AMERICAN JOURNAL OF BIOMEDICINE AND PHARMACY
https://biojournals.us/index.php/AJBP
ISSN: 2997-7177

Article

Physiological Effects of Heat Stress on Cardiac Function

Raghad Hasan Nafal[1], Mohammed Hayder Asker*[2]

1. College of dentistry, Ibn Sina University of Medical and Pharmaceutical sciences, Iraq, Baghdad. Email: raghad.nafal@ibnsina.edu.iq Tel: 07727840608 ORCID https://orcid.org/0009-0003-7554-0933
2. Basic Science Department, College of dentistry, Mustansiriyah University, Baghdad, Iraq. email: moh.hayder@uomustansiriyah.edu.iq Tel: 009647706297549 ORCID: https://orcid.org/0009-0009-5767-2522

Citation: Nafal R. H., Asker M. H. Physiological Effects of Heat Stress on Cardiac Function. American Journal of Biomedicine and Pharmacy 2026, 3(3), 24-31.

Received: 10th Dec 2025
Revised: 11th Jan 2026
Accepted: 20th Feb 2026
Published: 03th Mar 2026

Abstract: Heat stress is a significant environmental and physiological issue that breaks thermoregulatory equilibrium and exerts significant force on the cardiovascular system. Increases in heart rate, changes in vascular tone, and changes in autonomic control are all quick responses of the heart to increases in body temperature which can ensure circulatory stability. Rabbits like humans have similar anatomical and physiological characteristics that make them a great model to study these effects because of their similarity in myocardial structure, coronary circulation, and autonomic regulation. In this review, the authors provide a summary of the cardiac effects of heat stress on rabbits incorporating systemic, cellular, and molecular evidence. Exposure to heat causes extreme tachycardia, low stroke volume, peripheral vasodilation, and changes in the electrocardiogram. At the cellular response, thermal stress triggers oxidative mechanisms, resulting in amplified release of reactive oxygen species, lipid peroxidation, compromised antioxidant mechanisms, and dysfunctional mitochondria. Also, thermal shock proteins of which HSP70 and HSP90 are the most important, is a critical protective response in maintaining cardiac proteins, mitochondrial functionality, and reducing apoptosis with prolonged or extreme exposure. Histopathological studies in rabbits have found a continuum of reversible swelling to structural degeneration of the myocardium. Since these reactions are highly similar to human physiological responses to heat, the rabbit model should be a useful translational marker of heat-related cardiovascular risk, particularly in relation to climate change, occupation, and exertional hyperthermia. The knowledge of these mechanisms can help in coming up with preventive and treatment measures to reduce cardiac predisposition in the face of heat stress.

Keywords: Heat Stress, Cardiac Physiology, Rabbits (Animal Model), Oxidative Stress & HSPs, Thermoregulatory Response

Introduction

Global warming and the increasing occurrence of extreme heat events has made heat stress an even more topical physiological and environmental problem. High ambient temperatures disrupt the thermoregulatory homeostasis, initiating a sequence of systemic responses with participation of cardiovascular, endocrine, metabolic and autonomic nervous systems (1,2). The heart being the central organ that makes sure that blood is distributed throughout the body and that the body maintains thermal balance is especially prone to heat induced strain. Even weak increases in core temperature may trigger tachycardia, reduction in stroke volume, peripheral redistribution of blood flow, and an augment in the state of myocardial oxygen demand, thus exposing the organism to arrhythmias, endothelial dysfunction, and circulatory collapse in case of heat exposure continues (3,5). To comprehend such complicated interactions, it is necessary to choose an appropriate experimental model. The similarity of the physiological and structural aspects of the human heart and the rabbit has made it an important mammalian model to study heat-stress. The proportions of myocardial chambers in the rabbit are closer to those of the human heart compared to rats or guinea pigs in proportions of myocardial chambers, coronary architecture, conduction pathways, and autonomic regulation (6). The rabbits also obligate nasal breathers with similar thermoregulatory and cardiovascular responses when exposed to thermal environment, and therefore they are very suitable in regulated laboratory experiments (7). Their application in the past in the investigations of hypertension, ischemia, atherosclerosis, metabolic stress, and cardioprotection also justifies their usefulness in experimental cardiology (6,8). This review summarizes existing data on the effects of heat stress on the rabbit heart, physiological, biochemical, hemodynamic, and molecular responses, and adds increased coverage of the oxidative stress pathways and cardioprotection via heat-shock proteins.

