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The Journal of Basic and Applied Zoology (2023) 84:8
https://doi.org/10.1186/s41936-023-00331-z

The Journal of Basic and Applied Zoology

REVIEW

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A scoping review of the impact of heat stress on the organs of the Japanese quail (*Coturnix japonica*)

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Abstract

Background Heat stress negatively affects poultry welfare, including the Japanese quail, especially in sub-Saharan African countries. The quail is vital to research and protein food security, which are affected by global warming. This study identified and reviewed the literature on the impact of heat stress on the Japanese quail organs to provide context for the problem and ways to mitigate it.

Main body Eligible studies for this scoping review must be primarily animal-based experiments that include Japanese quail exposure to acute or chronic heat stress. Systematic reviews, theses and dissertations that meet these criteria were also eligible for use in this review. Reports that involved other types of quail species, eggs and or cell lines were not eligible and were excluded. The databases that were searched include MEDLINE (via PubMed), SCOPUS, CAB Abstracts (via CAB Direct) and Web of Sciences (All databases). A total of 4598 records were identified. After removing 105 duplicates, 4461 and 9 were excluded during the level 1 and 2 screening, respectively. Finally, 24 papers were included for data extraction. All eligible studies were primary animal experiments, and the average heat stress temperature level was 35.3 °C. Morphological findings of this scoping review include macrovesicular steatosis in the liver, necrosis of kidney tubular cells, dead and abnormal sperm cells in the testis, lung congestion, and neuronal degeneration resulting from heat stress exposure.

Conclusions Heat stress negatively impacts the organs of the Japanese quail, causing cell death in the liver, brain and testis, which will affect the production and survival of the Japanese quail. In addition, some cost-effective dietary strategies tested in mitigating heat stress were recommended.

Keywords Japanese quail, Heat stress, Morphological changes, Climate change, High temperature

Background

Global warming is still the major bioclimatic factor affecting poultry welfare (Nyoni et al., 2019). It propagates heat stress in birds, which leads to morbidity and mortality. The intergovernmental panel on climate change predict a continued global temperature rise in the coming years (IPCC, 2021). McKechnie and Wolf (2010) suggest that by 2050 several episodes of small bird mass mortality will occur due to evaporative water loss, caused by high environmental temperatures. One such small bird is the Japanese quail. Due to the quail reaching sexual maturity within six weeks from hatching, researchers have used it to study old age-related diseases and model

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it for osteoporosis and human hereditary diseases (Baer et al., 2015; Mizutani, 2003). In addition, the quail helps maintain protein food security in sub-Saharan African countries (Mnisi et al., 2021; Olorunfemi et al., 2016).

Oxidative stress plays a significant role in the mechanism of heat stress (Akbarian et al., 2016). For example, biochemical assays showed depletion of antioxidant enzymes and elevation of malondialdehyde (Sahin et al., 2017) and heat shock protein levels (Akdemir et al., 2015) in heat-stressed Japanese quail. Heat stress increases cellular energy demand, overwhelms mitochondrial energy production and leaks electrons from the electron transport chain that generates excessive reactive oxygen species (Akbarian et al., 2016). The reactive oxygen species interact with cellular components and cause lipid bilayer peroxidation, proteins and DNA damage (Akbarian et al., 2016). These processes lead to cell swelling and death, thus inciting inflammatory reactions and tissue damage (Swanson et al., 2010).

Researchers reported gross and histological changes in the organs of heat-stressed Japanese quail (Mehaisen et al., 2017). Still, no extensive evaluation of single or multiple organs in the Japanese quail affected by heat stress is available. Microscopic examination of organs could reveal insight into common phenomena. For example, heat stress reduced the quality and number of eggs produced by the quail, but the mechanism remains a mystery. However, De Moraes et al. (2021) immunolabelled calbindin-D28k (calcium transporter channel) in the gut of the quail and found that heat stress reduces calcium absorption. Hence, because morphological evaluation is essential to the overall understanding of the research in heat stress, we identified and analysed studies on the gross and histological changes in the organs of the Japanese quail.

Methodology

This scoping review was conducted following the JBI methodology for scoping reviews. Preferred reporting of items for systematic reviews and meta-analyses extension for scoping reviews (PRISMA-ScR) is used for reporting. A priori-registered protocol for this review can be found on the open science framework (OSF) website (https://doi.org/10.17605/OSF.IO/VMYQT).

