Adaptability of goats to heat stress: A review

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Abstract

In the environment, animals have to cope with a combination of natural factors. Extreme changes in these factors can alter homeostasis, which can lead to thermal or heat stress. This stress can be due to either high or low temperature. Energy transference for thermoregulation in homeothermic animals occurs through several mechanisms: conduction, convection, radiation and evaporation. When animals are subjected to thermal stress, physiological mechanisms are activated which may include endocrine, neuroendocrine and behavioral responses. Activation of the neuroendocrine system affects the secretion of hormones and neurotransmitters which act collectively as response mechanisms that allow them to adapt to stress. Mechanisms which have developed through evolution to allow animals to adapt to high environmental temperatures and to achieve thermo-tolerance include physical, physiological and biochemical changes like reduced feed intake and metabolic heat production, increased surface area of skin to dissipate heat, increased blood flow to take heat from the body core to the skin and extremities to dissipate the heat, increased numbers and activity of sweat glands, panting, increased water intake and color adaptation of integument system to reflect heat. Chronic exposure to thermal stress can cause disease, reduce growth, decrease productive and reproductive performance and, in extreme cases, lead to death. This paper aims to briefly explain the physical and physiological responses of mammals to thermal stress, like a tool for biological environment adaptation, emphasizing knowledge gaps and offering some recommendations to stress control for the animal production system.

Keywords: Adaptability, climate change, thermal stress, heat dissipation, heat tolerance

Introduction

Small ruminants like goats play a predominant role in the economy of million people, and have provided meat, milk, skin and fibre for centuries. Animals undergo various kinds of stress, i.e. physical, nutritional, chemical, psychological and heat stress. Among all, heat stress is the most concerning at present in the ever-changing climatic scenario. Climate change is the most serious long-term challenge faced by owners of small ruminants worldwide. Heat stress results in decreased growth, reproduction, production, milk quantity and quality, as well as natural immunity, making animals more vulnerable to diseases, and even death. Thus, heat stress results in great economic losses, emphasizing the necessity to objectively assess animal welfare. The increasing demand for animal products paralleled by the frequent hot climate is a serious threat for the agricultural sector. The ability of goats to cope with heat stress without harming their welfare and productive performance has been often overrated. To date, little attention has been paid to comprehensive detailed data on the adverse effect of heat stress on goats. Therefore, this review discusses in detail the behavioural, physiological, molecular/cellular, haematological, biochemical and immunological responses of goats under heat stress conditions, and review suggests various strategies for alleviation of heat stress.

The demand for livestock (including small ruminants) products has been largely driven by the rapid growth of the human population, increases in income and urbanization [1]. The livestock sector is increasingly organized in long market chains that employ more than 1.3 billion people globally and directly support the livelihoods of 600 million poor smallholder farmers in the developing world [1]. Globally, small ruminants play an important role in the economy of millions of people who earn their livelihood by rearing these animals in different climatic conditions [2,4].

Goats are among the species with a wide geographical distribution, playing an important role in the agricultural revolution and advance of human civilization. The goats are thought to have been domesticated around 10,000 years ago [5, 6], in the so-called ‘Fertile Crescent’ of the Middle East [7]. This species plays a predominant role in the sustenance of the livelihoods of impoverished families, especially in rural areas [8, 9]. Goats owe their popularity to their multipurpose ability to provide meat, milk, skin, offal, horn, dung for fuel, and fiber [2, 6].

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Also, these animals are well adapted under different geographical and environmental conditions including extreme and harsh climates \cite{10}, and perform better than other domesticated ruminants. Goats tend to tolerate heat better than other species \cite{11, 12}. Worldwide, there are more than 600 goat breeds \cite{6}, and these breeds differ in their capacity to overcome climatic conditions. Goats with loose skin and floppy ears are more heat tolerant than other goats \cite{12}. Angora goats have a decreased ability to respond to heat stress (HS) as compared to other breeds of goats \cite{12}. However, despite their extreme tolerance, the productivity of these animals often declines due to heat stress \cite{10}. Therefore, proper breed selection is a very valuable tool for sustaining animal production under an increasingly challenging environment \cite{13}. Nevertheless, importing high-producing breeds from temperate to desert and tropical areas does not always work well because of poor adaption to heat stress. Crossbreeding is a common strategy to resolve this problem.

Stress is described as the cumulative detrimental effect of a variety of factors on the health and performance of animals, or also described as the magnitude of forces external to the body which tend to displace its systems from their ground state \cite{11}. Animals undergo various kinds of stressors, i.e. physical, nutritional, chemical, psychological and heat/thermal stress. Among all, heat stress is the most concerning issue nowadays in the ever-changing climatic scenario \cite{14}, and it is one of the most important stressors especially in the tropical, subtropical \cite{15}, arid \cite{13}, and semiarid \cite{11, 16} regions of the world. Heat stress is the perceived discomfort and physiological strain associated with an exposure to an extreme and hot environment \cite{4}.

Climate change is the most serious long-term challenge faced by small ruminants’ owners in much of the world, as it impacts animals’ production and health \cite{14}. Environmental factors such as ambient temperature, solar radiation and relative humidity have direct and indirect effects on animals \cite{17}. High ambient temperature is the major concern that challenges the animal’s ability to maintain energy, thermal, water, hormonal and mineral balance \cite{13}. The intergovernmental panel on climate change reported that the period from 1983 to 2012 was the warmest 30-year period of the last 1,400 years in the Northern Hemisphere \cite{18}. They predict that by the year 2100, the increase in global surface temperature may be 3.7–4.8°C \cite{19}. It is expected 20–30% of livestock to be at risk of extinction \cite{20} due to changes in weather and climate events. There is evidence that climate change, especially elevated temperature, has already changed the overall abundance, seasonality and spatial spread of farmed small ruminants \cite{21}. Animal welfare outcomes show that heat stress compromises animal welfare and it is commonly stated that heat stress causes mortality in goats under inappropriate transport conditions \cite{22}. However, unlike the situation in cows \cite{23} there are no reports so far on mortality due to heat stress under conventional farming conditions, even in those raised in areas exposed to extreme heat stress (e.g., in Saudi Arabia).