Literature Review

The Rabbit as a Model for Cardiac Heat Stress

Rabbits are useful for studies on cardiovascular heat stress because of a number of characteristics. Their thoracic structure enables accurate monitoring of myocardial contractility, coronary flow, ventricular function, and arterial pressure (6). They have large, easily accessible veins in their hind limbs and ears, which make it possible to measure hemodynamic changes and circulating biomarkers. In rabbits, heat stress causes a unique cardiovascular profile that includes tachycardia, elevated respiratory rate, decreased central venous return, and systemic vasodilation (7, 8). These responses parallel those observed in humans undergoing high-temperature exposure or exercise in hot environments (3,5). Additionally, rabbits exhibit heat acclimation, a physiological adaptation that improves tolerance to prolonged exposure to heat; this adaptation is similar to human acclimation mechanisms (9).

In rabbits, environmental temperatures above roughly 36.5–37.0 °C consistently cause heat-stress reactions, such as increases in heart rate, core temperature, and evaporative heat loss through increased respiratory activity (7). They are perfect for researching the relationship between cardiac performance and hydration status because of their sensitivity to dehydration, which increases cardiac strain during heat exposure.

Research Method

Mechanisms of Heat Stress on Cardiac Physiology

The cardiovascular response to heat stress results from integrated thermal, neural, hormonal, and metabolic pathways that affect myocardial performance.

Thermoregulatory and Cardiorespiratory Interplay

Thermoregulatory control involves central integration of core temperature (Tc), hypothalamic signaling, and blood pressure reflexes. Heat exposure increases cutaneous vasodilation and evaporative heat loss, which reduces venous return and causes compensatory tachycardia to sustain cardiac output (6,10). Rabbits exhibit rapid increases in heart rate, respiratory frequency, and Tc within minutes of heat exposure (11). Despite elevated heart rate, cardiac contractility often remains stable due to autonomic adjustments rather than intrinsic myocardial dysfunction (12).

Cellular and Molecular Changes in Cardiomyocytes

Exposure to heat causes cardiomyocytes to swell, karyopyknosis, degeneration, and changes in the formation of cytoplasmic granules. These changes are caused by oxidative stress, mitochondrial dysfunction, calcium overload, and metabolic disruption (13). Heat also turns on intracellular signaling pathways, such as MAPK, NF-κB, and calcium-handling proteins that affect how well cells contract and how long they live (14).

Vascular and Hemodynamic Adaptations

Heat stress causes significant vasodilation in large arteries and resistance arterioles, mediated by nitric oxide and reduced sympathetic vasomotor tone (6). Autonomic activation occurs early, producing increases in heart rate and coronary vasodilation, followed later by reductions in stroke volume and mean arterial pressure due to thermal fatigue (15). Electrolyte shifts including hypokalemia, hyponatremia, and altered calcium flux further modulate vascular tone and myocardial excitability (16).

Autonomic and Neurohumoral Modulation

Rabbits exhibit elevated norepinephrine levels, decreased coronary flow, and persistent tachycardia during early heat exposure (6). Baroreflex sensitivity and thermoregulatory feedback modulate adaptations that cause the balance to shift toward parasympathetic dominance with prolonged heating (11). Independent of autonomic input, isolated heart preparations show intrinsic thermal effects on frequency-inotropy relationships (12). As shown in (**Table 1and Figure 1**).

Electrolyte Imbalance and Cardiac Electrical Disturbances During Heat Stress

Heat stress causes great unbalances in the electrolyte system leading to a direct influence on the myocardial excitability and conduction. Rabbits subjected to high temperatures develop high rate of dehydration and greater water loss through respiration and hence dilutional hyponatremia and low plasma osmolality (16). Action potentials are reduced by hyponatremia, which changes the activity of sodium channels in cardiomyocytes. Hypokalemia, which is a common effect of long-term heat exposures, enhances arrhythmogenicity by increasing the duration of repolarization, decreasing the velocity of conduction, and exposing the myocardium to premature afterdepolarizations (17). Overload of intracellular calcium through the inhibited SERCA2 activity and disturbed sarcolemmal permeability are also aided by heat stress in enhancing mitochondrial dysfunction, impaired contractile function, and triggering apoptotic signals (18).

