



HAL
open science

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

May Bin-Jumah, Mohamed E. Abd El-Hack, Sameh A. Abdelnour, Yasmeen A. Hendy, Hager A. Ghanem, Sara A. Alsafy, Asmaa F. Khafaga, Ahmed E. Noreldin, Hazem Shaheen, Dalia Samak, et al.

► To cite this version:

May Bin-Jumah, Mohamed E. Abd El-Hack, Sameh A. Abdelnour, Yasmeen A. Hendy, Hager A. Ghanem, et al.. Potential use of chromium to combat thermal stress in animals: A review. *Science of the Total Environment*, 2020, 707, pp.135996. 10.1016/j.scitotenv.2019.135996 . hal-02421792

HAL Id: hal-02421792

<https://hal.science/hal-02421792>

Submitted on 21 Dec 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

1 **Potential use of chromium to combat thermal stress in animals: a review**

2

3 May Bin-Jumah¹, Mohamed E. Abd El-Hack², Sameh A. Abdelnour³, Yasmeeen A. Hendy⁴,
4 Hager A. Ghanem⁴, Sara A. Alsafy⁴, Asmaa F. Khafaga⁵, Ahmed E. Noreldin⁶, Hazem Shaheen⁷,
5 Dalia Samak⁸, Maha A. Momenah¹, Ahmed A. Allam⁹, Abdullah A. AlKahtane¹⁰, Saad
6 Alkahtani¹⁰, Mohamed M. Abdel-Daim^{10,11}, Lotfi Aleya^{12*}

7

8 ¹Department of Biology, Faculty of Science, Princess Nourah bint Abdulrahman University,
9 Riyadh 11474, Saudi Arabia

10 ²Department of Poultry, Faculty of Agriculture, Zagazig University, Zagazig 44511, Egypt

11 ³Department of Animal Production, Faculty of Agriculture, Zagazig University, Zagazig 44511,
12 Egypt

13 ⁴Faculty of Veterinary Medicine, Damanhour University, Damanhour 22511, Egypt

14 ⁵Department of Pathology, Faculty of Veterinary Medicine, Alexandria University, Edfina
15 22758, Egypt

16 ⁶Department of Histology and Cytology, Faculty of Veterinary Medicine, Damanhour
17 University, Damanhour 22511, Egypt

18 ⁷Department of Pharmacology, Faculty of Veterinary Medicine, Damanhour University,
19 Damanhour 22511, Egypt

20 ⁸Department of Veterinary Forensic Medicine and Toxicology, Faculty of Veterinary Medicine,
21 Damanhour University, Damanhour 22511, Egypt

22 ⁹Department of Zoology, Faculty of Science, Beni-suef University, Beni-suef, 65211 Egypt

23 ¹⁰Department of Zoology, Science College, King Saud University, Riyadh 11451, Saudi Arabia

24 ¹¹Department of Pharmacology, Faculty of Veterinary Medicine, Suez Canal University, Ismailia
25 41522, Egypt

26 *¹²Bourgogne Franche-Comté University, Chrono-Environnement Laboratory, UMR CNRS
27 6249, 25030 Besançon Cedex, France (*Corresponding author: lotfi.aleya@univ-fcomte.fr)

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44 Abstract

45 Heat stress (HS) has adverse effects on the body: it decreases body weight, feed efficiency, feed
46 intake, carcass quality, and nutrient digestibility. Chromium (Cr) can prevent lipid peroxidation
47 induced by HS through its strong antioxidant activities, especially when it is added to the poultry
48 diet. It improves the action of insulin and nutrient metabolism (of lipids, proteins, nucleic acid,
49 and carbohydrates) through activation of enzymes associated with such pathways. The results of
50 the studies on Cr added to diets with concentrations of 0.05 mg Cr/kg of Cr-methionine led to
51 improved feed efficiency and DM intake by cows and Holstein dairy calves exposed to high
52 environmental temperatures. Moreover, calves that received Cr at levels of 0.05 mg/kg of body
53 weight tended to have higher serum concentrations of glucose and higher ratios of insulin to
54 glucose. In heat-stressed pigs, Cr addition (200 ppb) increased blood neutrophils by about 37%.
55 Several studies have asserted that Cr can inhibit inflammation in lactating cows by promoting the
56 release of Hsp72, assisting production of IL-10 and inhibiting degradation of I κ B α in HS
57 conditions. In addition, Cr supplementation was observed to possibly have positive impacts on
58 both cell-mediated and humeral immunity in heat-stressed buffalo calves. Studies over the last
59 two decades have shown with certainty that chromium supplementation has an impact on many
60 variables in chickens. Moreover, Cr is believed to increase insulin action in insulin-sensitive
61 tissues (i.e., adipose and muscles), resulting in increased farm animal productivity through the
62 improvement of feed intake, growth rate, carcass quality, reproductive parameters and immune
63 functions.

64 **Keywords:** Heat stress; chromium; growth; thermoregulation; heat shock proteins.

65

66

67 **1. Introduction**

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

78 HS alters lipid, protein and carbohydrate metabolism. It also alters homeorhetic
79 adaptations, which are largely caused by increased circulating insulin (Baumgard and Rhoads,
80 2013). Hence, identification of nutritional approaches to ameliorate the effects of HS on health
81 and production has become of interest recently (Khafaga et al., 2019). Alternation in utilization
82 and substrate uptake is also a result of HS, but this phenomenon is not yet fully understood.
83 When temperatures are high, metabolic adaptations occur to increase chances of survival. For
84 example, feed intake in Holstein cattle during summer was found to result in lower insulin
85 concentrations in summer than in winter and spring (Abdelnour et al., 2019). Likewise, plasma
86 insulin was lower in heat-stressed lactating sows compared to a control group, although glucose
87 concentration was the same (de Braganca and Prunier, 1999). In addition, Sevi et al. (2002)
88 reported that plasma non-esterified fatty acids (NEFA) increased in sheep but declined in
89 lactating cows due to heat exposure (Itoh et al., 1998; Shwartz et al., 2009; Wheelock et al.,

90 2010). Under stress conditions, Cr requirements are higher due to increased urinary excretion
91 (Chang and Mowat, 1992; Pechova and Pavlata, 2007; Yari et al., 2010).

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

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

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

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

113 **2. Heat stress in animals**

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

129 Moreover, HS often alters the physiological mechanisms of the rumen, with resultant
130 increases in health problems and metabolic disorders (Nardone et al., 2010; Soriani et al., 2013).
131 Nonaka et al. (2008) concluded that heat-stressed animal suffer from diminished acetate
132 production and from increased propionate and butyrate production due to alterations in rumen
133 function. As a result, stressed animals consume less roughage and undergo alteration of rumen
134 pH and microbial population (Hall, 2009), diminished rumination and rumen motility (Nardone
135 et al., 2010; Soriani et al., 2013), decreased salivary production, and less dry-matter intake

136 (DMI) (Nardone et al., 2010; Soriani et al., 2013). Also, HS resulted in decreased animal growth,
137 carcass quality and fertility, and in increased mortality rate and care costs (Baumgard and
138 Rhoads, 2013; Mayorga et al., 2019).