Heat stress influences ovarian function and embryonic development which results in decreased fertility \cite{4}. Heat stress redistributes the body resources including protein and energy at the cost of decreased growth, reproduction, production and health of animals \cite{4}. In addition, heat stress reduces milk yield and quality \cite{24}. The general homeostatic responses to heat stress in goats include raised respiration rate, body temperature and water consumption, decreased feed intake, and dry matter intake \cite{4, 22, 25, 26}. Also, heat stress lowers natural immunity, making animals more vulnerable to diseases \cite{27}. Collapse and even death can result if the heat load experienced by the animal becomes excessive \cite{28}.

**Behavioural responses of goats to heat stress**

Despite the numerous published studies on the impact of heat stress on productive and reproductive parameters, little is published about the behavioural changes in goats during heat stress. However, animals behave in various ways during heat stress, and that can provide insights on how and when to cool them. The range of behavioral responses affects heat exchange between the animal and its environment by reducing heat gain from radiation and increasing heat loss via convection and conduction \cite{29}. Behavioural responses of goats under heat stress include: bunching in the shade \cite{11}, slobbering, panting, open-mouth breathing, decreasing feed intake and increasing water consumption \cite{26}. In severe cases of heat stress in goats, lack of coordination, trembling and down animals may be seen. In addition, desert animals usually use nocturnal activity (most active during the night) to reduce heat load in hot conditions \cite{30}.

Seeking shade is a conspicuous form of behavioral adaptation. If shade is not available, animals will change their posture to the vertical position in respect to the sun in order to reduce the effective area for heat exchange \cite{30}. Animals can change posture, i.e. stand or spread out to increase surface area for heat loss and reduce activity \cite{31}. Under severe heat stress, animals moisten their body surface with water, saliva or nose secretions \cite{11}. Animals may react either by physiological or behavioral responses, but most often a combination of both \cite{32}. For example, goats expressed decreased urination and defecation under heat stress conditions \cite{33, 34}. The reason for reduced urination frequency could be due to increased respiratory and cutaneous cooling mechanisms which might lead to severe dehydration, thereby leading to a reduction in their urination frequency \cite{34}. Also, the reduction in defecating frequency could be an adaptive mechanism of these animals to conserve body water \cite{34}. In extreme heat, grazing ruminants decrease their grazing time, tend to lie down to reduce their locomotion and spend more time in the shade \cite{11, 35}. Standing and lying are behavioral adaptive mechanisms to prevent additional heat load from the ground and to facilitate effective heat dissipation \cite{33, 34}. It was concluded that heat-treated goats (4–8 h heat exposure for 18 days) showed an elevation in standing time (445 vs. 390 min), and spent less time lying down (50 vs. 90 min) as compared to control goats.

Interaction between stress and nutrition results in nutrient deficiency as heat stress is associated with marked reduction in feed intake \cite{36}. There is also a direct effect of heat stress on the feeding centre of the hypothalamus, resulting in a hormonal response, which could also decrease metabolic rate \cite{36, 37}. Heat-stressed animals decrease feed intake in an attempt to create less metabolic heat because the heat increment of feeding is an important source of heat production \cite{38}. Also, the maintenance requirements increased by 30% because of heat stress \cite{39} and the energy intake would not be enough to cover the daily requirements which results in an apparent body weight loss \cite{40}. In fact, heat-stressed animals enter a bioenergetic state similar (but not to the same extent) to the negative energy balance observed in early lactation \cite{41}. Negative energy balance is associated with a variety of metabolic and hormonal changes; it is likely that many of the negative effects of heat stress on production,
animal health and reproduction indices are mediated by the reduction in energy balance [41]. Literature reported a marked loss of feed intake and body weight of animals exposed to heat stress. Feed intake reduction due to heat stress has been reported in goats [40, 42]. In addition, body weight, daily feed intake and gain decreased under heat stress conditions in goats [9]. Loss of body weight during heat stress might be attributed to the increase in energy expended for heat dissipation through respiratory evaporation, and subsequently to the reduction in the amount of water available for storage [9, 43]. Dairy goats decreased their dry matter intake by 30% under heat stress conditions [24]. Numerous nutritional changes through researcher guidance to producers/farmers in diet, are needed during heat stress to maintain feed intake, increase nutrient density and minimize the negative effect of heat stress [36].

Water is one of the most important nutrients required for the maintenance of life, and it is involved in many physiological functions essential for performance of small ruminants. Water is essential for the adjustment of body temperature, growth, reproduction, lactation mechanisms, digestion pattern, nutrient exchanges and transport to and from cells in blood, excretion of waste products and heat balance [2]. Water requirements are regulated by dry matter intake (during drought, animals require more water as they are forced to select more fibrous and less digestible feed), environmental temperature (animals use more water for evaporative cooling in hot weather), and loss of water from body evaporation (body surfaces and the respiratory tract), urine, feces, and milk [44]. Unlike feed nutrients, water does not receive adequate consideration to ensure optimal performance of ruminant animals, mainly those raised under hot conditions. Small ruminants may experience moderate to severe water restriction during a variety of commonly occurring environmental conditions (i.e., drought periods, shipment, when grazing in areas far from watering sources), and their requirements for water in dry areas are high due to high temperature and radiation load from the sun [2]. Goats are characterized by a remarkable tolerance to drought conditions. In general, goats are better at conserving water than sheep and possibly due to their browse diet [6, 14, 35]. Goat breeds differ in their capacity to cope with hot periods without water, for example, Black Bedouin and Barmer goats can live on a once very four days watering regime [23]. Unlike feed nutrients, water does not receive adequate consideration to ensure optimal performance of ruminant animals, mainly those raised under hot conditions. Small ruminants may experience moderate to severe water restriction during a variety of commonly occurring environmental conditions (i.e., drought periods, shipment, when grazing in areas far from watering sources), and their requirements for water in dry areas are high due to high temperature and radiation load from the sun [2]. Goats are characterized by a remarkable tolerance to drought conditions. In general, goats are better at conserving water than sheep and possibly due to their browse diet [6, 14, 35]. Goat breeds differ in their capacity to cope with hot periods without water, for example, Black Bedouin and Barmer goats can live on a once every four days watering regime [13, 43], and desert goats raised under traditional systems may be watered only once every three to six days, when water is scarce [46]. Goats kept under heat stress conditions doubled their water consumption [22, 24]. Increased water intake was mainly used by heat-stressed goats for boosting heat loss by sweating and panting [40]. In this regard, total water evaporation from water input was three to six times greater in the heat-stressed goats than the controlled ones [40].