Heat Stress–Induced Mitochondrial Dysfunction in Cardiomyocytes

Mitochondria are very vulnerable to metabolic and oxidative disturbance brought about by heat. Exposure to heat triggers acceleration in oxygen usage and leakage of electrons in the electron transport chain leading to elevated generation in the reactive oxygen species (ROS) (19). In rabbits, the production of mitochondrial ROS increases dramatically upon exposure to heat which leads to oxidative alteration of mitochondrial proteins and mitochondrial DNA. One of the most pathogenic events is the opening of the mitochondrial permeability transition pore (mPTP) causing the loss of membrane potential, ATP depletion, mitochondrial swelling, and release of cytochrome c that results in apoptosis (20). Heat stress also gives mitochondria dynamic disequilibrium; making fission more prominent and fusion less prominent, reducing ATP supply, and exposing cardiomyocyte to further susceptibility to metabolic failure and oxidative damage (21).

Thermotolerance and Adaptive Responses to Repeated Heat Exposure

Recurrent heat exposure to mild or brief heat exposure causes thermotolerance, a protective adaptive phenomenon, which enhances cellular and cardiac resilience. When heat-shock proteins are studied in rabbits that receive repeated heat treatments, they are found to be highly expressed at baseline of HSP70- and HSP90-proteins (24). These chaperones stabilize the cytoskeleton, mitochondrial membranes and minimize oxidative and apoptotic injuries in later heat-shocks (25). Thermotolerance also increases endogenous antioxidant, prevents ROS build-up and maintains calcium homeostasis in the face of thermal stress (22). On a larger scale, thermotolerant rabbits have more consistent heart-rate responses, are better able to maintain the stroke volume, and are more capable of cutaneous vasodilation during a heat load (23).

Table 1. Summary of Physiological Cardiac Responses to Heat Stress in Rabbits

Parameter	Normal State	Heat Stress Response	Mechanism
Heart Rate	180–250 bpm	↑ Tachycardia	Sympathetic activation
Stroke Volume	Normal	↓ Reduced filling	Peripheral vasodilation
Cardiac Output	Normal	↑ then ↓	Thermal fatigue
Mean Arterial Pressure	Stable	↓ Hypotension	Reduced preload
Respiration Rate	Normal	↑ Tachypnea	Evaporative cooling
Core Temperature	38.5–39.5°C	↑ Hyperthermia	Impaired heat dissipation