Inclusion criteria

Studies that reported Japanese quail of any age and sex were eligible; any other type of quail, such as Common quail or California quail, were excluded. Studies that exposed the Japanese quail to acute or chronic heat stress and either continuous or cyclical exposure were included. In contrast, studies on Japanese quail exposure to cold stress were excluded. Furthermore, gross morphological and histological studies of Japanese quail organs subjected to heat stress were included. In addition, morphological studies of cell cultures, eggs, and molecular analyses were excluded. Finally, morphological studies of Japanese quail organs not exposed to heat stress were excluded. This scoping review considers all primary experiments involving the Japanese quail; however, systematic reviews, theses, and dissertations that meet the criteria were selected.

Search strategy

The search strategy for this scoping aimed to locate both published and unpublished studies. A three-step approach was used to identify records for this scoping review. The first step was conducted using key terms (Japanese quail, Heat stress, Morphology) to identify major keywords and the availability of literature related to the topic. This step was part of the pilot study conducted, details of which can be found in the registered protocol. The second step is the search of databases and grey literature using the search query. The databases searched for records are MEDLINE (via PubMed), SCOPUS, CAB Abstracts (via CAB Direct), and Web of Sciences (All databases). Grey literature search was conducted in ProQuest (ebook central, agricultural sciences database, biological sciences database, environmental science database, health and medical collection, science database, ProQuest dissertation and theses global), Biorxiv & Medrxiv, and Google scholar. All the searches were conducted on the 27th and 28th of June 2022 (Additional file 1: Appendix 1). The search results from CAB abstracts were sorted based on relevance, and the first 1075 records were exported. A similar approach was used for searches of ProQuest (first 500 records) and Google scholar (first 204 records), as suggested by Haddaway et al. (2015). This limitation was applied to avoid redundancy because the titles of CAB abstract results were screened up to the first 8000, which showed no record related to the topic after the first 1000 records. The third step was the search for eligible records in the references cited by the included studies.

An example of the search query used in the CAB Abstract is as follows:

("Japanese quail") OR ("Coturnix japonica") OR ("Coturnix coturnix japonica") AND ("Heat stress") OR ("Thermal stress") OR ("Heat exposed") OR ("Thermal exposed") OR ("Heat exposure") OR ("Thermal exposure") AND (Morphology) OR (Morphometry) OR (Histology) OR (Histological) OR (Morphological) OR (Morphometric).

Source of evidence selection

Following the search, all identified citations were exported as a.ris file and collated, then uploaded into EndNote 20.2.1 (The EndNote Team, 2013). After that, the collated records from the databases and grey literature sources were exported from EndNote as one.txt file. This makes it easier to import into the Rayyan web application for systematic reviews (Ouzzani et al., 2016). At this point, all the records identified as eligible from the pilot study were uploaded into the Rayyan Web application just before the removal of duplicates. After uploading the documents into the Rayyan web application, duplicates were removed immediately. Subsequently, the title and abstracts of the records were screened by two reviewers based on the following questions:

1. Is the study on Japanese quail or involved Japanese quail?
2. Is the experimental design on heat exposure or involved heat exposure?
3. Does the study outcome include gross morphology, morphometry, or histology of any organ?

All the records that ticked 'yes' in the three questions were selected for full-text screening. However, any study that answered 'no' to one question was excluded. Any conflict between the reviewers from the level 1 screening was resolved by consensus. Then, level 2 screening of the full texts was conducted based on the following questions:

1. Does the study report explicitly gross or histological evaluation of any organ of the Japanese quail?
2. Does the study design have a control group and a heat-stressed group to compare heat stress effect on organs?
3. Does the study outcome explicitly mention the effects of heat stress on any organ of the Japanese quail?

The criteria for the full-text screening are that a study must answer 'yes' in the first question and another 'yes' in the second or third question to be eligible. If a study answered 'no' in question 1, it is excluded, and if it answered 'no' in both question 2 and question 3, it is excluded. Conflicts were resolved by consensus.

All the eligible studies were included for data extraction without critical appraisal. The vital information necessary for the scoping review question did not warrant strict methodology appraisal.