Physiological responses of goats to heat stress

High ambient temperature has potentially several physiological adverse effects that result in a tremendous economic loss for the goat industry. These include aberration of reproductive functions, oxidative stress, enzymatic dysfunction, electrolyte imbalances, promoting an unfavorable endocrine balance and reducing feed intake, and meat quality [47-49]. Physiological parameters like respiration rate, heart rate and rectal temperature give an immediate response to heat stress [50], and consequently the level of animal discomfort/comfort. Changes in respiration rate, heart and/or pulse rate and rectal temperature have been frequently used as indices of physiological adaptability to heat stress in small ruminants [4, 48, 51]. Increased body temperature and respiration rate are the most important signs for heat stress in goats [33]. However, it is important to mention that complexity and a suite of physiological changes due to heat stress response can differ from species to species, individual to individual, and the hormonal status of the animal.

Respiratory Rate: The respiration rate (breaths/min) can change frequently and it is indirectly influenced by the animal’s activities (metabolism and muscle activity) [52], and environmental conditions [35]. Respiration rate is a practical and reliable measure of heat load and an indicator of heat stress [9, 35]. Respiration rate per minute was found to be increased by the effect of environmental temperature [53]. Increased respiration is an attempt to increase heat loss by evaporative cooling. The changes of metabolism and muscle activity of goats also changes pulsation and respiration rates [52]. Heat loss via high respiration rate was reported as higher than that via other ways [52]. The respiration rate is recorded by counting flank movements per minute from a distance of 4–5 m without disturbing the animals [54] or from a non-obstructive distance [48]. The basal reference respiration rate is 15–30 breaths/min in goats [54]. Thus, measuring respiration rate and deciding if an animal is panting, and qualifying the severity of heat stress according to panting rate (breaths/min) (low: 40–60, medium: 60–80, high: 80–120, and severe: >200) appears to be the most accessible and easiest method for evaluating the impact of heat stress on animals under extreme conditions [11, 35]. In this regard, [35] suggested that the respiration rate approaching 300 breaths/min with open-mouthed panting is indicative of severe heat stress. Increased respiration rate following heat stress has been reported in goats: 22–162 breaths/min [55], 23 breaths/min [9]. The increased respiration rate is probably indicating an effort of animals to maintain their normal body temperature by increasing their heat dissipation through increasing respiratory evaporation [40].

Heart and Pulse Rates: The heart rate is the regular beat rate of the arteries as the blood is pumped through them to the heart [56]. Heart rate (expressed through beats/min) can be rapidly altered due to animal biological activities or by external factors such as temperature. Normal heart rates range from 90 to 95 beats/min for goats [56]. Heat exposure showed a higher heart rate of 74 to 91 beats/min in goats [9, 33]. The heart rate increases under heat stress conditions, and this increases blood flow from the core to the surface of the body to give a chance for more heat to be lost by sensible (conduction, convention and radiation) and insensible (diffusion water from the skin) means [48]. However, heart rate reflects primarily the homeostasis of circulation along with the general metabolic status. Heat stress reduces the heart rate, and the marked acceleration of the heart rate occurred during the hottest part of the day [55] have suggested that heart rate decreased because of the general effort of the animal to decrease heat product. Pulsation rate per minute was found to be increased by the effect of environmental temperature [53]. Increase in heart rate and pulse rate is attributed to two causes. One is the increase in muscular activity controlling the rate of respiration, concurrent with elevated respiration rate. The second is the reduction in resistance of peripheral vascular beds and arteriovenous anastomoses. Increase in
pulsation rate increases blood flow from the core to the surface as a result of it more heat is lost by sensible (loss by conduction, convection and radiation) and insensible (loss by diffusion water from the skin) means. The increase in cardiac output and cutaneous blood flow by heat stress, due to blood redistribution from deep splanchnic to more peripheral body regions, have been implicated in goat [11, 35].

Rectal Temperature: The body temperature is a good measure of heat tolerance in animals. It represents the resultant of all heat gain and heat loss processes of the body. Rectal temperature is considered as a good index of body temperature even though there is a considerable variation in different parts of the body core at different times of the day. Rectal temperature of goats was found to be elevated with high environmental temperature in several studies [52]. Maintenance of body temperature is under neuronal control in a negative feedback system [58]. Temperature sensitive neurons (warm and cold), which are found in the preoptic region of the anterior hypothalamus, are considered a thermostat with a desired set point [59]. Temperature sensors are also found in the skin and deep tissues of the body (e.g., thorax, around the great veins of the abdomen and in the abdominal viscera) [59]. Fever and hyperthermia are two distinct causes of high body temperature. Fever is a complex reaction to pyrogens that not only cause the body’s thermoregulatory set point to rise, but also stimulates an acute-phase reaction and activates numerous metabolic, endocrinologic and immunologic systems and behaviours [58, 60]. While hyperthermia represents a failure in thermoregulation (uncontrolled heat production, poor heat dissipation or an external heat load), this does not involve a thermoregulatory set point [58, 60], and the microbial products and pyrogenic cytokines are not directly involved [60]. It is likely that most cases of elevated body temperature after stroke are due to fever, and not to hyperthermia [60]. The temperature in the rectum is representative of deep body temperature [61]. It represents the result of all heat gain and heat loss processes of the body [4]. Rectal temperature is an indicator of thermal balance and may be used to assess the adversity of heat stress which can affect growth, lactation and reproduction [60]. A rise in rectal temperature of 1°C or less is enough to reduce performance in most livestock species [62], which makes body temperature a sensitive indicator of the physiological response to heat stress because it is nearly constant under normal conditions [13]. The physiological adjustments that animal makes to prevent body temperature from rising during heat stress help prevent death from heat stroke, but also reduce productivity [13].