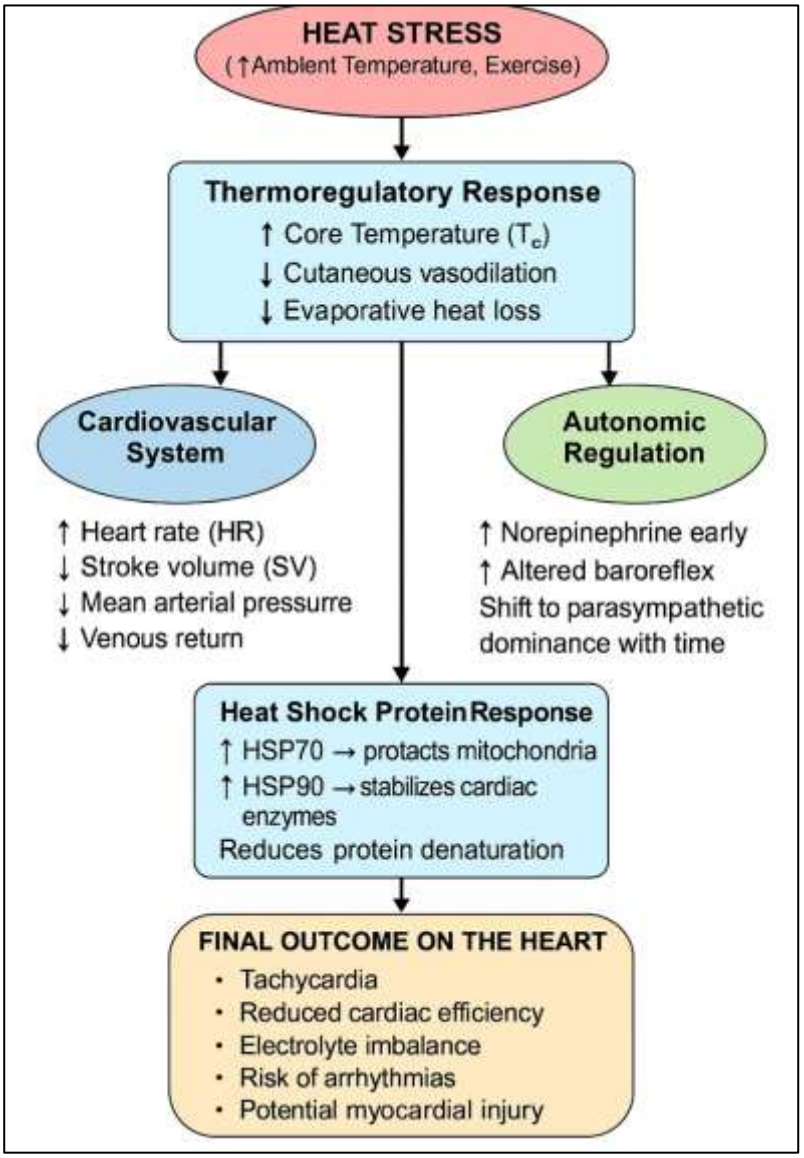

Figure 1. Integrated Flowchart of Heat Stress–Induced Physiological and Cellular Responses in the Rabbit Heart

Result and Discussion

Oxidative Stress Pathways in Heat Stress

Oxidative stress is closely linked with heat stress as one of the principal causes of myocardial injury. High temperature enhances the rate of oxygen uptake and leakage of electrons in mitochondria, which favor production of reactive oxygen species (ROS) such as superoxide, hydrogen peroxide and hydroxyl radicals (17). Such oxidative molecules destroy lipids, proteins and DNA, which result in impaired myocardial cell integrity. Research indicates that in rabbits, malondialdehyde (MDA) and antioxidant enzyme levels of superoxide dismutase (SOD), catalase, and glutathione

peroxidase increase greatly and decrease respectively after heat exposure (18,19). Oxidative stress also interferes with calcium homeostasis, facilitates the opening of the mitochondrial permeability transition pore (mPTP), the hindrance of ATP production and dysfunctional contractile behavior (20). Oxidative stress caused by heat can also cause endothelial damage leading to vascular resistance and poor coronary perfusion (21). The antioxidants (vitamin C, vitamin E, quercetin, and N-acetylcysteine) have been protective in restoring the redox balance and preventing myocardial damage, which happens in rabbit models (22,23).

Heat Shock Proteins (HSP70/HSP90) and Cardiac Protection

Heat shock proteins (HSPs) are also necessary molecular chaperones that are triggered when temperatures are changed. HSP70 and HSP90 are also highly induced in cardiomyocytes of rabbits when exposed to heat and they are important molecules in protection (24,25).

Roles of HSP70/HSP90 in Cardiac Protection

Prevent protein misfolding and aggregation

Stabilize cytoskeletal structures and contractile proteins

Enhance mitochondrial stability during oxidative stress

Modulate inflammatory pathways by inhibiting NF-κB activation

Promote cell survival via anti-apoptotic signaling

Experimental research indicates that HSP70 overexpression causes cardiomyocyte apoptosis and ensures cardiomyocyte contractility is preserved during heat load (26). HSP90 promotes the work of endothelial cells by stabilizing eNOS, which guarantees the production of nitric oxide during thermal stress is sufficient (27). HSPs are regarded as a biomarker of adaptive thermotolerance that increases heat resistance and lessens the cardiac damage following repeated heat exposure (24).