139 It is therefore necessary to develop protocols to overcome the negative impacts of HS.
140 Nutritional intervention is considered to be an economical method for increasing production in
141 summer (Mayorga et al., 2019). Indeed, dietary chromium enhances cellular glucose uptake
142 (Chen et al., 2006) by increasing the binding of insulin to its extracellular receptors (NRC, 1994;
143 Vincent, 2015). In addition, studies showed that average daily feed intake (ADFI), reproduction,
144 immune response and growth performance are improved by Cr supplementation (Burton et al.,
145 1993b; Hayirli et al., 2001; Hung et al., 2014; Lindemann et al., 1995; Sadri et al., 2009; Sales
146 and Jancik, 2011; Yasui et al., 2014). The adverse effect of HS in ruminants and their body
147 reactions against it are summarized in Figure 1. Similarly, the adverse effect of HS on animal
148 performance, production and reproduction is summarized in Figure 2.

149 **3. General properties of chromium and sources**

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

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

167 **4. Mode of action of chromium in animal nutrition**

168 Chromium chloride, chromium polynicotinate, and chromium picolinate (CrP, Figure 3)
169 are considered to be nutritional supplements and micronutrients. Several investigations
170 concluded that chromodulin is a naturally occurring biomolecule that binds to trivalent Cr and
171 could explain the action of Cr in metabolism of lipids and carbohydrates (Davis and Vincent,
172 1997). Chromodulin is able to stimulate insulin-dependent glucose metabolism in adipocytes
173 (Yamamoto et al., 1988). Moreover, it could activate the membrane phosphotyrosine
174 phosphatase in adipocyte membranes (Davis et al., 1996).

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

178 In addition, CrP has the potential to control levels of blood sugar in diabetes, control blood
179 pressure levels, and reduce cholesterol. Cr acts as a cofactor for insulin; therefore, it activates
180 insulin receptor kinase and increases the number of insulin receptors. CrP attenuates weight gain,

181 but the mechanism for this is unknown (Anton et al., 2008). It may have an action through its
182 influence on the balance of energy to either decrease feed intake or increase energy expenditure.

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

186 Stress stimulates the hypothalamus to produce corticotropin, which stimulates the pituitary
187 to produce the adrenocorticotrophic hormone, which in turn stimulates the adrenal cortex to
188 release corticosterone. Corticoids depress the immune system and reduce the concentration of
189 serum protein. They also raise blood glucose levels and decrease the utilization of glucose, thus
190 functioning as antagonists to Cr, which influence the release of corticosteroids. The role of Cr³⁺
191 against cellular glucose uptake is summarized in Figure 4.

192 **5. Impacts of chromium in heat-stressed animals**

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

196 **5.1 Thermoregulatory responses**

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

204 Most studies indicated that Cr decreases RT to overcome the effects of HS (Kargar et al.,
205 2018b). Mousavi et al. (2019a) found no effect of Cr-methionine on diarrhea, pneumonia,
206 medication days or RT in heat-stressed calves. Also, Kumar et al. (2015a) found no effect of 0.5,
207 1 or 1.5 mg of inorganic Cr/kg on pulse rate (PR), RR or RT in heat-stressed buffalo calves. An-
208 Qiang et al. (2009) measured the values of RR and RT for cows undergoing Cr supplementation
209 (3.6, 7.2 or 10.8-milligram chromium/head per day) and cows without any supplementation and
210 found no differences. According to the previous results, Cr has no impact on somatic cell count
211 and or on RT, PR or RR in lactating cows (Qi et al. 2018b). A separate study indicated that Cr
212 propionate (200 ppb) has no effect on RR, skin temperature (ST) or body temperature (BT) in
213 heat-stressed pigs (Mayorga et al., 2019).

214 **5.2 Growth performance**

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

224 Feed efficiency and average daily gain increased in the case of calves in their growth stage
225 fed Cr at a level of 4 mg/head (Chang and Mowat, 1992). This result is due to the increase in
226 total levels of immunoglobulins in serum (Burton, 1995; Burton et al., 1996; Chang and Mowat,

227 1992). Moreover, the supplementation of 0.05 mg Cr/kg of body weight of Cr-methionine in
228 cows' diets increased feed efficiency and DMI (Arthington et al., 1997). Supplementation of 3.6,
229 7.2 and 10.8 mg chromium/head/day to heat-stressed dairy cows resulted in a significant increase
230 in DMI ($p < 0.05$) according to An-Qiang et al. (2009). Mousavi et al. (2019a) reported that
231 supplementation of Cr to dairy calves under HS resulted in increases in DMI ($P = 0.002$) and in
232 average daily gain (ADG) ($p = 0.02$) but had no effect on effectiveness of feed ($P = 0.93$) or on
233 body weight ($p = 0.14$). On the other hand, Kargar et al. (2018b) found that dietary
234 supplementation of chromium improved the intake of feed and growth rate in dairy Holstein
235 calves exposed to high environmental temperature (83.3 units). Also, the addition of Cr at a level
236 of 0.05 mg/kg of body weight to a milk substitute or to diets for cattle during the pre- and post-
237 weaning periods led to increases, at the end of the experiment, in feed intake, DM intake and
238 average body weight gain, by 16.4%, 11.85% and 7.07% respectively. Cr supplementation
239 improves growth rate and body weight by enhancing the absorption and digestion of nutrients
240 (Ghorbani et al., 2012; Kargar et al., 2018a). Moreover, in finisher gilts exposed to high
241 temperatures, the application of nano-chromium tripicolinate (400 ppb) resulted in a reduction in
242 cortisol level by 25% and an increase in feed intake by 6% (Hung et al., 2014). Mayorga et al.
243 (2019) discovered that final body weight increased in heat-stressed finishing pigs when fed with
244 200 ppb of chromium propionate.

245 Ruminant activity was reported to decrease as a result of environmental heat load
246 (Soriani et al., 2013). Decreased rumen motility as a result of a slowing in the fractional digesta
247 passage rate has led to a decrease in feed intake (Nikkhah, 2012). Although the mechanism by
248 which Cr affects rumination patterns is unclear, the insulin-potentiating pathway may be
249 involved. In contrast with previous results, Cr supplementation given over 120 days to Murrah

250 buffalo calves had no significant effect on feed conversion ratio (FCR), ADG or intake of DM
251 (Kumar et al., 2015a). Similar results recorded by Qi et al. (2018a), Subiyatno et al. (1996)
252 showed that Cr has no influence on DM intake. Also, the results of tests performed under normal
253 conditions by Bunting et al. (2000) and Ghorbani et al. (2012) showed that Cr has no influence
254 on feed intake or total DMI. The timing of supplementation of Cr to the diet (pre-partum or
255 immediately post-partum) had an impact on the response.