Domestic animals are homeotherms which tend to maintain a constant body temperature through a balance of heat gain and loss. Its variation above and below normal is a measure of the animal’s ability to resist stress environmental factors. However, [63] reported rectal temperature between 39.2°C and 39.8°C for goats. Heat exposure increased goats’ rectal temperature from 37°C to 41°C [9, 64]. In contrast, no rectal temperature changes were reported in goats [33, 55] exposed to heat treatments. A daily change in respiration rate per minute from the effect of environmental temperature may not be parallel with change in body temperature and pulsation number (31). Higher values of means of these parameters (RR, RT, HR) have been reported than that of values in thermo-neutral zone [64, 65].

Haematological responses of goats to heat stress

The blood profile of animals is sensitive to changes in the environmental temperature and is an important indicator of physiological responses to the stressing agent [9]. Determination of blood parameters may be important in establishing the effect of heat stress. Heat stress has an effect on animals as revealed by changes in hematological parameters, i.e. red blood cells, white blood cells, hemoglobin, lymphocytes, neutrophil, eosinophil, monocyte, granulocytes, packed cell volume and blood pH. When exposed to heat stress, goats showed an increased amount of red blood cells, packed cell volume, haemoglobin, white blood cells, neutrophil, eosinophil, lymphocyte and monocyte [33]. Also, packed cell volume, haemoglobin and red blood cells were higher under heat stress in goats [9]. In contrast, heat stress decreases packed cell volume and haemoglobin [66], and while white blood cells in goats [9]. Another explanation of the increase in packed cell volume and hemoglobin levels could be either increased un-attack of free radicals on the red blood cells membrane, which is rich in lipid content, and ultimate lysis of red blood cell [67] or availability of adequate nutrients for synthesis of haemoglobin as the animal consumes more feed or decreases voluntary intake under heat stress [4].

Biochemical responses of goats to heat stress

The acid-base balance is a complex physiological process to maintain a stable pH in an animal’s body. The body utilizes different mechanisms to combat any change in acid-base balance, i.e. chemical buffering, respiratory adjustment of blood carbonic acid (H₂CO₃) and excretion of hydrogen ions or bicarbonate (HCO₃⁻) by the kidneys [68]. Metabolic acidosis and alkalosis involving HCO₃⁻ as well as respiratory acidosis and alkalosis related to partial pressure of CO₂ may occur under heat stress. The vital limits of pH variation for mammals are between 7.35 and 7.45 [68, 69] and regulated by a complex system of buffers (H₂CO₃ and HCO₃⁻). Blood pH increased under heat stress in goats (66). The increase in pH may be due to reduced H₂CO₃ (70), total CO₂, HCO₃⁻ [40] and base excess in blood and extra-cellular fluid [60]. The secretion of HCO₃⁻ in urine and its reabsorption suggest a large requirement and turnover of body HCO₃⁻ to maintain blood pH during heat stress [40]. Blood biochemical parameters reflect the health (detecting possible diseases) and the metabolic status of an animal (evaluating the body’s internal condition, the function of organs [e.g. kidneys and liver], and metabolic processes in the body), which are widely used in clinical situations. heat stress affects biochemical parameters, i.e. alkaline phosphatase, alanine aminotransferase, aspartate transaminase, lactate dehydrogenase, total protein, albumin, globulin, glucose, cholesterol, blood urea nitrogen, non-ester fatty acids, beta-hydroxybutyrate, creatinine, triiodothyroxine, thyroxine, cortisol, prolactin, sodium, potassium, chloride, calcium, magnesium, iron, manganese, copper, zinc and oxidative stress parameters (glutathione peroxidase, glutathione reductase, superoxide dismutase and lipid peroxides).

Enzymes: Metabolic regulators are important in elucidating a picture of modulation in physiological mechanisms during stressed conditions and are best assessed by determining the enzymes governing various metabolic reactions in plasma/serum [4]. Enzyme levels reflect the metabolic activities during stress. Heat stress reduces alkaline phosphatase and lactate dehydrogenase activity in goats [50].
The decrease in these enzymes during heat stress is due to the decrease in thyroid activity during heat stress [50]. Serum level of aspartate transaminase and alanine aminotransferase is helpful in the diagnosis of the welfare of animals. The serum alanine aminotransferase value increases during heat stress in goats [71].

Proteins: Significant decrease in total protein concentration in goats has been reported during heat stress [72]. Total plasma protein, albumin and globulin levels decrease in goats subjected to heat stress [50]. This may be due to an increase in plasma volume as a result of heat stress, which results in a decrease in plasma protein concentration. In contrast, heat stress increased total protein and albumin in goats [9] and could be due to dehydration which has been reported to occur as a result of increased respiration rate.

Glucose, cholesterol, blood urea nitrogen, non-ester fatty acids and beta-hydroxybutyrate: Studies on glucose, cholesterol, blood urea nitrogen, non-ester fatty acids and beta-hydroxybutyrate in response to heat stress are conflicting. Glucose and cholesterol levels show greater differences under heat stress conditions than in the comfort zone. Heat stress conditions decrease glucose and cholesterol levels in goats [43]. The decrease in glucose level could be related to the decrease in availability of nutrients and lower rate of propionate production [73], or due to the increase in plasma glucose utilization to provide energy for muscular expenditure required for high muscular activity associated with increased respiration rate [74]. The decrease in cholesterol level may have a relation with the increase in total body water or the decrease in acetate concentration, which is the primary precursor for the synthesis of cholesterol [4]. Heat stress had no effect on glucose and blood urea nitrogen in goats [40]. Non-ester fatty acids and beta hydroxybutyrate are most indicative of the animal’s energy status [40]. reported a reduction in feed intake and body weight under heat stress was not accompanied by body fat mobilization as non-ester fatty acid concentration did not vary between heat-stressed and control goats. Exposure to heat stress resulted in higher beta-hydroxybutyrate concentration in goats [75].