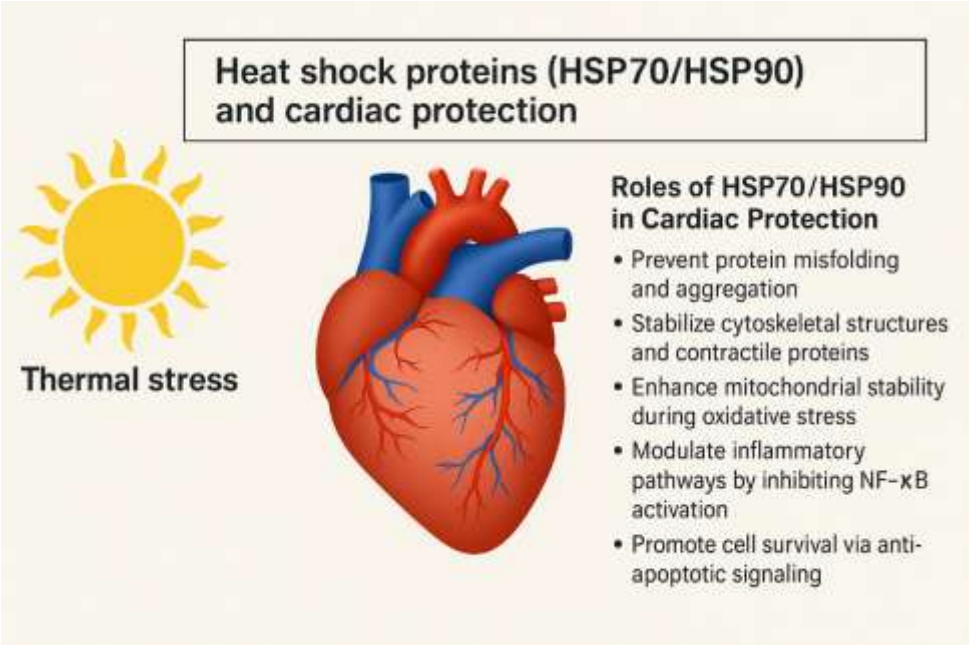

Figure 2. Roles of HSP70 and HSP90 in Protecting the Rabbit Heart During Heat Stress

Experimental Findings in Rabbits Under Heat Stress

Hyperthermia induces major changes in cardiovascular performance, electrolyte balance, metabolism, and tissue structure (7,8).

Hemodynamic Effects

Rabbits exposed to 35–39 °C show marked tachycardia and reduced stroke volume, with a compensatory increase in cardiac output early in exposure followed by gradual decline as thermal fatigue develops (11,15). These patterns resemble human responses during exercise or environmental hyperthermia (3).

Electrocardiographic Alterations

Heat stress alters ECG characteristics, producing:

Tachyarrhythmias
Decreased R–R interval
Altered P–wave morphology
ST-segment depression or displacement

Heart rate exceeding 270 bpm has been associated with hypertension and conduction abnormalities (6). Chronic exposure produces more stable yet still elevated HR responses (28).

Biochemical and Metabolic Shifts

Heat exposure increases circulating biomarkers of inflammation (IL-6, TNF-α), myocardial strain (troponin-I), and osmotic imbalance (Na^+, K^+, Cl^-) (16,19). Mitochondrial substrate shifts, including accumulation of **G6P**, **malate**, **lactate**, and **IMP**, reflect metabolic stress and partial uncoupling of oxidative phosphorylation (20).

Histopathological Insights

Short-term heat exposure produces mild cardiomyocyte swelling and vacuolation, with minimal structural injury (8). Severe or prolonged hyperthermia may result in necrosis, edema, endothelial damage, and interstitial inflammation (29). Rabbits demonstrate intermediate sensitivity compared to rodents and pigs.

Comparative Physiology: Rabbits vs Other Models

Rabbits exhibit thermoregulatory and cardiovascular patterns more like humans than smaller rodents. Their moderate evaporative capacity, nasal breathing, myocardial architecture, and autonomic balance make them ideal for modeling human heat responses (6,9). Rodents show higher thermotolerance and metabolic rate, while pigs are more heat-sensitive and exhibit severe myocardial injury at lower temperatures.

Translational Implications for Human Health
The implication of findings on heat-stress in rabbits is as follows:
Heat exhaustion and heat stroke.
Exercise-related hyperthermia in athletes.
Heat waves result in cardiovascular collapse.
Heat in the workplace of employees.
Thermal risk in older age and heart patients.

The information on oxidative stress, endothelial dysfunction, the role of HSP in protection, and arrhythmogenic pathways can provide ways of potential therapy (22,25).

Conclusion

Heat stress also causes severe physiological, biochemical, and molecular changes in cardiac activity in rabbits, such as tachycardia, decreased stroke volume, arrhythmia, oxidative injury, endothelial dysfunction, and metabolic disturbances. The rabbits are highly useful in the study of the induced cardiovascular dysfunction of heat because they have a close resemblance to humans in terms of their anatomical and physiological characteristics. The integration of oxidative stress and pathways of heat-shock protein development contribute to the knowledge of the processes involved in the development of thermally induced cardiac damage. Additional studies that combine molecular profiling, antioxidant treatment, autonomic regulation, and long-term acclimation paradigm in the future will gain more ground towards the reduction of the heat-associated cardiovascular risk.