Data extraction

The reviewers developed a unique data extraction tool (Additional file 1: Appendix 2) during the protocol development and tested it during the pilot study. The data extracted from the records are the study's country and aim. The total number of Japanese quail used, the age, sex, weight range and the species name used were extracted as the essential characteristics of the bird's sample. The species name used is vital to understanding the standing conflict in using the scientific name of the Japanese quail. The data extracted regarding heat stress include the type and duration of the exposure, the temperature level for both the heat stress group and the thermoneutral group, and the study duration. The type of heat stress exposure can be either continuous or cyclic. Continuous heat exposure is when the temperature above the thermoneutral level is maintained for 24 h throughout the experimental period for the heat stress group. While cyclic exposure is when the higher temperature level is increased over certain hours and then reduced to a thermoneutral temperature for the remaining hours and repeated the next day. The duration of the study can be acute or chronic. Acute exposure is when the period of heat stress exposure, whether continuous or cyclic, is 24 h or less, while chronic exposure is more than 24 h. The Japanese quail body temperature measurement method used by the researchers is also extracted to know if the body temperature of the Japanese quails was monitored. The second level of data extraction is the organ(s) of interest in the study, the descriptive and quantitative data reported. The descriptive data is simply the observed changes affected by exposure to heat stress on the organ(s) of interest.

In contrast, the quantitative data is the measurements reported in the study, i.e., villus height, crypt depth etc. Numerical values were not extracted because no meta-analysis or meta-synthesis was intended for this scoping review. The study title was added during data extraction, which was not in the protocol, for the completeness of the data and to help reviewers navigate through the data table quickly and precisely.

Data analysis and presentation

The critical component of this scoping review, which is the impact of heat stress on Japanese quail organs, is summarised narratively. The basic features of the included studies and the data on heat stress are presented in figures where appropriate. In addition, a flow chart of the screening process of the sources is presented. No meta-analysis or meta-synthesis of the extracted data was conducted.

Results

Studies inclusion

The identification, screening, inclusion, and exclusion process of records is summarised in Fig. 1. This scoping review identified 4598 records through databases and grey literature searches. Following the removal of