Hormones: Hormones (i.e. thyroxine, triiodothyroxine, prolactin, leptin, adiponectin, growth hormone, glucocorticoids, mineralocorticoids, catecholamines and antidiuretic) are involved in thermal adaptation and could be important indicators for assessment of stress in animals [66, 76]. Decreased thyroid hormone level during heat stress is an adaptive response and affects the hypothalamic-pituitary-adrenal to decrease thyrotropin releasing hormone [37], which enables animals to reduce metabolic rate and heat production [36], and reduces the amount of heat produced by the cells [28]. In goats, [50] and [66] reported a decrease in plasma concentration of triiodothyroxine and thyroxine levels. Cortisol plays an important role in all types of stress. An increased cortisol level during heat stress was reported in goats [66]. The prolactin level increased in goats under heat stress [66].

Electrolytes: Heat stress challenges the animal’s ability to maintain its mineral balance. The serum concentrations of sodium, potassium and chloride decreased in goats subjected to heat stress due to the fact that heat-stressed animals lost more potassium and chloride in sweat than non-heatstressed animals, and the blood volume expanded where water is transported in the circulatory system for evaporative cooling [66].

Oxidative stress parameters: Heat stress stimulates excessive production of free radicals such as reactive oxygen species (superoxide anion radicals, hydroxyl radical, hydrogen peroxide and singlet oxygen) which are continuously produced in the course of normal aerobic metabolism, and they can damage healthy cells if not eliminated [77]. Normal cells have the capacity to detoxify superoxide radicals using antioxidant enzymes (superoxide dismutase, glutathione peroxidase, glutathione reductase and catalase) and non-enzymatic antioxidants including vitamins (C, A and E), and proteins (albumin, transferrin, glutathione) [78, 79] reported that oxidative stress increases in goats during summer as superoxide dismutase increases.

Molecular / cellular responses of goats to heat stress
It is widely accepted that changes in gene expression are an integral part of the cellular response to thermal stress. Although the heat shock proteins (HSPs) are perhaps the best-studied examples of genes whose expression is affected by heat shock, it has become apparent in recent years that thermal stress also leads to induction of a substantial number of genes not traditionally considered to be HSPs. Some of these genes are affected by a wide variety of different stressors and probably represent a nonspecific cellular response to stress, whereas others may eventually found to be specific to certain types of stress. In mammalian cells, nonlethal heat shock produces changes in gene expression and in the activity of expressed proteins, resulting in what is referred to as a cell stress response [90]. This response characteristically includes an increase in thermotolerance (i.e., the ability to survive subsequent, more severe heat stresses) that is temporally associated with increased expression of HSPs. Thermal-induced changes in gene expression occur both during hyperthermia as well as hypothermia. About 50 genes not traditionally considered HSPs have been found to undergo changes in expression during or after heat stress. Many of these genes will likely to be proved as important mediators and effectors of the cell stress response. The cellular response is one component of the acute systemic response to heat stress. High temperature results in alterations and damages at the cellular level. Cell components (i.e. unfolding and subsequent aggregation of proteins) are negatively affected by heat stress [81, 82]. Protein synthesis is particularly affected by heat stress but recovers quickly [77], whereas resumption of DNA synthesis requires a period of time [83]. The cellular response includes: activation of heat shock factors, increased expression of heat shock proteins, increased glucose and amino acid oxidation, reduced fatty acid metabolism, activation of endocrine and immune systems via extracellular secretion of heat shock proteins [84]. Heat shock factors exist in multiple isoforms in mammals, i.e. heat shock factors 1, 2 and 4. Heat shock factor 1 is the central transcription factor involved in the heat shock response [85]. Heat shock factor 1 is activated in response to heat stress and oxidative stress [86]. Heat shock factor 2 is primarily transcribed in response to the inhibition of proteasome activity and thus complements the response of heat shock factor 1 to an increase in misfolded proteins [87]. Heat shock proteins contribute to cell survival by reducing the accumulation of damaged or abnormal polypeptides within...
cells [88]. They play a crucial role in intracellular transport, maintenance of proteins in an inactive form, and the prevention of protein degradation [89]. Heat shock proteins 27, 60, 70, 90 and 110 are major heat shock proteins in mammalian cells [90], each with different functions and cellular locations [91]. Heat shock proteins are the best studied genes whose expressions are affected by heat stress. Expression of many heat shock proteins [32, 40, 60, 70, 90, 110] is increased during heat stress [51]. Heat shock protein 70 is used as a biomarker of cellular stress [77], and plays a heightened role in cryoprotection [92] and its expression level is indicative of magnitude and duration of heat stress [93]. In the nucleus, heat shock factor trimmer complexes bind promoters containing heat shock elements to activate heat stress target gene transcription [4, 84].

**Immunological responses of goats to heat stress**

Heat stress impairs immune function and increases disease susceptibility [94]. The immune system is classified into two categories: innate and adaptive immunity. Components of the innate defense include the physical barrier of the skin and mucous epithelia, leukocytes (macrophages, neutrophils and natural killer cells), non-immune cells (epithelial and endothelial cells), and certain soluble mediators (cytokines, eicosanoids and acute phase proteins). Inflammation is one of the hallmarks and first responses of the innate immune system to infection, and is associated with heat, redness, pain, swelling and impaired function. It has two main functions: remove the injurious agents and initiate the tissue healing process [95, 96]. The local inflammation that develops at the site of infection induces the acute phase response. The acute phase response is a complex systemic innate-defense system activated by trauma, infection, inflammation and stress to prevent tissue damage, eliminate any infective organisms and activate the repairing processes to restore homeostasis. It is induced by the release of inflammatory cytokines, especially Interleukin-1, Interleukin-6 and tumor necrosis factor-α from the macrophages or blood monocytes at the site of inflammatory lesions or infections. The liver is the main site of synthesis of most acute phase proteins. Cytokines therefore act as mediators between the local site of injury and the hepatocytes (liver) to produce and release the acute phase proteins [97].

