motility of reticulum and rumen through enhancing the entry of glucose into the cells. They also reported an increase in rumination time when glucose was infused intravenously (2.75 mmol/kg) to dairy cows. However, supplemental Cr did not affect blood insulin concentration at weaning or rumination time during the pre-weaning period in their study, despite the fact that rumination patterns changed (decreased rumination frequency and increased rumination duration and interval). Therefore, the relationship between blood insulin concentration and rumination patterns needs to be investigated further.

Chromium supplementation had little impact on insulin and blood glucose levels for both control and heat-stressed calves (Ghorbani et al., 2012; Yari et al., 2010). Kumar et al. (2015a) reported a reduction in blood insulin concentration in buffalo calves under HS when 1.0 and 1.5 mg Cr/kg of DMI was supplemented, but not in the case of 0.5 mg Cr/kg. Consistent with these results, Bunting et al. (2000) found that blood glucose decreased and insulin levels increased when 0.5 mg of Cr/kg of DMI was supplemented to dairy calves. Chromium supplementation increased both insulin concentrations and the ratio of insulin to glucose, suggesting that high levels of insulin were needed in order to make blood free from glucose (weak insulin sensitivity) and that resistance to insulin increased over that time period (Bunting et al., 2000).

5.5. Hormones

After 0.05 mg of Cr-methionine/kg of body weight was given in supplementation to dairy calves exposed to HS, Mousavi et al. (2019a) observed no notable effect on thyroxin (T3, T4, T3/T4 ratio), and cortisol hormone activities. However, they also reported that calves fed with Cr recorded high insulin levels and insulin-to-glucose ratios compared to those in the control group. Similarly, Kargar et al. (2018b) reported that chromium supplementation (0.05 mg/kg of body weight) had no influence on serum levels of T3, T4 or cortisol when measured at pre- and post-weaning. Calves fed 0.04 mg Cr/kg of body weight showed no difference in T3 or T4 blood concentration.

The same results were observed in buffalo calves that received 0.5, 1.0, and 1.5 mg of Cr/kg of DMI (Kumar et al., 2015a). However, Cr supplementation of 0.03 mg of Cr/kg of body weight increased blood T4 concentration and reduced T3-to-T4 ratio in dairy calves (Ghorbani et al., 2012). On the other hand, it was reported that raising Cr doses (from 0 to 0.02 and 0.04 mg Cr/kg of body weight) resulted in a quadratic decline in serum T4, whereas blood T3 decreased only with the higher Cr dose supplementation in dairy calves (Yari et al., 2010).

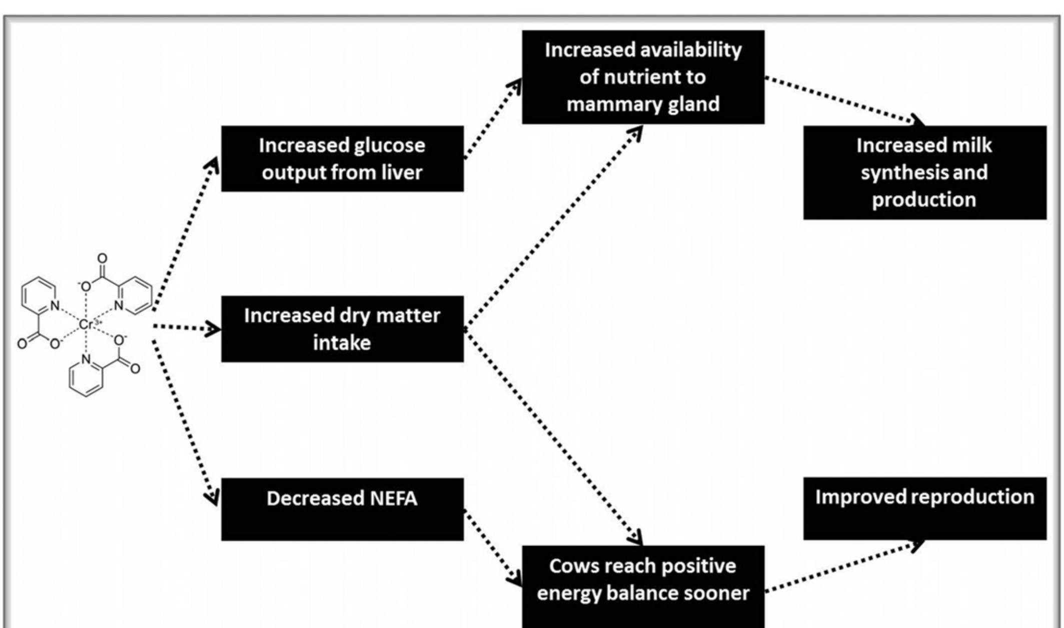

Fig. 5. The beneficial effect of Chromium on glucose and non-esterified fatty acids (NEFA) metabolism in dairy cattle.

5.6. Antioxidants

Cr supplementations do not influence malondialdehyde (MDA) or glutathione peroxidase (GPx) serum levels, but the concentration of superoxide dismutase (SOD) tended to increase in calves receiving Cr-methionine at levels of 0.05 mg Cr/kg of body weight at weaning. Furthermore, serum activities of catalase in calves fed Cr-methionine was higher after weaning ($p < 0.001$) (Jin et al., 2017). Moreover, Mousavi et al. (2019a) revealed a significant reduction of creatine kinase as a response to yeast-chromium (Cr yeast, 8 mg/d) dietary supplementation to lactating heat-stressed cows; this result may be linked to application of different types of animals, suitable doses of chromium, and its chemical forms.