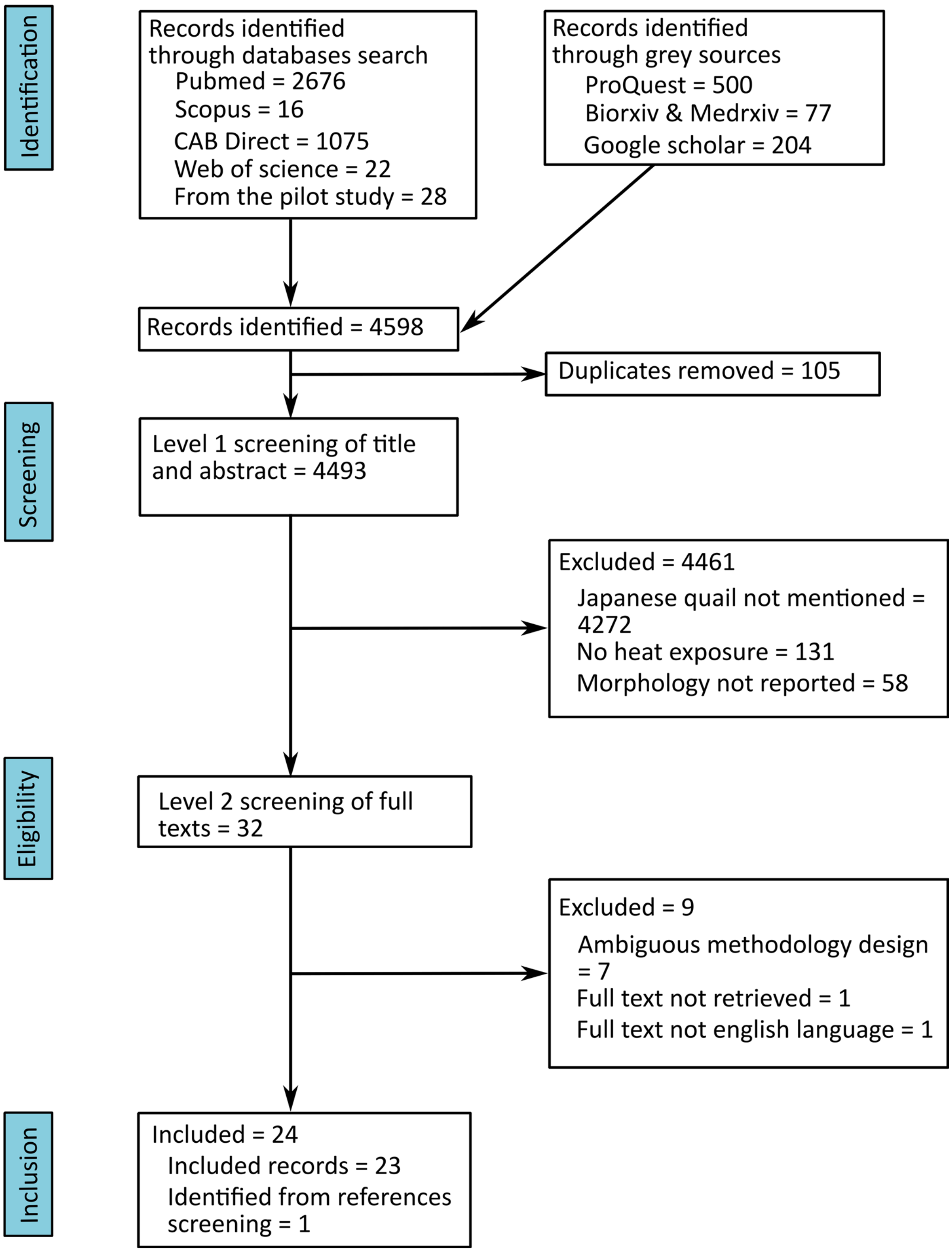

Fig. 1 The flow chart of study selection showing the stages of identification, screening and inclusion

105 duplicates, 4493 records were screened at the level 1 title and abstracts. We excluded 4461 records for the following reasons: 4272 experiments did not use or involve Japanese quail, 131 used Japanese quail without heat stress, and 47 studies exposed Japanese quail to heat stress but did not report morphological outcomes. Other reasons for excluding records are studies conducted on Japanese quail eggs (7) and cell lines (4). However, amongst the 131 records that used Japanese quail without heat stress exposure, 36 reported morphological outcomes. Although excluded, it is significant to outline this observation because this scoping review is interested in morphological consequences.

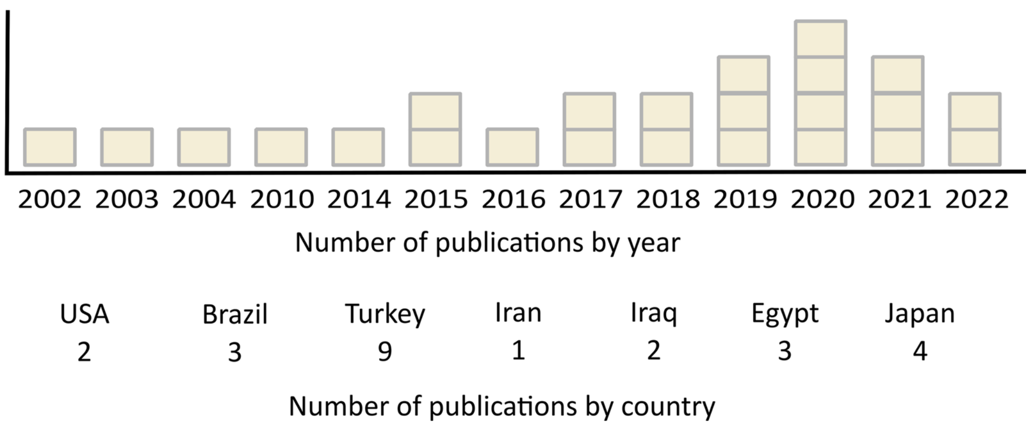

Fig. 2 A diagram showing the distribution of included studies' per year and country

In screening 32 full texts, we excluded nine records for the following reasons: seven records had an ambiguous methodology, one full text was not in the English language, and one unfound full text (Additional file 1: Appendix 3).