**Cytokines:** Leptins are a kind of circulating adipocytokines whose concentration increases rapidly when the animal is exposed to hot environment [98]. The studies showed that expression of leptin mRNA is higher during winter season as compared to summer season [98]. The leptin is a pleiotropic hormone in caprine and changed leptin expressions in peripheral blood mononuclear cells (PBMCs) in vivo may represent an adaptive mechanism to environmental temperatures in goats suffering from severe thermal stress [98]. Under stress conditions Hypothalamus-Pituitary Axis gets stimulated which stimulates the production of catecholamine and glucocorticoids. Cytokine production and modulation of stress occur due to production of interleukins. Interleukins can act locally and systemically. Their action locally is to modulate cellular immune response. Systemically they change behavior, metabolism and neuro-endocrine secretion. IL-6 is considered as the primary mediator of metabolic response to inflammation by inducing production of a broad array of acute phase proteins. IL-1 and IL-6 inherently link muscle protein degradation with production of hepatic acute phase proteins as a response to inflammatory stimuli [99]. Production of these pro inflammatory cytokines directly affects bone growth and found to modulate the mechanism of proteins, fats and carbohydrates [100].

**Acute Phase Proteins:** The acute phase proteins are defined as proteins whose plasma concentrations increase or decrease classifying them into positive (i.e. C-reactive protein, serum amyloid A, haptoglobin), and negative (i.e. albumin, transferrin) acute phase proteins, respectively. The maximum concentration is usually reached within 24–48 hours after stimulation and declines with recovery from the infection [97]. In ruminants, there are two major acute phase proteins: haptoglobin and serum amyloid A which both increase during tissue injury and disease [101, 102]. Acute phase proteins are recognized as promising tools to assess welfare, health and performance in animal production [103]. The data on the use of acute phase proteins as biomarkers and potential indicators of stress in goats are rare. Goats exposed to heat stress increased circulating haptoglobin when they were metabolically challenged [40].

**Nitric Oxide Synthases:** Nitric oxide is a gaseous lipophilic free radical. It has three isoforms such as NOS type 1 or neuronal (nNOS), NOS type 2 or inducible (iNOS) and NOS type 3 or endothelial (eNOS) [104]. Nitric oxide regulates vascular hemostasis, hematopoiesis and peripheral immune response. Even in a small concentration, physiological and cellular activities are affected. Nitric oxide is required for full expression of active vasodilatation of the skin during hyperthermia. The effects of thermal stress on mRNA and protein expression of iNOS, eNOS and cNOS of goats in vivo during winter, moderate and summer season revealed that there is a higher relative mRNA expression of iNOS, eNOS and cNOS during summer [105]. The interaction between nitric oxide and HSPs plays an important role in the adaptive enhancement of resistance to thermal stress. iNOS protects the heart from myocardial ischaemia occurring due to heat stress [106].

**Role of interleukins in combating heat stress**

Interleukins are a group of cytokines (secreted proteins and signal molecules) that were first seen to be expressed by white blood cells (leukocytes) [107]. The function of the immune system depends in a large part on interleukins, and rare deficiencies of a number of them have been described, all featuring autoimmune diseases or immune deficiency. The majority of interleukins are synthesized by helper CD4 T lymphocytes, as well as through monocytes, macrophages, and endothelial cells. They promote the development and differentiation of T and B lymphocytes, and hematopoietic cells.

T lymphocytes regulate the growth and differentiation of T cells and certain B cells through the release of secreted protein factors [108]. These factors, which include interleukin 2 (IL2), are secreted by lectin- or antigen-stimulated T cells, and have various physiological effects. IL2 is a lymphokine that induces the proliferation of responsive T cells. In addition, it acts on some B cells, via receptor or specific binding [109] as a growth factor and antibody production stimulant [110]. The protein is secreted as a single glycosylated polypeptide, and cleavage of a signal sequence is required for its activity [109]. Solution NMR suggests that the structure of IL2 comprises a bundle of 4 helices (termed A-D), flanked by
2 shorter helices and several poorly defined loops. Residues in helix A, and in the loop region between helices A and B, are important for receptor binding. Secondary structure analysis has suggested similarity to IL4 and granulocyte-macrophage colony stimulating factor (GMCSF) [110].

Interleukin 6 (IL6), also referred to as B-cell stimulatory factor-2 (BSF-2) and interferon beta-2, is a cytokine involved in a wide variety of biological functions [111]. It plays an essential role in the final differentiation of B cells into immunoglobulin-secreting cells, as well as inducing myeloma/plasmacytoma growth, nerve cell differentiation, and, in hepatocytes, acute-phase reactants [111, 112]. A number of other cytokines may be grouped with IL6 on the basis of sequence similarity [111-113]. These include granulocyte colony stimulating factor (GCSF) and myelomonocytic growth factor (MGF). GCSF acts in hematopoiesis by affecting the production, differentiation, and function of 2 related white cell groups in the blood [113]. MGF also acts in hematopoiesis, stimulating proliferation and colony formation of normal and transformed avian cells of the myeloid lineage. Cytokines of the IL6/GCSF/MGF family are glycoproteins of about 170 to 180 amino acid residues that contain four conserved cysteine residues involved in two disulphide bonds [113]. They have a compact, globular fold (similar to other interleukins), stabilised by the two disulphide bonds. One half of the structure is dominated by a 4-alpha-helix bundle with a left-handed twist; the helices are anti-parallel, with two overhand connections, which fall into a double-stranded anti-parallel beta-sheet [114]. The fourth alphahelix is important to the biological activity of the molecule [112].