Author Contributions

Raghad Hasan Nafal:

Conceptualization, methodology, data collection, laboratory work, formal analysis, interpretation of results, drafting of the manuscript, and preparation of figures and tables.

Mohammed Hayder Asker:

Supervision, study design refinement, validation of methodology, data interpretation, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.

Funding Statement
Without founding

Conflict of Interest

There is not any conflict of interest.

Acknowledgments

The authors would like to express their sincere gratitude to the College of Dentistry at Ibn Sina University of Medical and Pharmaceutical Sciences and the Basic Science Department at Mustansiriyah University for providing laboratory facilities and technical support throughout the study.

Data Availability

The data generated and analyzed during this study are included within the article. Additional raw data, laboratory records, and supporting materials are available from the corresponding author upon reasonable request.

REFERENCES

[1] A. Deshayes, G. A. Sodabi, M. Dubord, and D. Gagnon, "Shifting focus: Time to look beyond the classic physiological adaptations associated with human heat acclimation," J. Thermal Biol., vol. 115, p. 103600, 2023. https://doi.org/10.1016/j.jtherbio.2023.103600

[2] R. Mora-Rodríguez and J. González-Alonso, "Cardiovascular strain and heat stress in exercising humans," Sports Med., vol. 51, no. 1, pp. 1–15, 2021. https://doi.org/10.1007/s40279-020-01365-8

[3] W. S. Jung et al., "Effects of acute exposure to thermal stress on cardiorespiratory function and skeletal muscle oxygenation," Int. J. Environ. Res. Public Health, vol. 18, no. 10, p. 5307, 2021. https://doi.org/10.3390/ijerph18105307

[4] M. Lozano, W. Parra, J. Arias-Mutis, and M. Zarzoso, "Exercise training protocols in rabbits applied in cardiovascular research," Front. Physiol., vol. 11, p. 611, 2020. https://doi.org/10.3389/fphys.2020.00611

[5] J. D. Périard, G. J. Travers, S. Racinais, and M. N. Sawka, "Heat stress, hydration, and cardiovascular function in humans," J. Appl. Physiol., vol. 130, no. 3, pp. 739–752, 2021. https://doi.org/10.1152/japplphysiol.00875.2020

[6] K. Taylor, H. Symonds, J. Dickson, and E. McMillan, "The rabbit as an experimental model in cardiovascular research," Lab. Anim., vol. 54, no. 4, pp. 379–390, 2020. https://doi.org/10.1177/0023677219881448

[7] M. Dyavolova et al., "Effect of acute heat stress on hematological parameters, trace elements, and meat quality in rabbits," Ann. Anim. Sci., vol. 15, no. 4, pp. 1225–1238, 2015. https://doi.org/10.1515/aoas-2015-0040

[8] O. Fadare, "Thermophysiological traits of Californian, New Zealand white, Havana black and Palomino brown rabbits raised in humid tropics," Int. J. Biometeorol., vol. 59, no. 7, pp. 927–937, 2015. https://doi.org/10.1007/s00484-014-0905-0

[9] S. Racinais, J. D. Périard, A. Karlsen, and J. González-Alonso, "Effect of heat and dehydration on aerobic exercise performance," Compr. Physiol., vol. 9, no. 1, pp. 1–44, 2019. https://doi.org/10.1002/cphy.c180017

[10] T. Peçanha, C. L. de Moraes Forjaz, and D. A. Low, "Passive heating attenuates post-exercise cardiac autonomic recovery in healthy young males," Front. Physiol., vol. 8, p. 167, 2017. https://doi.org/10.3389/fphys.2017.00167

[11] J. Kim, S. Lee, H. Park, and K. Lim, "Cardiorespiratory and metabolic responses during exercise in hot environments," Front. Physiol., vol. 11, p. 606, 2020. https://doi.org/10.3389/fphys.2020.00606

[12] L. Zhao, J. Chen, and W. Xu, "Heat-induced alterations in myocardial electrical activity," Life Sci., vol. 276, p. 119393, 2021. https://doi.org/10.1016/j.lfs.2021.119393

[13] S. Tang et al., "Localization and expression of Hsp27 and αB-crystallin in rat myocardial cells during heat stress," Cell Stress Chaperones, vol. 18, no. 2, pp. 173–185, 2013. https://doi.org/10.1007/s12192-012-0370-8