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

265 ***5.3 Milk yield and composition***

266 Adding (4 g/head/day) of dietary chelated chromium to the diet of heat-stressed dairy cows
267 has no effect on milk fats, protein, lactose, or the non-fat percentage of solids (Alsaady et al.,
268 2004). A significant rise ($p < 0.05$) in milk protein, fat and lactose levels by 1.043%, 1.066% and
269 1.020% respectively was recorded by Nikkhah (2012) when heat-stressed dairy cows were
270 supplied with 0.05 mg Cr/kg. Moderate levels of Cr resulted in an increase in the ingestion of
271 feed, DM effectiveness and a decline in insulin levels, leading to a significant augmentation in
272 milk secretion as a result of increased mammary nutrient flow (Winkelman and Overton, 2012).

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

284 ***5.4 Blood variables***

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

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

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

317 did not change in chromium tripicolinate nanoparticles-treated pigs (400 ppb) compared to those
318 in the control group (Hung et al., 2014).

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

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

336 **5.5 Hormones**

337 After 0.05 mg of Cr-methionine/kg of body weight was given in supplementation to dairy
338 calves exposed to HS, Mousavi et al. (2019a) observed no notable effect on thyroxin (T3, T4,
339 T3/T4 ratio), and cortisol hormone activities. However, they also reported that calves fed with Cr

340 recorded high insulin levels and insulin-to-glucose ratios compared to those in the control group.
341 Similarly, Kargar et al. (2018b) reported that chromium supplementation (0.05 mg/kg of body
342 weight) had no influence on serum levels of T3, T4 or cortisol when measured at pre- and post-
343 weaning. Calves fed .04 mg Cr/kg of body weight showed no difference in T3 or T4 blood
344 concentration.

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

351 **5.6 Antioxidants**

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

360 On the other hand, (Qi et al., 2018a) reported that supplementation of chromium picolinate
361 (3.5 mg of Cr/cow daily) under hot conditions did not have an effect on antioxidant activities
362 such as serum total antioxidant capacity (T-AOC), SOD activity, or MDA levels of lactating

363 cows (Qi et al. 2018a). Qi et al. (2018a) moreover suggested that Cr can inhibit inflammation in
364 lactating cows by promoting the release of Hsp72, facilitating the production of IL-10, and
365 inhibiting the degradation of I κ B α under HS conditions.

366 **5.7 Immunity**

367 Kumar et al. (2015a) observed that 1mg Cr/kg DM had positive impacts on both cell-
368 mediated and humeral immunity in heat-stressed buffalo calves. Kumar et al. (2015a)
369 investigated different levels: 0.5, 1.0 and 1.5 mg of inorganic Cr/kg DM of the diet of buffalo
370 calves under high environmental temperature conditions: buffalo calves receiving 1.5 mg/kg DM
371 of Cr ($p < 0.01$) showed the highest immune status values and plasma Cr concentration during
372 the stages of the experiment. It was found that buffalo calves receiving 1.5 mg/kg of DM of Cr
373 exhibited a boost in the proliferation of B or T lymphocyte values (+16.50%), the phagocytic
374 activity of neutrophils (13.72%), fluorescence recovery after use of the photobleaching (FRAP)
375 technique (27.88%) and immunoglobulin of plasma (13.14%) compared with the control buffalo
376 calves (Kumar et al., 2015a). The negative influence of HS on cows can be reduced through
377 improved immunological activities under the effect of chromium supplementation. A significant
378 enhancement in lymphocytes proliferation and blastogenesis in inorganic Cr given as
379 supplementation to periparturient buffaloes was reported by several researchers (Burton et al.,
380 1993a; Chang and Mowat, 1992; Kumar et al., 2015b).

381 It was reported that beef calves given supplementation of 15 mg/kg DM of Cr) had a slight
382 improvement in cell-mediated immunity. Supplementation of Cr may have improved immune
383 status by increasing immunoglobulin (IgM) and decreasing blood cortisol levels in buffalo calves
384 compared to those in the control group, although an increase in cortisol level after exposure to
385 high temperatures was also observed (Abdelnour et al., 2019; Kumar et al., 2015b). This led to

386 depression in immunity by preventing proliferation of lymphocytes, the activation of
387 lymphocytes factors, and the production of T-cell growth factors (Munck et al., 1984; Roth and
388 Kaeberle, 1982). Wang et al. (2007) recorded that supplementation of 200 ppb Nano- Cr/kg in
389 pigs increased the serum levels of IgG and IgM by 20.6% and 13.2% respectively. Likewise,
390 serum total levels of Ig and IgM increased after supplementation of Cr yeast to the diets of
391 stressed calves (Burton et al., 1993a). On the other hand, Kegley and Spears (1995) found that Cr
392 nicotinate and Cr yeast supplementation for stressed calves had no impact on total levels of IgM.
393 To develop immunoglobulin concentration and the proliferation of lymphocytes, advanced
394 antioxidants are needed for the production of immunoglobulin (Bach et al., 2000).

395 **5.8 Heat shock proteins (HSPs)**

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

402

403 **6. Conclusion and future perspectives**

404 The rapidly changing climate, global warming, and accompanying rapid growth in
405 population size are sounding the alarm for the development of critical strategies to manage
406 livestock productivity and reproducibility. As shown in this current review, HS has an effect on
407 the nutritional metabolic and antioxidant status of livestock. When exposed to HS conditions,
408 animals maintain thermoregulation and homeostasis via metabolic and physiological adjustments

409 that can have a negative influence on growth performance. Feed intake is lowered, and growth
410 rates consequently decrease. Alterations in nutrient partitioning and utilization as well as in
411 immune and metabolic functions have also been reported. Cr restores productivity, performance,
412 nutrient digestibility, antioxidant profile and immune status while decreasing lipid peroxidation,
413 cholesterol and fat content in animals after exposure to HS. Therefore, dietary supplementation
414 with Cr may be recommended as a nutritional strategy to modulate the negative effects of HS in
415 broilers.

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

427

428 **Acknowledgment**

429 This review was funded by the Deanship of Scientific Research at Princess Nourah bint
430 Abdulrahman University, through the Fast-track Research Funding Program. In addition, this

431 project was supported by King Saud University, Deanship of Scientific Research, College of