The relative mRNA expression of IL-2 and IL-6 was found significantly higher in winter as compared to summer in tropical as well as temperate region goats [115]. Similar type of findings was also observed by [116, 117] in studies on rats, which explained that under stress conditions, the HPA axis gets stimulated, which stimulated secretion of catecholamine and glucocorticoids, which modulate immune cells and thus cytokine production and modulation of cold stress occurs due to higher expression of proinflammatory cytokines like IL-2 and IL-6. [118] observed that acute heat stress enhanced the secretion of IL-2 by splenic lymphocytes significantly in broiler chickens. Many studies indicated that acute or chronic stress induces immunomodulatory effects in animal models. The decrease in IL-6 expression during summer may be due to inhibition of expression of IL-6, mediated through activating transcription factor 3 by heat shock factor 1 as observed in murine cells [119]. Thermoregulatory protective mechanism develops with age of animal and is well developed in adults as compared to infants and aged ones [120]. The higher expression of IL-2 and IL-6 in adults as compared to young ones suggests that these genes help in thermal protection in better way in adults as compared to young ones.

**Estimation of degree of heat stress / measure of heat load**

The degree of heat stress experienced by animals is estimated by the temperature-humidity index (THI) that includes both ambient temperature and relative humidity [123]. Measuring the heat load imposed on an animal using air temperature (dry bulb temperature) can be misleading. A more useful measure is the wet bulb temperature, which takes relative humidity into account [122]. When the temperature is expressed in °C, the equation to determine THI for goats according to (121) is as follows: THI = Dry Bulb Temperature °C − [(0.31 − 0.31 Relative Humidity) (Dry Bulb Temperature °C − 14.4)]. The values obtained indicate the following: <22.2 = absence of heat stress; 22.2 to <23.3 = moderate heat stress; 23.3 to <25.6 = severe heat stress and ≥25.6 = extreme severe heat stress [123].

When temperature is measured in °F, the equation is as follows: THI = Dry Bulb Temperature °F − [(0.55 − 0.55 Relative Humidity) (Dry Bulb Temperature °F − 58)]. The obtained values indicate the following: values <82 = absence of heat stress; 82 to <84 = moderate heat stress; 84 to <86 = severe heat stress and ≥86 = extreme severe heat stress [123]. Comparisons based on THI between dairy goats and dairy cows revealed that goats are more adapted than cows to the effect of heat stress i.e., extreme heat stress: THI ≥ 84 for cows and ≥ 90 for goats [14]. It is worth to mention here that THI does not take into account the effect of radiation [35], and since most goat farming occur under grazing situations, THI poorly reflected heat stress. In fact, heat stress is much higher under grazing situations than as reflected by the THI.

**Thermoregulatory and heat dissipating mechanisms by goats**

Goats are homeotherms, and can maintain near constant body temperature under a wide range of environmental conditions [124]. Thermoregulation is the mean by which an animal maintains its body temperature and it involves a balance between heat gain and loss [125]. The range of temperature when the animal needs no additional energy to maintain its body temperature is called thermoneutral zone. Animals function most efficiently within their thermoneutral zone, while above the upper and below the lower critical temperatures, the animals are stressed and the environment constrains the production process. The thermoneutral zone is about 12–24°C for goats in the hot regions of the world [126, 127]. Heat stress occurs in animals when there is an imbalance between heat production within the body and its dissipation. Most of the adjustments made by an animal involve dissipating heat to the environment and reducing the production of metabolic heat [11, 35]. Exposure of animals to heat stress leads to drastic changes, including a decrease in feed intake efficiency and utilization, disturbances in water, protein, energy and mineral balances, enzymatic reactions, hormonal secretions and blood metabolites, reduction in fecal and urinary water losses and an increase in sweating, respiration and heart rates [11].

Animals maintain their body temperature within tight limits over a wide range of ambient temperatures by balancing heat loss or gain and heat production [125]. Elevation of body temperature is the most obvious measure indicating that an animal is exposed to an unacceptable heat load [128]. The exposure of goats to elevated ambient temperatures induces an increase in the dissipation of excess body heat in order to negate the excessive heat load. Dissipation of excess body heat is excluded by evaporation of water from the respiratory tract and skin surface via panting and sweating, respectively. As ambient temperature approaches skin temperature, the rate of heat dissipation through sensible heat loss decreases [122]. As heat stress progresses, there is recruitment of evaporative processes, primarily sweating and increased respiration rate [25]. When heat stress becomes more severe, the depth of respiration increases back to near normal tidal volume while the respiration rate remains elevated above normal [122]. Evaporation of water requires a vapour pressure gradient for loss of heat energy as water evaporates to the surrounding air, but in very humid conditions this gradient is reduced, and
Strategies for alleviation of heat stress

From the above discussed sections, it could be concluded that the changes in the biological functions of goats due to exposure to heat stress include depression in feed intake, disturbance in the metabolism of water, protein, energy and mineral balances, enzymatic reactions, hormonal secretions and blood metabolites. Therefore, a variety of methods should be adopted by small ruminant producers/owners to overcome the negative effects of heat stress, including the use of shades, feeding and grazing strategies, providing water, handling time, the use of fans and evaporative cooling, and site selection of animals’ housing [11, 13, 15, 16, 17].

Shade is the easiest method to reduce the impact of high solar radiation, and it is applicable under extensive conditions. The use of shades, fans or evaporative cooling is not possible in intensive systems as goats are grazed in the open during most of the day, and this necessitates other strategies (i.e. portable shades) to counteract the adverse effects of heat stress [3].