Characteristics of included studies

All the studies included in this scoping review are primary experiments; we did not identify systematic or scoping reviews, theses, or dissertations. The characteristics of included studies are summarised in Additional file 1: Appendix 4. Nine studies were conducted in Turkey, Japan—4, Brazil—3, Egypt—3, the United States of America—2, Iraq—2, and Iran—1. The first study identified was conducted in the year 2002, which means in 20 years, few experiments (24 included studies) evaluated the gross or microscopic features of heat stress in Japanese quail organs (Fig. 2). Chronic heat exposure was the format in 22 records, while only two studies were acute heat stress experiments. However, the heat exposure was continuous in 13 records and cyclic in 11 records. The average exposure in cyclic experiments was 7.6 h (min = 4, max = 12). The temperature levels for thermoneutral groups averaged 23.4 °C (min = 22, max = 26), while the mean heat stress temperature was 35.3 °C (min = 32, max = 42). None of the records describes the method of the birds' body temperature check, which could have been either cloacal or skin temperature measurement.

Review findings

Figure 3 summarises the effects of heat on the major organs of the Japanese quail. Heat stress increased gizzard weight (Furtado et al., 2022), but other organs remained unaffected, as Rodrigues et al. (2022) reported. In the intestines: heat stress decreased villus height and area of the small intestines; reduced number of goblet cells; caused crypt epithelium hyperplasia; and decreased Calbindin-D28k (epithelial calcium transporter channel) activity in the duodenum (De Moraes et al., 2021; Mehaisen et al., 2017; Sandikci et al., 2004). In addition, heat stress decreased villus width in a report by Mehaisen et al. (2017) but remained the same in a report by Sandikci et al. (2004). Furthermore, heat stress activates Kupffer cells; causes macrovesicular steatosis, severe congestion, bile accumulation, extramedullary haematopoiesis, hepatocyte degeneration, and necrosis in the liver (De Moraes et al., 2021; Mohamed et al., 2015; Ozcelik et al., 2014; Pu et al., 2019b, 2020; Sritharet et al., 2002). In the kidneys, heat stress causes fatty change, hydropic degeneration, congestion and necrosis of renal tubular cells; enhances mononuclear cell infiltration; increases calbindin-D28k activity in the proximal and distal tubules (De Moraes et al., 2021; Mohamed et al., 2015).

Heat stress reduces ejaculate volume, sperm motility, and concentration; kills or distorts sperm cells; and causes disorganization and degeneration of the germinal cells layer in the testis. It increased immature spermatids and spermatogonia production and dilated the seminiferous tubule (Razooqi et al., 2019; Turk et al., 2015, 2016). Furthermore, heat stress reduced the number of primary and secondary uterine folds and lowered Calbindin-D28k activity in the uterus (De Moraes et al., 2021). Heat-stressed quail showed low oviduct and ovarian weight; reduced follicle number; and empty oviduct uterovaginal junctions (Hassan et al., 2003; Pu et al., 2019a).

Heat stress decreased nuclei per millimetre of muscle fibre in fast-growing Japanese quail but increased mean muscle fibre diameter. Authors reported varied results on muscle colour: (Tekce et al., 2020a) reported lower lightness L* values but subsequently reported no changes in values (Tekce et al., 2020b). The remaining authors