432 Science Research Center.

433

434 **References**

- 435 Abd El-Hack ME, Alagawany M, Noreldin AE (2019) Managerial and Nutritional Trends to
436 Mitigate Heat Stress Risks in Poultry Farms, in: Negm, A.M., Abu-hashim, M. (Eds.),
437 Sustainability of Agricultural Environment in Egypt: Part II: Soil-Water-Plant Nexus.
438 Springer International Publishing, Cham: 325-338.
- 439 Abdelnour SA, Abd El-Hack ME, Khafaga AF, Arif M, Taha AE, Noreldin AE (2019) Stress
440 biomarkers and proteomics alteration to thermal stress in ruminants: A review. *J therm*
441 *biol* 79: 120-134.
- 442 Alagawany M, Farag MR, Abd El-Hack ME, Patra A (2017) Heat stress: effects on productive
443 and reproductive performance of quail. *World's Poult Sci J* 73(4), 747-756.
- 444 Alsaiady M, Alshaikh M, Al-Mufarrej S, Al-Showeimi T, Mogawer HH, Dirrar A, (2004) Effect
445 of chelated chromium supplementation on lactation performance and blood parameters of
446 Holstein cows under heat stress. *Anim Feed Sci Tech* 117: 223-233.
- 447 An-Qiang L, Zhi-Sheng W, An-Guo Z (2009) Effect of Chromium Picolinate Supplementation
448 on Early Lactation Performance, Rectal Temperatures, Respiration Rates and Plasma
449 Biochemical Response of Holstein Cows under Heat Stress. *Pak J Nutr* 8: 940-945.
- 450 Anderson RA (1998) Effects of chromium on body composition and weight loss. *Nutrition*
451 *reviews* 56: 266-270.
- 452 Anton SD, Morrison CD, Cefalu WT, Martin CK, Coulon S, Geiselman P, Han H, White CL,
453 Williamson DA (2008) Effects of chromium picolinate on food intake and satiety.
454 *Diabetes technology & therapeutics* 10: 405-412.

- 455 Arthington JD, Corah LR, Minton JE, Elsasser TH, Blecha F (1997) Supplemental dietary
456 chromium does not influence ACTH, cortisol, or immune responses in young calves
457 inoculated with bovine herpesvirus-1. *J anim sci* 75: 217-223.
- 458 Bach A, Huntington GB, Calsamiglia S, Stern MD (2000) Nitrogen metabolism of early lactation
459 cows fed diets with two different levels of protein and different amino acid profiles. *J*
460 *Dairy Sci* 83: 2585-2595.
- 461 Baile CA, Forbes JM (1974) Control of feed intake and regulation of energy balance in
462 ruminants. *Physiol Rev* 54(1):160.
- 463 Bareille N, Faverdin P (1996) Modulation of the feeding response of lactating dairy cows to
464 peripheral insulin administration with or without a glucose supply. *Reprod nutr develop*
465 36: 83-93.
- 466 Baumgard LH, Rhoads RP Jr (2013) Effects of heat stress on postabsorptive metabolism and
467 energetics. *Annual review anim bioscie* 1:311-337.
- 468 Berman AJ (2005) Estimates of heat stress relief needs for Holstein dairy cows. *J Anim Sci*
469 83(6):1377–1384.
- 470 Bouraoui R, Lahmar M, Majdoub A, Djemali M, Belyea R (2002) The relationship of
471 temperature-humidity index with milk production of dairy cows in a Mediterranean
472 climate *Anim Res* 51(6):479–491.
- 473 Bunting LD, Tarifa TA, Crochet BT, Fernandez JM, Depew CL, Lovejoy JC (2000) Effects of
474 dietary inclusion of chromium propionate and calcium propionate on glucose disposal
475 and gastrointestinal development in dairy calves. *J Dairy Sci* 83: 2491-2498.
- 476 Burton JL (1995) Supplemental chromium: its benefits to the bovine immune system. *Anim Feed*
477 *Sci Tech* 53: 117-133.

- 478 Burton JL, Mallard BA, Mowat DN (1993a) Effects of supplemental chromium on immune
479 responses of periparturient and early lactation dairy cows. *J anim scie* 71: 1532-1539.
- 480 Burton JL, Mallard BA, Mowat DN (1993b) Effects of supplemental chromium on immune
481 responses of periparturient and early lactation dairy cows¹. *J anim scie* 71: 1532-1539.
- 482 Burton JL, Nonnecke BJ, Dubeski PL, Elsasser TH, Mallard BA (1996) Effects of supplemental
483 chromium on production of cytokines by mitogen-stimulated bovine peripheral blood
484 mononuclear cells. *J Dairy Sci* 79: 2237-2246.
- 485 Chang X, Mowat DN (1992) Supplemental chromium for stressed and growing feeder calves. *J*
486 *anim scie* 70: 559-565.
- 487 Chen G, Liu P, Pattar GR, Tackett L, Bhonagiri P, Strawbridge AB, Elmendorf JS (2006)
488 Chromium activates glucose transporter 4 trafficking and enhances insulin-stimulated
489 glucose transport in 3T3-L1 adipocytes via a cholesterol-dependent mechanism.
490 *Molecular endocrinology* (Baltimore, Md.) 20, 857-870.
- 491 Davis CM, Sumrall KH, Vincent JB (1996) The biologically active form of chromium may
492 activate a membrane phosphotyrosine phosphatase (PTP). *Biochem* 35: 12963–12969.
- 493 Davis CM, Vincent JB (1997) Isolation and characterization of a biologically active chromium
494 oligopeptide from bovine liver. *Arch Biochem Biophys* 339: 335–343
- 495 de Braganca MM, Prunier A (1999) Effects of low feed intake and hot environment on plasma
496 profiles of glucose, nonesterified fatty acids, insulin, glucagon, and IGF-I in lactating
497 sows. *Domestic anim endocrinol* 16: 89-101.
- 498 El-Kholy MS, El-Hindawy MM, Alagawany M, Abd El-Hack ME, El-Sayed SA (2018) Use of
499 acetylsalicylic acid as an allostatic modulator in the diets of growing Japanese quails
500 exposed to heat stress. *J Therm Biol* 74: 6-13.

- 501 Farghly M.F, Abd El-Hack ME, Alagawany M, Saadeldin IM, Swelum AA (2018) Ameliorating
502 deleterious effects of heat stress on growing Muscovy ducklings using feed withdrawal
503 and cold water. *Poult Sci* 98(1): 251-259.
- 504 Forbes J (2007) *Voluntary food intake and diet selection in farm animals: Second edition.*
- 505 Ghorbani A, Sadri H, Alizadeh AR, Bruckmaier RM (2012) Performance and metabolic
506 responses of Holstein calves to supplemental chromium in colostrum and milk. *J Dairy*
507 *Sci* 95: 5760-5769.
- 508 John B (2004) Vincent Recent advances in the nutritional biochemistry of trivalent chromium.
509 *Proceedings of the Nutrition Society* 63: 41–47
- 510 Hall MB (2009) Heat stress alters ruminal fermentation and digesta characteristics, and behavior
511 in lactating dairy cattle. In: Chilliard Y, Glasser F, Faulconnier Y, Bocquier F, Veissier I,
512 Doreau M, editors. *Proceeding of 11th International Symposium on Ruminant*
513 *Physiology*. Wageningen, The Netherlands: Wageningen Academic Publication; 2009. p.
514 204.
- 515 Hayirli A, Bremmer DR, Bertics SJ, Socha MT, Grummer RR (2001) Effect of chromium
516 supplementation on production and metabolic parameters in periparturient dairy cows. *J*
517 *Dairy Sci* 84: 1218-1230.
- 518 Hua Y, Clark S, Ren J, Sreejayan N (2012) Molecular mechanisms of chromium in alleviating
519 insulin resistance. *J Nutr Biochem* 23: 313-319.
- 520 Hung AT, Leury BJ, Sabin MA, Collins CL, Dunshea FR (2014) Dietary nano-chromium
521 tripicolinate increases feed intake and decreases plasma cortisol in finisher gilts during
522 summer. *Tropic anim health prod* 46: 1483-1489.