Accessibility of animals to shade during summer is simple, easy, cheap and an efficient tool to minimize heat stress [11, 64]. Providing goats access to shade allows a reduction in rectal temperature and respiration rate in goats [132]. A well-designed shade structure reduces heat load by 30–50% [133]. Shelters do not need to be complicated or elaborate, trees and shrubs can serve as shelters for animals from solar radiation [134], and are usually the least-cost alternative. If natural shelter is not available, many goat producers use Quonset huts, plastic calf hutches, polydomes and/or carports to provide shelters for grazing animals. In addition, hay or straw shades, solid shade provided by sheet metal painted with white on top [135], and aluminum sheets [136] are the most effective and cheap materials.

Ration modifications can greatly help in reducing the negative effect of heat stress, and these adjustments may include changes in feeding schedules (feeding at cool hours, feeding intervals), grazing time, and ration composition such as dietary fiber adjustment, the use of high-quality fiber forage, increased energy density (supplemental protected fat) and use of feed additives [buffers (sodium bicarbonate), niacin, antioxidants and fungal culture (yeast culture)]. During summer, the feeding behavior for most of the animals changes and they tend to consume more feed during the cooler periods of the day [136]. Therefore, feeding animals during the cooler periods of the day encourages them to maintain their normal feed intake and prevents the co-occurrence of peak metabolic and climatic heat load [128]. Also, feeding animals at more frequent intervals helps to minimize the diurnal fluctuation in ruminal metabolites and increase feed utilization efficiency in the rumen [137]. Another point to be taken into account to alleviate heat stress is the grazing time. In extreme heat, animals decrease their grazing time and spend more time in the shade, especially during the heat of the day. They graze during the period of the milder weather during the day, i.e. before sunrise, at dawn and during the night [8]. Careful ration modifications during heat stress are important in achieving the optimum animal performance. Decreasing the forage to concentrate ratio can result in more digestible rations that may be consumed in greater amounts [138]. Feed containing low fiber rations during hot weather is logical since heat production is highly associated with metabolism of acetate compared with propionate [139]. More nutrient-dense diets are usually preferred during the heat stress period [140].

Dairy goats supplemented with 4% fat during summer had lower rectal temperature. Soybean oil fed to goats kept under heat stress increased milk fat content [34]. Feed additives have been proposed to offset the consequence of heat stress. For example, antioxidants such as vitamin C and E protect the body defense system against excessive production of free radicals (antioxidants are free radical scavengers) during heat stress and stabilize the health status of the animal [5, 140, 141] found that vitamin C supplementations to goats are effective in alleviating heat stress. Vitamin E and C supplementations decreased rectal temperature and respiration rate [66], and alleviated heat stress in goats [142]. One of the best practices to reduce heat stress is to provide adequate fresh and cool drinking water [11, 130].

The water requirements of goats increase under heat stress conditions, thus, it is essential that animals have a continuous access to adequate, cool and fresh water. This is done by having adequate watering devices (making sure pressure is adequate to refill waterers), and providing more water sources in the pasture [139].

In addition, handling animals should be kept at minimum. Goats can be handled (i.e. milking, transportation) in the early morning or late evening time [130], and the afternoon work should be avoided when body temperature is already high. One of the effective methods for prevention of heat stress is to delay afternoon milking for 1–2 hours [139]. Also, it may be necessary to install fans or other cooling systems in barns and similar structures [139, 143]. Cooling goats by spraying could reduce heat stress symptoms and improve animal welfare [24].

Direct wetting of animals is often used as an emergency measure and can be an effective protective method [134]. Sprayed and ventilated heat-stressed goats for 1 h/day would show improved milk yields [144].
consumed more feed (18%) and water (7%) and produced more milk (21%) \[144\]. The site selection of animals’ housing is fundamental to decrease exposure and minimize the effect of heat stress. Proper selection of the housing site to emphasize factors for enhancing heat dissipation (minimal radiation, air temperature and humidity, and maximal air velocity) will have long-term protection benefits \[143\]. Fully enclosed shelters are not recommended for hot climates because of the decreased natural air velocity, therefore, it is preferred to use partially enclosed shelters \[143\]. Apart from nutritional and managerial strategies, genetic selection is one important aspect. Improvement of adaptability by simultaneous heterosis and crossbreeding is a better option in the hand of goat breeders for producing better offspring capable of withstanding heat stress \[145\]. Genetic variability for the response to climatic change can be used to select the most tolerant and robust animal to cope up with future climatic changes \[146\].

Conclusion
Livestock genetic improvement should take into account not only production traits (milk yield, weight gain and wool production), but also the interaction of those traits with the environmental factors (i.e. air temperature, relative humidity and solar radiation). Heat stress exerts negative effects on productivity and well-being in small ruminants. The exposure of goats to heat stress negatively affects biological functions, changes antioxidant levels and various hormones which are reflected in the impairment of their health, production and reproduction. Goats show various responses to heat stress at behavioural, physiological, molecular/cellular, haematological, biochemical and immunological levels. Heat stress adversely affects animals’ comfort, water consumption, feed intake, milk yield and quality, meat quality, and reproduction and fertility. Thus, management strategies must be applied to counter hot/humid environmental conditions. Control is based on the provision of drinking water, adjustments in animals’ diets during heat stress (such as increase in the energy density of rations, the use of feed additives, etc.), use of cooling mechanisms (shade and fans), the use of strategies to reduce the impact of heat stress on fertility (i.e. timed mating programs during summer), and scheduling animal activities in the early morning and evening when temperatures are not as extreme. For optimal results, the people who care for animals should have appropriate education and experience, understand the species requirements and have good observational skills. It is to be noted that awareness of heat stress is the first step towards its management. In addition, effective participation, coordination and active cooperation among scientists, technicians, meteorologists, veterinarians, nutritionists and local agricultural organizations are required to successfully include these factors as a basis for strategic and operational management decisions to improve production systems. There is a need to intensify agricultural extension staff/farmer relationships and researcher/agricultural extension staff linkage to improve farmers’ knowledge, skills and practices on the use of heat stress management techniques. Finally, it is hoped that this review serves as guidance to researchers and contributes to ongoing efforts to promote heat stress management, and therefore will contribute to agricultural sustainability.

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