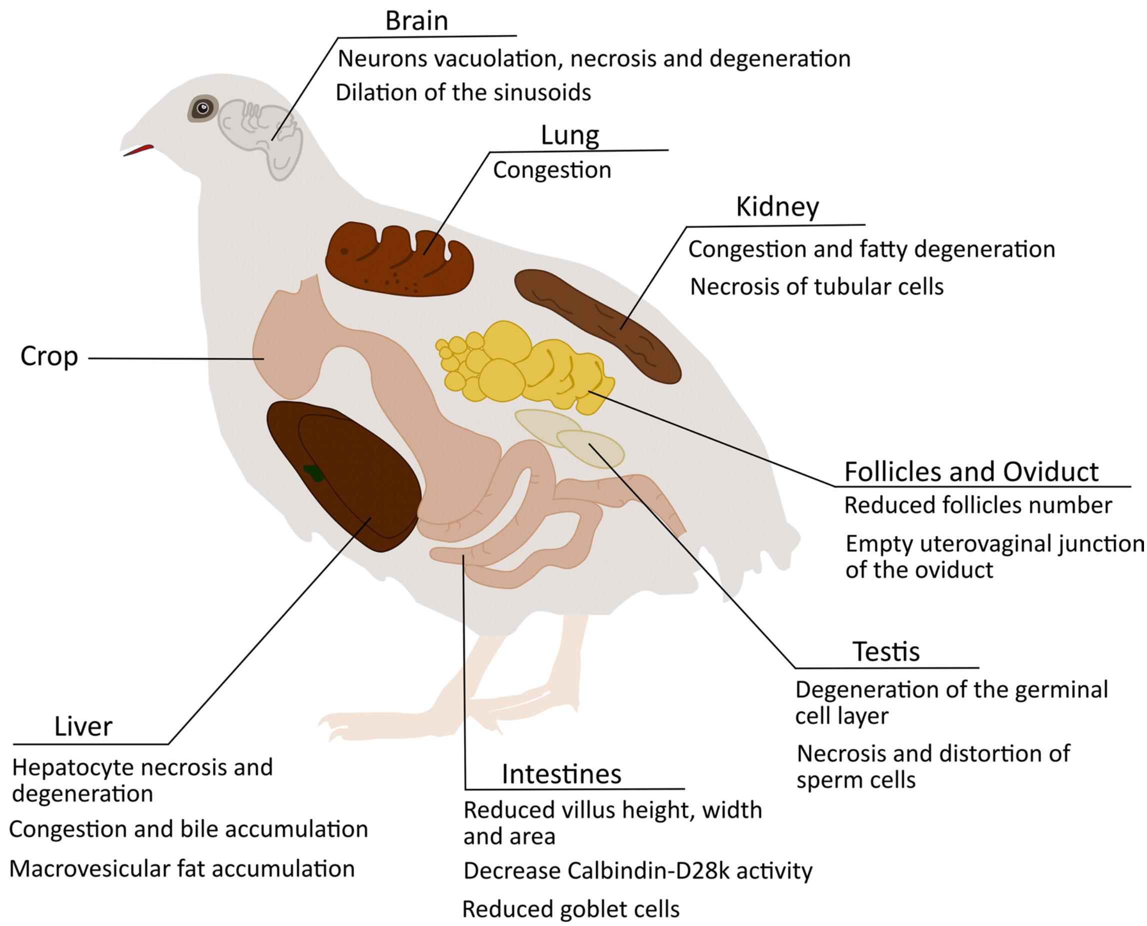

Fig. 3 A diagram of the Japanese quail showing the negative impact of heat stress on vital organs. Note that Calbindin-D28k is a calcium transporter channel, and its decreased activity will reduce calcium absorption

reported high lightness L* value, low redness a* and yellowness b* values (Imik et al., 2010; Jimenez & De Jesus, 2021; Jimenez et al., 2018; Kaplan & Koksal, 2021).

Heat-stressed quails showed signs of brain damage, including enlargement of blood sinusoids, vacuolation, necrosis and degeneration of the neurons (Mohamed et al., 2015; Shahri, 2020). In the spleen, heat stress caused lymphocyte infiltration; promoted necrosis, degeneration, disintegration, congestion and bleeding of the lymphatic nodules and pulp tissue (red and white); and dilated the sinusoids (Al-Ali et al., 2017). In addition, heat stress caused lung congestion (Mohamed et al., 2015) and degenerated pituitary gland cells (Sritharet et al., 2002). Finally, heat stress increased tonic immobility and asymmetric lengths of the beak, outer toe, eye, and nostril (Sarica & Ozdemir, 2018).

Phytochemicals used to mitigate heat stress

Some of the phytochemicals used to mitigate heat stress are listed below. Phytochemicals could act directly to scavenge reactive oxygen species or participate in the inflammatory process (see Fig. 4). In contrast, other phytochemicals contain natural antioxidants to enhance the antioxidant capacity but have no direct effect.