On the other hand, (Qi et al., 2018a) reported that supplementation of chromium picolinate (3.5 mg of Cr/cow daily) under hot conditions did not have an effect on antioxidant activities such as serum total antioxidant capacity (T-AOC), SOD activity, or MDA levels of lactating cows (Qi et al., 2018a). Qi et al. (2018a) moreover suggested that Cr can inhibit inflammation in lactating cows by promoting the release of Hsp72, facilitating the production of IL-10, and inhibiting the degradation of IκBα under HS conditions.

5.7. Immunity

Kumar et al. (2015a) observed that 1 mg Cr/kg DM had positive impacts on both cell-mediated and humeral immunity in heat-stressed buffalo calves. Kumar et al. (2015a) investigated different levels: 0.5, 1.0 and 1.5 mg of inorganic Cr/kg DM of the diet of buffalo calves under high environmental temperature conditions: buffalo calves receiving 1.5 mg/kg DM of Cr ($p < 0.01$) showed the highest immune status values and plasma Cr concentration during the stages of the experiment. It was found that buffalo calves receiving 1.5 mg/kg of DM of Cr exhibited a boost in the proliferation of B or T lymphocyte values (+16.50%), the phagocytic activity of neutrophils (13.72%), fluorescence recovery after use of the photobleaching (FRAP) technique (27.88%) and immunoglobulin of plasma (13.14%) compared with the control buffalo calves (Kumar et al., 2015a). The negative influence of HS on cows can be reduced through improved immunological activities under the effect of chromium supplementation. A significant enhancement in lymphocytes proliferation and blastogenesis in inorganic Cr given as supplementation to periparturient buffaloes was reported by several researchers (Burton et al., 1993a; Chang and Mowat, 1992; Kumar et al., 2015b).

It was reported that beef calves given supplementation of 15 mg/kg DM of Cr) had a slight improvement in cell-mediated immunity. Supplementation of Cr may have improved immune status by increasing immunoglobulin (IgM) and decreasing blood cortisol levels in buffalo calves compared to those in the control group, although an increase in cortisol level after exposure to high temperatures was also observed (Abdelnour et al., 2019; Kumar et al., 2015b). This led to depression in immunity by preventing proliferation of lymphocytes, the activation of lymphocytes factors, and the production of T-cell growth factors (Munck et al., 1984; Roth and Kaeberle, 1982). Wang et al. (2007) recorded that supplementation of 200 ppb Nano-Cr/kg in pigs increased the serum levels of IgG and IgM by 20.6% and 13.2% respectively. Likewise, serum total levels of Ig and IgM increased after supplementation of Cr yeast to the diets of stressed calves (Burton et al., 1993a). On the other hand, Kegley and Spears (1995) found that Cr nicotinate and Cr yeast supplementation for stressed calves had no impact on total levels of IgM. To develop immunoglobin concentration and the proliferation of lymphocytes, advanced antioxidants are needed for the production of immunoglobulin (Bach et al., 2000).

5.8. Heat shock proteins (HSPs)

Heat-stressed lactating Holstein cows with a chromium diet (Cr yeast, 8 mg/d) were found to have a significant elevation ($p < 0.05$) of blood HSP mRNA expression on d 44 of exposure, and Kumar et al. (2015b) found that the addition of 1.5 mg of Cr/kg to the diet of heat-stressed buffalo calves decreased Hsp70 significantly. Similarly, Qi et al. (2018a) confirmed that the supplementation of 3.5 mg Cr/kg daily to the diets of heat-stressed lactating cows increased Hsp72 significantly (11.68 ppb) compared to those that did not receive Cr (6.21 ppb).

6. Conclusion and future perspectives

The rapidly changing climate, global warming, and accompanying rapid growth in population size are sounding the alarm for the development of critical strategies to manage livestock productivity and reproducibility. As shown in this current review, HS has an effect on the nutritional metabolic and antioxidant status of livestock. When exposed to HS conditions, animals maintain thermoregulation and homeostasis via metabolic and physiological adjustments that can have a negative influence on growth performance. Feed intake is lowered, and growth rates consequently decrease. Alterations in nutrient partitioning and utilization as well as in immune and metabolic functions have also been reported. Cr restores productivity, performance, nutrient digestibility, antioxidant profile and immune status while decreasing lipid peroxidation, cholesterol and fat content in animals after exposure to HS. Therefore, dietary supplementation with Cr may be recommended as a nutritional strategy to modulate the negative effects of HS in broilers.

Proper nutritional management of livestock so that animals maintain energy balance could have a positive effect on reproductive status and resulting embryos, future progeny and production. More in-depth studies using genomic and metabolomic technologies are needed to clearly investigate the genomic and epigenetic mechanism of action of HS on livestock development. Most of the literature discussing the effect of HS and/or NEB on livestock health is based on in vivo chromium effects. Because of its marked role in poultry performance and production, Cr could be considered as one of the very essential components in poultry feed during times of HS. Furthermore, the effect of Cr diet interaction with livestock health status during HS is a new area that should be considered for future research. Another future consideration is proper attention on breeding programs, for selection of HS-tolerant breeds, instead of only selection for high-production breeds.

Declaration of competing interest

All authors declare that they do not have any conflicts of interests that could inappropriately influence this manuscript.

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