- 523 Ibrahim WM, Oda SS, Khafaga AF (2017) Pathological Evaluation of The Effect of Zinc Oxide
524 Nanoparticles on Chromium-Induced Reproductive Toxicity in Male Albino Rats. Alex J
525 Vet Sci 53 (2): 24-32.
- 526 Itoh F, Obara Y, Rose MT, Fuse H, Hashimoto H (1998) Insulin and glucagon secretion in
527 lactating cows during heat exposure. J anim sci 76: 2182-2189.
- 528 Jin D, Kang K, Wang H, Wang Z, Xue B, Wang L, Xu F, Peng Q (2017) Effects of dietary
529 supplementation of active dried yeast on fecal methanogenic archaea diversity in dairy
530 cows. Anaerobe 44: 78-86.
- 531 Johnson JS, Sanz Fernandez MV, Patience JF, Ross JW, Gabler NK, Lucy MC, Safranski TJ,
532 Rhoads RP, Baumgard LH (2015) Effects of in utero heat stress on postnatal body
533 composition in pigs: II. Finishing phase. J anim sci 93: 82-92.
- 534 Kadzere CT, Murphy MR, Silanikove N, Maltz E (2002) Heat stress in lactating dairy cows: A
535 review. Livest Prod Sci 77(1):59–91.
- 536 Kargar S, Mousavi F, Karimi-Dehkordi S (2018a) Effects of chromium supplementation on
537 weight gain, feeding behaviour, health and metabolic criteria of environmentally heat-
538 loaded Holstein dairy calves from birth to weaning. Arch anim nutr 72: 443-457.
- 539 Kargar S, Mousavi F, Karimi-Dehkordi S, Ghaffari MH (2018b) Growth performance, feeding
540 behavior, health status, and blood metabolites of environmentally heat-loaded Holstein
541 dairy calves fed diets supplemented with chromium. J Dairy Sci 101: 9876-9887.
- 542 Kegley EB, Spears JW (1995) Immune response, glucose metabolism, and performance of
543 stressed feeder calves fed inorganic or organic chromium. J anim sci 73: 2721-2726.

- 544 Kegley EB, Spears JW, Brown TT Jr (1997) Effect of shipping and chromium supplementation
545 on performance, immune response, and disease resistance of steers. *J anim sci* 75: 1956-
546 1964.
- 547 Kerr BJ, Yen JT, Nienaber JA, Easter RA (2003) Influences of dietary protein level, amino acid
548 supplementation and environmental temperature on performance, body composition,
549 organ weights and total heat production of growing pigs. *J anim sci* 81: 1998-2007.
- 550 Khafaga A., Noreldin AE, Taha AE (2019) The adaptogenic anti-ageing potential of resveratrol
551 against heat stress-mediated liver injury in aged rats: Role of HSP70 and NF-kB
552 signalling. *J therm biol* 83: 8-21.
- 553 Kumar M, Kaur H, Deka RS, Mani V, Tyagi AK, Chandra G (2015a) Dietary Inorganic
554 Chromium in Summer-Exposed Buffalo Calves (*Bubalus bubalis*): Effects on Biomarkers
555 of Heat Stress, Immune Status, and Endocrine Variables. *Biologic trace element res* 167:
556 18-27.
- 557 Kumar M, Kaur H, Deka RS, Mani V, Tyagi AK, Chandra G (2015b) Dietary inorganic
558 chromium in summer-exposed buffalo calves (*Bubalus bubalis*): effects on biomarkers of
559 heat stress, immune status, and endocrine variables. *Biologic trace element res* 167: 18-
560 27.
- 561 Lacetera N, Bernabucci U, Ronchi B, Nardone A (1996) Body condition score, metabolic status
562 and milk production of early lactating dairy cows exposed to warm environment. *Riv*
563 *Agric Subtrop Trop* 90(1):43–55.
- 564 Le Bellego L, van Milgen J, Noblet J (2002) Effect of high temperature and low-protein diets on
565 the performance of growing-finishing pigs. *J anim sci* 80: 691-701.

- 566 Lindemann MD, Wood CM, Harper AF, Kornegay ET, Anderson RA (1995) Dietary chromium
567 picolinate additions improve gain:feed and carcass characteristics in growing-finishing
568 pigs and increase litter size in reproducing sows. *J anim sci* 73: 457-465.
- 569 Loyau T, Bedrani L, Berri C, Métayer-Coustard S, Praud C, Coustham V (2015) Cyclic
570 variations in incubation conditions induce adaptive responses to later heat exposure in
571 chickens: a review. *Animal* 9: 76-85.
- 572 Lukaski HC, Bolonchuk WW, Siders WA, Milne DB (1996) Chromium supplementation and
573 resistance training: effects on body composition, strength, and trace element status of
574 men. *Amer J clinic nutr* 63: 954-965.
- 575 Marouani N, Tebourbi O, Mahjoub S, Yacoubi MT, Sakly M, Benkhalifa M, Rhouma KB (2012)
576 Effects of hexavalent chromium on reproductive functions of male adult rats. *Reprod*
577 *biol* 12: 119-133.
- 578 Mayorga EJ, Kvidera SK, Seibert JT, Horst EA, Abuajamieh M, Al-Qaisi M, Lei S, Ross JW,
579 Johnson CD, Kremer B, Ochoa L, Rhoads RP, Baumgard LH (2019) Effects of dietary
580 chromium propionate on growth performance, metabolism, and immune biomarkers in
581 heat-stressed finishing pigs¹. *J anim sci* 97: 1185-1197.
- 582 McNamara JP, Valdez F (2005) Adipose tissue metabolism and production responses to calcium
583 propionate and chromium propionate. *J Dairy Sci* 88: 2498-2507.
- 584 Mirzaei M, Ghorbani GR, Khorvash M, Rahmani HR, Nikkhah A (2011) Chromium improves
585 production and alters metabolism of early lactation cows in summer. *J anim physiol anim*
586 *nutr* 95: 81-89.