1. *Berberis vulgaris* has antioxidant and anti-inflammatory properties. It reduced hepatic MDA and improved antioxidant enzymes, NF-kB, HSP70, Nrf2 and HO-1 (Sahin et al., 2013).
2. Capsaicinoids contain an alkaloid that Inhibits lipid peroxidation and ROS generation. It reduced serum and ovarian MDA and improved antioxidant enzymes, NF-kB, protein kinase, Nrf2 and HO-1 (Sahin et al., 2017).
3. Rosemary oil has antioxidant and free radical scavenging activities. It improves the testicular weight, sperm count and gonado-somatic index. It decreased testicular MDA and increased rGSH, GSH-Px and CAT (Turk et al., 2016).

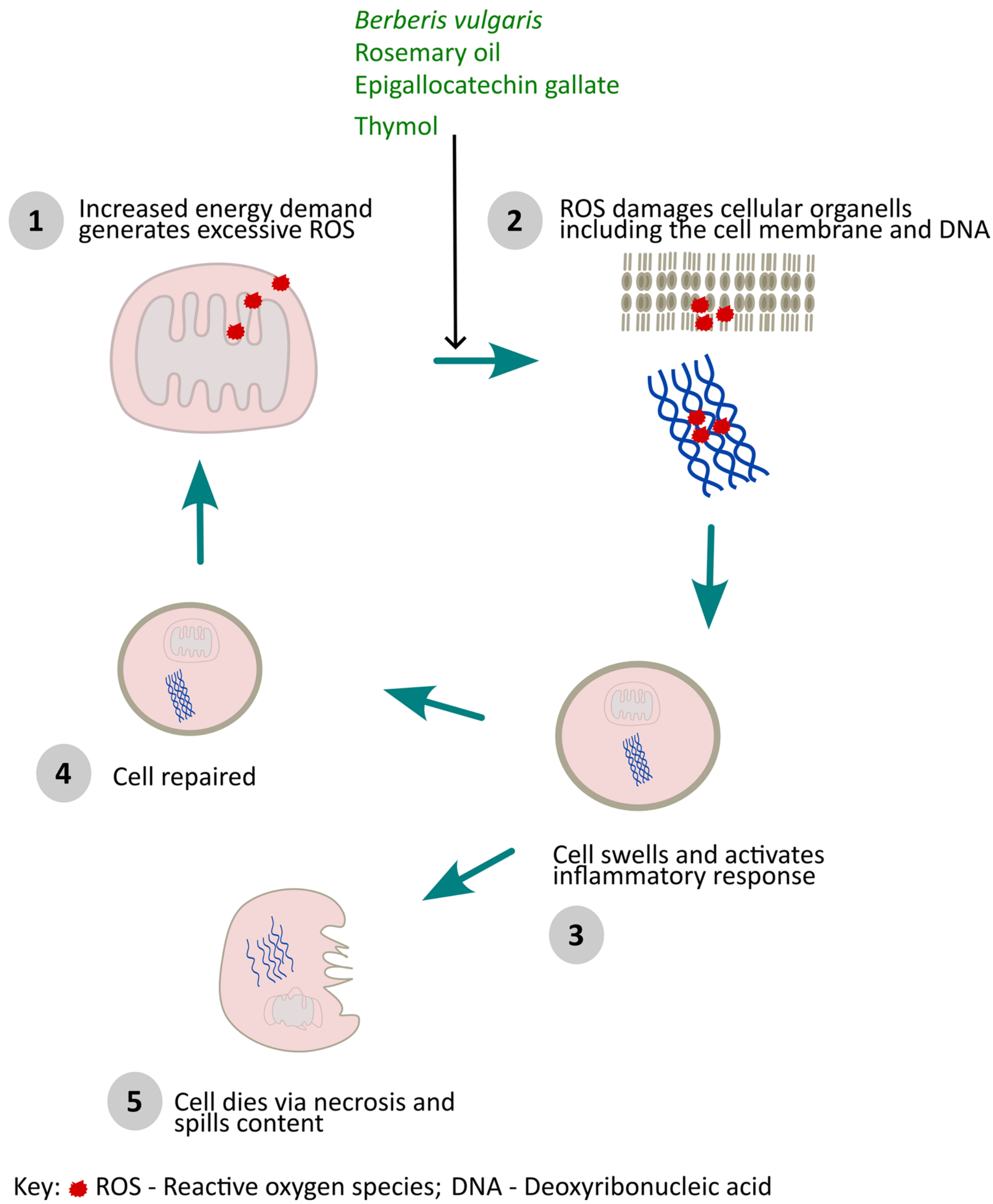

Fig. 4 A diagram of oxidative stress in heat stress showing the process of ROS generation and action. The phytochemicals shown (Berberis vulgaris, Rosemary oil, Epigallocatechin gallate and Thymol) have direct antioxidant action by scavenging ROS