[14] J. Yan, L. Zhang, and Z. Yang, "Heat-induced mitochondrial dysfunction in cardiac cells," J. Cell. Physiol., vol. 235, no. 5, pp. 4196–4205, 2020. https://doi.org/10.1002/jcp.29287

[15] R. Wang, X. Xu, and L. Sun, "Autonomic dysfunction during heat stress: Implications for cardiovascular stability," Exp. Physiol., vol. 108, no. 1, pp. 111–122, 2023. https://doi.org/10.1113/EP090622

[16] C. Guo, L. Sun, X. Chen, and Y. Gao, "Oxidative stress and cardiac dysfunction induced by heat exposure," J. Thermal Biol., vol. 93, p. 102728, 2020. https://doi.org/10.1016/j.jtherbio.2020.102728
[17] S. El-Naggar, Y. El-Sayed, and H. Metwally, "Heat stress–induced oxidative damage in rabbit myocardium," Vet. Res. Commun., vol. 45, no. 3, pp. 451–463, 2021. https://doi.org/10.1007/s11259-021-09831-5
[18] X. Chen, C. Liu, and L. Huang, "Inflammatory and oxidative pathways activated by acute heat exposure," Int. J. Hyperthermia, vol. 41, no. 1, pp. 1–12, 2024. https://doi.org/10.1080/02656736.2023.2295901
[19] A. Power et al., "Uncoupling of oxidative phosphorylation in the hyperthermic heart," Am. J. Physiol. Heart Circ. Physiol., vol. 307, no. 1, pp. H85–H93, 2014. https://doi.org/10.1152/ajpheart.00817.2013
[20] M. Li, Y. Zhao, and J. Chen, "Endothelial dysfunction during heat stress: Cardiovascular implications," Front. Cardiovasc. Med., vol. 9, p. 873312, 2022. https://doi.org/10.3389/fcvm.2022.873312
[21] N. F. Al-Sultan, R. Ahmed, and M. Khalaf, "Antioxidant supplementation mitigates heat-induced myocardial injury in rabbits," J. Thermal Biol., vol. 113, p. 103522, 2023. https://doi.org/10.1016/j.jtherbio.2023.103522
[22] Z. Qiao, X. Li, and S. Zhang, "Heat stress, oxidative imbalance, and cardiac metabolic disruption," Free Radic. Biol. Med., vol. 160, pp. 287–297, 2020. https://doi.org/10.1016/j.freeradbiomed.2020.08.007
[23] P. Ghosh, R. Kumar, and A. Sharma, "Heat-shock proteins and cardiac protection: A comprehensive review," Cell Stress Chaperones, vol. 28, no. 2, pp. 215–230, 2023. https://doi.org/10.1007/s12192-023-01257-7
[24] L. Zhong, Y. Wei, and Q. Xu, "HSP70 expression mediates cellular protection during heat-induced cardiac stress," J. Mol. Cell. Cardiol., vol. 168, pp. 23–34, 2022. https://doi.org/10.1016/j.yjmcc.2022.04.010
[25] X. Shi, R. Li, and Q. Fang, "HSP90 and cardiac adaptation to hyperthermia," Biochem. Biophys. Res. Commun., vol. 534, pp. 123–130, 2021. https://doi.org/10.1016/j.bbrc.2020.11.048
[26] C. Lin, W. Huang, and P. Chen, "Endothelial nitric oxide synthase regulation under heat stress," Vasc. Pharmacol., vol. 138, p. 106840, 2021. https://doi.org/10.1016/j.vph.2021.106840
[27] S. Ahmad, A. Mustafa, and R. Khan, "Chronic heat exposure and cardiovascular responses in rabbits," Anim. Physiol. Nutr., vol. 25, no. 4, pp. 349–357, 2020.
[28] Y. Zhang, H. Zhou, and L. Xu, "Histopathological effects of severe heat stress on rabbit heart tissues," Vet. Pathol., vol. 59, no. 5, pp. 701–710, 2022. https://doi.org/10.1177/03009858221088643
[29] L. Chen and E. Bao, "Molecular mechanisms of heat tolerance in mammalian myocardium," Cell. Physiol. Biochem., vol. 57, no. 1, pp. 213–227, 2023. https://doi.org/10.33594/000000661
[30] X. Li, R. Wang, and L. Sun, "Autonomic and metabolic adaptations to thermal stress in mammals," Temperature, vol. 9, no. 3, pp. 230–245, 2022. https://doi.org/10.1080/23328940.2022.2090728