- 587 Mousavi F, Karimi-Dehkordi S, Kargar S (2019a) Effect of chromium supplementation on
588 growth performance, meal pattern, metabolic and antioxidant status and insulin
589 sensitivity of summer-exposed weaned dairy calves. *Animal* 13: 968-974.
- 590 Mousavi F, Karimi-Dehkordi S, Kargar S, Khosravi-Bakhtiari M (2019b) Effects of dietary
591 chromium supplementation on calf performance, metabolic hormones, oxidative status,
592 and susceptibility to diarrhea and pneumonia. *Anim Feed Sci Tech* 248: 95-105.
- 593 Munck A, Guyre PM, Holbrook NJ (1984) Physiological functions of glucocorticoids in stress
594 and their relation to pharmacological actions. *Endocrine reviews* 5: 25-44.
- 595 NRC, National Research Council (1994). The role of chromium in Animal nutrition. National
596 Academy Press, Washington DC.
- 597 Nardone A, Ronchi B, Lacetera N, Ranieri M.S, Bernabucci U (2010) Effect of climate changes
598 on animal production and sustainability of livestock systems. *Livest Sci* 130(1-3):57-69.
- 599 Nikkhah A (2012) Eating time modulations of physiology and health: life lessons from human
600 and ruminant models. *Iran J Basic Med Sci* 15: 891-899.
- 601 Nonaka I, Takusari N, Tajima K, Suzuki T, Higuchi K, Kurihara M (2008) Effects of high
602 environmental temperatures on physiological and nutritional status of prepubertal
603 Holstein heifers. *Livest Sci*, 113(1):14-23.
- 604 Pantelic M, Jovanovic LJ, Prodanovic R, Vujanac I, Duric M, Culafic T, Vranjes-Duric S,
605 Koricanac G, Kirovski D (2018) The impact of the chromium supplementation on insulin
606 signalling pathway in different tissues and milk yield in dairy cows. *J anim physiol anim*
607 *nutr* 102: 41-55.
- 608 Pechova A, Pavlata L (2007) Chromium as an essential nutrient: A review. *Vet Medicina* 52: 1-
609 18.

- 610 Qi Z, Gao J, Zhao C, Zhang Y, Liu Y, Wang X, Li H (2018a) PSXVII-30 Effects of dietary
611 supplementation of yeast chromium and dihydropyridine on serum biochemical indices
612 and HSP70 mRNA expression of lactating dairy cows in summer. *J anim sci* 96: 448-449.
- 613 Qi Z, Gao J, Zhao C, Zhang Y, Liu Y, Wang X, Li H (2018b) PSXVII-30 Effects of dietary
614 supplementation of yeast chromium and dihydropyridine on serum biochemical indices
615 and HSP70 mRNA expression of lactating dairy cows in summer. *J anim sci* 96: 448-449.
- 616 Rhoads RP, Baumgard LH, Suagee JK, Sanders SR (2013) Nutritional interventions to alleviate
617 the negative consequences of heat stress. *Adv Nutr* 4(3):267–276.
- 618 Ross JW, Hale BJ, Seibert JT, Romoser MR, Adur MK, Keating AF, Baumgard LH (2017)
619 Physiological mechanisms through which heat stress compromises reproduction in pigs.
620 *Molec reprod develop* 84: 934-945.
- 621 Roth JA, Kaeberle ML (1982) Effect of glucocorticoids on the bovine immune system. *J Amer*
622 *Vet Med Assoc* 180: 894-901.
- 623 Sadri H, Ghorbani GR, Rahmani HR, Samie AH, Khorvash M, Bruckmaier RM (2009)
624 Chromium supplementation and substitution of barley grain with corn: Effects on
625 performance and lactation in periparturient dairy cows. *J Dairy Sci* 92: 5411-5418.
- 626 Saeed M, Abbas G, Alagawany M, Kamboh AA, Abd El-Hack ME, Khafaga AF, Chao S (2019)
627 Heat stress management in poultry farms: A comprehensive overview. *J therm biol.*
- 628 Sahin K, Sahin N, Kucuk O (2002) Effects of dietary chromium and ascorbic acid
629 supplementation on digestion of nutrients, serum antioxidant status, and mineral
630 concentrations in laying hens reared at a low ambient temperature. *Biologic trace element*
631 *res* 87: 113-124.

- 632 Sales J, Jancik F (2011) Effects of dietary chromium supplementation on performance, carcass
633 characteristics, and meat quality of growing-finishing swine: a meta-analysis. *J anim sci*
634 89: 4054-4067.
- 635 Sevi A, Albenzio M, Annicchiarico G, Caroprese M, Marino R, Taibi L (2002) Effects of
636 ventilation regimen on the welfare and performance of lactating ewes in summer. *J anim*
637 *sci* 80: 2349-2361.
- 638 Shwartz, G., Rhoads, M.L., VanBaale, M.J., Rhoads, R.P., Baumgard, L.H., 2009. Effects of a
639 supplemental yeast culture on heat-stressed lactating Holstein cows. *J Dairy Sci* 92, 935-
640 942.
- 641 Soltan MA (2010) Effect of dietary chromium supplementation on productive and reproductive
642 performance of early lactating dairy cows under heat stress. *J anim physiol anim nutr* 94:
643 264-272.
- 644 Soriani N, Panella G, Calamari L (2013) Rumination time during the summer season and its
645 relationships with metabolic conditions and milk production. *J Dairy Sci* 96: 5082-5094.
- 646 Spiers DE, Spain JN, Sampson JD, Rhoads RP (2004) Use of physiological parameters to predict
647 milk yield and feed intake in heat-stressed dairy cows. *J Therm Biol* 29 (7-8):759–764.
- 648 Subiyatno A, Mowat D, Yang WZ (1996) Metabolite and hormonal responses to glucose or
649 propionate infusions in periparturient dairy cows supplemented with chromium. *J Dairy*
650 *Sci* 79: 1436-1445.
- 651 Upadhyay RC, Ashutosh, Singh SV (2009) Impact of climate change on reproductive functions
652 of cattle and buffalo. In: Aggarwal P.K, editor. *Global Climate Change and Indian*
653 *Agriculture*. New Delhi: ICAR:107–110.
- 654 Vincent JB (2001) The bioinorganic chemistry of chromium(III). *Polyhedron* 20, 1-26.

- 655 Vincent JB (2014) Is chromium pharmacologically relevant? *Journal of trace elements in*
656 *medicine and biology: organ of the Society for Minerals and Trace Elements (GMS)* 28:
657 397-405.
- 658 Vincent JB (2015) Is the Pharmacological Mode of Action of Chromium (III) as a Second
659 Messenger? *Biological trace element research* 166, 7-12.
- 660 Vincent JB (2017) New Evidence against Chromium as an Essential Trace Element. *J nutr* 147:
661 2212-2219.
- 662 Wang M, Xu Z, Zha L, Lindemann M (2007) Effects of chromium nanocomposite
663 supplementation on blood metabolites, endocrine parameters and immune traits in
664 finishing pigs. *Anim Feed Sci Tech* 139: 69-80.
- 665 West JW (2003) Effects of heat-stress on production in dairy cattle. *J Dairy Sci* 86 (6):2131–
666 2144.
- 667 Wheelock JB, Rhoads RP, Vanbaale MJ, Sanders SR, Baumgard LH (2010) Effects of heat stress
668 on energetic metabolism in lactating Holstein cows. *J Dairy Sci* 93: 644-655.
- 669 Winkelman LA, Overton TR (2012) The effects of increasing doses of 2 preparations of long-
670 acting insulin on short-term plasma profiles of glucose and insulin in lactating dairy
671 cows. *J Dairy Sci* 95: 6974-6982.
- 672 Yamamoto A, Wada O, Suzuki H (1988) Purification and properties of biologically active
673 chromium complex from bovine colostrum. *J Nut* 118: 39–45.
- 674 Yang W, Mowat D, Subiyatno A, Liptrap R (1996) Effects of chromium supplementation on
675 early lactation performance of Holstein cows. *Can J Anim Sci* 76: 221-230.
- 676 Yari M, Nikkhah A, Alikhani M, Khorvash M, Rahmani H, Ghorbani GR (2010) Physiological
677 calf responses to increased chromium supply in summer. *J Dairy Sci* 93: 4111-4120.

678 Yasui T, McArt JA, Ryan CM, Gilbert RO, Nydam DV, Valdez F, Griswold KE, Overton TR
679 (2014) Effects of chromium propionate supplementation during the periparturient period
680 and early lactation on metabolism, performance, and cytological endometritis in dairy
681 cows. *J Dairy Sci* 97: 6400-6410.

682

683

684

685

686

687

688

689

690

691

692

693

694

695

696

697

698

699

700

701 **Figure legends**

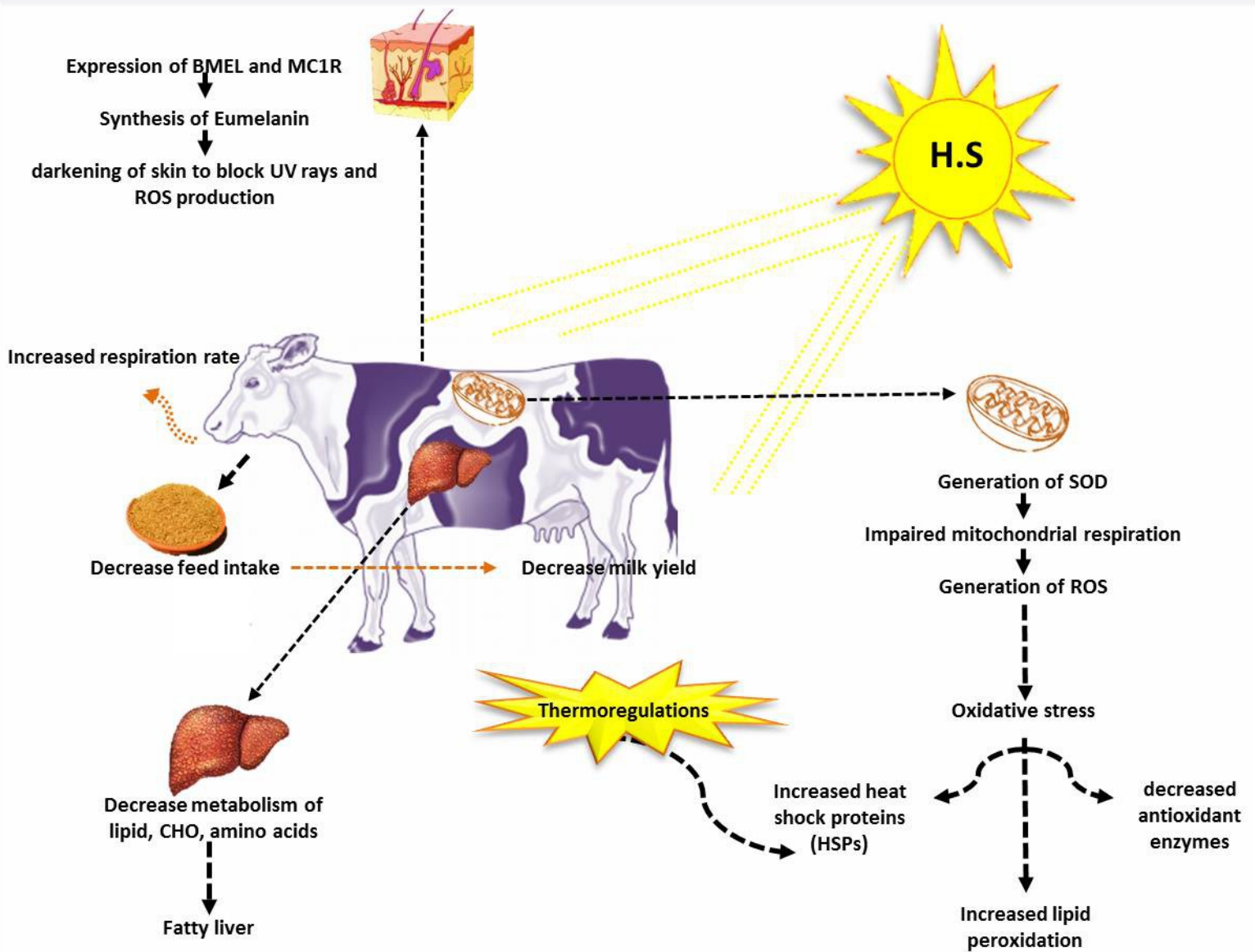
702 **Figure 1.** Summary of heat stress adverse impacts and body reactions in ruminants.

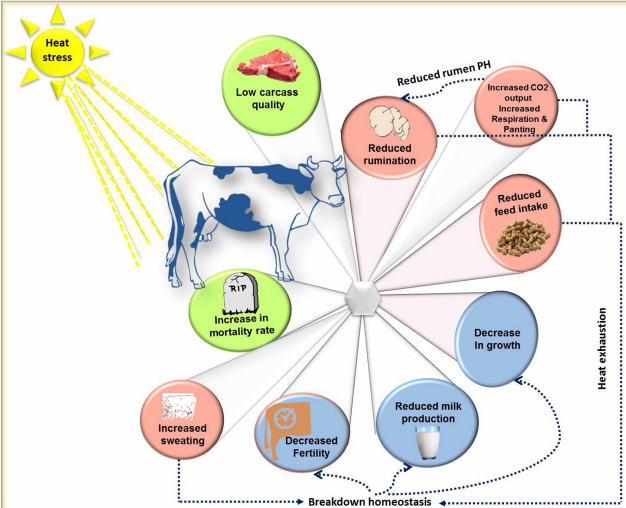
703 **Figure 2.** Effect of heat stress on animal performance, production and reproduction.

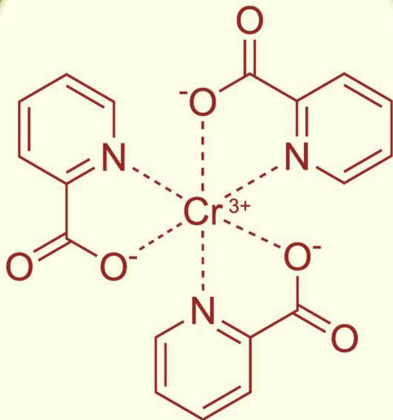
704 **Figure 3.** Chemical formula of Cr III picolinate.

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

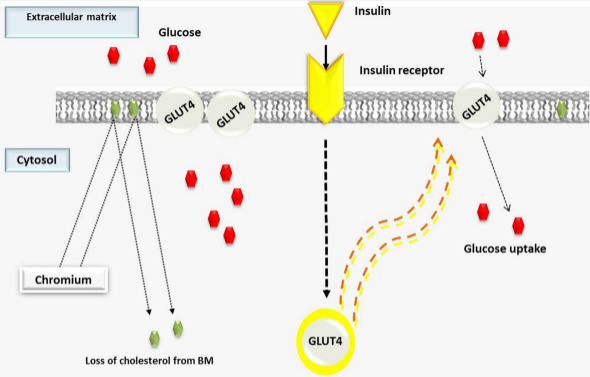
711 **Figure 5.** The beneficial effect of Chromium on glucose and non-esterified fatty acids (NEFA)
712 metabolism in dairy cattle.







Chromium(III) Picolinate





Increased glucose
output from liver

Increased dry matter
intake

Decreased NEFA

Increased availability
of nutrient to
mammary gland

Increased milk
synthesis and
production

Cows reach positive
energy balance sooner

Improved reproduction

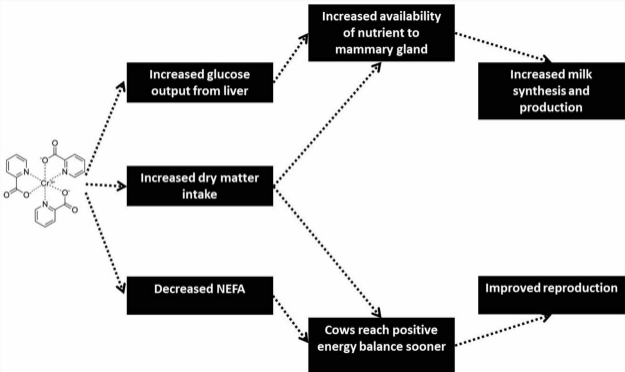


Table 1. The main findings related to Cr supplementation in heat stressed-animals

Parameter	Species	Form & dosage	Findings	References
1-Thermoregulatory responses	Dairy calves.	<ul style="list-style-type: none"> • Cr-methionine (0.05 mg /kg BW0.75). • Cr (0.05 mg/kg BW0.75). • Cr-methionine at 0.05 mg/kg BW0.75 - 	<ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • (Mousavi et al., 2019b) • (Kargar et al., 2018b) • (Mousavi et al., 2019a) • (Mousavi et al., 2019a)
	Buffalo calves.	<ul style="list-style-type: none"> • Cr (0.5, 1 or 1.5 mg inorganic Cr/kg 	<ul style="list-style-type: none"> • No effect on PR, RR and RT in heated buffalo calves. 	<ul style="list-style-type: none"> • (Kumar et al., 2015)
	Cows.	<ul style="list-style-type: none"> • (3.6, 7.2 or 10.8 milligram chromium/head per day) 	<ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • (An-Qiang et al., 2009) • (Qi et al., 2018)
	Pigs.	<ul style="list-style-type: none"> • Cr propionate (200ppb). 	<ul style="list-style-type: none"> • No effect on RR, ST and BT in heat stressed pigs. 	<ul style="list-style-type: none"> • (Mayorga et al., 2019)

2- Growth performance	Cows.	<ul style="list-style-type: none"> • Cr yeast. • Cr–methionine at 0.05 mg Cr/kg. • Cr (3.6, 7.2 and 10.8 mg chromium/head/day) 	<ul style="list-style-type: none"> • Increased feed intake in heat stressed lactating dairy cows compared with control group (21.24 and 19.56kg/day, respectively 21.24 and 19.56kg/day, respectively. • Increases feed efficiency and dry matter intake. • Significant increase ($p < 0.05$) as reported in the DMI. 	<ul style="list-style-type: none"> • (Alsaiady et al., 2004) • (Arthington et al., 1997) • (An-Qiang et al., 2009)
	Calves.	<p style="text-align: center;">-</p> <ul style="list-style-type: none"> • 0.05 mg/kg BW0.75 Cr. <p style="text-align: center;">-</p> <ul style="list-style-type: none"> • 4 mg/head. <p style="text-align: center;">-</p>	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • (Mousavi et al., 2019a) • (Kargar et al., 2018a) • (Ghorbani et al., 2012) • (Chang and Mowat, 1992) • (Burton et al., 1996)

		-	<p>immunoglobulins in serum.</p> <ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • (Kumar et al., 2015) • (Bunting et al., 2000)
	Pigs	<ul style="list-style-type: none"> • 200ppb of Chromium propionate. 	<ul style="list-style-type: none"> • Final body weight has increased in heat stressed finishing pigs. 	<ul style="list-style-type: none"> • (Mayorga et al., 2019)

<p style="writing-mode: vertical-rl; transform: rotate(180deg);">3-Milk yield and composition</p>	<p>Dairy cows.</p>	<ul style="list-style-type: none"> • (4g/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. 	<ul style="list-style-type: none"> • 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). 	<ul style="list-style-type: none"> • (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.	<ul style="list-style-type: none"> • Chromium yeast (6mg/head /day). • 0.05 mg of supplemental Cr/kg of BW 0.75 • Chromium picolinate (3.5 mg of Cr/cow daily). • 3.5m g/kg of Cr/cow. 	<ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • (Soltan, 2010). • (Yari et al., 2010) • (Jin et al., 2017) • (Qi et al., 2018)
	Calves.	<ul style="list-style-type: none"> • Cr-methionine (0.05 mg /kg BW 0.75). • Chromium at level 0.05 mg/kg BW 0.75 	<ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • (Mousavi et al., 2019a) • (Kargar et al., 2018b; Yari et al., 2010) • (Ghorbani et al., 2012)

	<ul style="list-style-type: none"> • 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 BW0.75). • Raising Cr doses (from 0 to 0.02 and 0.04 mg Cr/kg of BW0.75). 	<ul style="list-style-type: none"> • 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, respectively, when dairy calves were supplemented with cr. - Hormones: <ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • (Kumar et al., 2015) • (Bunting et al., 2000) • (Mousavi et al., 2019a) • (Kargar et al., 2018b) • (Kumar et al., 2015) • (Ghorbani et al., 2012) • (Yari et al., 2010)
--	---	--	---

	Cows	<ul style="list-style-type: none"> • (Cr-Yeast, 8mg/d). 	<p>- Antioxidants:</p> <ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • (Mousavi et al., 2019a)
	Calves.	<ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • (Kumar et al., 2015) • (Burton et al., 1993) • (Kegley and Spears, 1995). • (Kumar et al., 2015), (Qi et al., 2018)
	Pigs.	<ul style="list-style-type: none"> • Chromium propionate supplementation (200 ppb). • Chromium tripicolinate nanoparticles (400 ppb). • 200 µg/kg Cr as Cr-Nano. 	<ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • (Mayorga et al., 2019) • (Hung et al., 2014) • (Wang et al., 2007)