4. Epigallocatechin gallate (EGCG) is found in green tea, and it has free radicals scavenging properties. It reduced hepatic expressions of COX-2, c-Jun and c-Fos, HSP60, HSP70 and HSP90 (Orhan et al., 2013).
5. Thymol has direct antioxidant activity. Its supplementation in birds' diets increased albumin concentrations and inflammatory responses; decreased antibody titers and H/L ratio (Nazar et al., 2019).
6. *Alchemilla vulgaris* contains high levels of flavonoids which activate antioxidant enzymes. Its addition to the quail diet improved egg production but not eggshell quality (Akdemir et al., 2019).
7. The microalgae *Arthrospira Platensis* contains vitamins, gamma-linoleic acid, phycocyanins, phenolic acids, beta-carotene, and chlorophyll. It decreased serum MDA and H/L ratio (Hajati et al., 2020).
8. Chromium is involved in carbohydrate, lipid and protein metabolism and enhances insulin actions

at the receptor level. It reduced serum cholesterol, MDA, NF-kB and HSPs 60, 70,90 (Akdemir et al., 2015). In addition, chromium improves feed intake, weight gain and final body weight. It inhibits hepatic NF-kB expression and increases IkBα (Orhan et al., 2012). It also enhanced egg production, humoral (SRBC, Newcastle) and cellular (PHA-P) immune response (Gitoee et al., 2018).

9. *Moringa oleifera* comprises significant concentrations of vitamins A, B, and C, proteins, phosphorus, calcium, flavonoids, carotenoids, tocopherols, selenium, and vitamin E. It improves feed intake, egg production, and weight gain (Abou-Elkhair et al., 2020).
10. Digestarom® is a blend of 8% peppermint, 2% eugenol or clove, 3.4% anethole or anise and thyme and sodium chloride. It improved weight gain and feed intake. It also enhances the H/L ratio and MDA. Improved cooking loss and water-holding capacity of the meat (Kaplan & Koksal, 2021).
11. The grape seed contains high tocopherol antioxidants. It reduced total plasma cholesterol, glucose, triglyceride, AST, and ALT levels. It also reduced hepatic and kidney MDA levels (Erişir et al., 2018).
12. Methionine is involved in the production of glutathione. It reduced MDA levels and increased GSH, GPx, and uric acid concentration activity (Del Vesco et al., 2014).
13. Selenium is involved in glutathione production and improves the expression of avian uncoupling protein (Del Vesco et al., 2017).
14. Alpha-lipoic acid is involved in the cycling of antioxidants, including vitamins C and E and GSH. It reduced MDA levels and increased GSH, Cat and SOD activity (Halici et al., 2012).
15. Worker honeybees produce propolis, but its specific antioxidant activity is unknown. It improves feed intake and live weight gain; alleviates intestinal desquamation and increases crypt depths; decreases corticosterone, MDA, and TNF-α and increases levels of T3 (Mehaisen et al., 2017, 2019).

Discussion

We found that heat stress harm the intestines, liver, spleen, kidney, male and female reproductive organs, lungs, and brain. These negative impacts of heat stress on several organs of the Japanese quail affect its welfare and reproduction and can lead to mortality.

The decreased villus height and width of the intestines induced by heat stress (De Moraes et al., 2021) reduces the surface area for nutrient absorption affecting body weight gain. In addition, reduced Calbindin-D28k in the intestines (De Moraes et al., 2021) reduced calcium absorption causing low egg quality (Akdemir et al., 2019), the number of eggs, and the delay in egg lay (Mehaisen et al., 2019).

Liver cell death led to a widespread inflammatory response and fibrosis, causing steatosis, bile accumulation, degeneration and necrosis (De Moraes et al., 2021). These processes will end in liver failure and mortality. In addition, tubular cell necrosis leads to renal failure and loss of function. Perhaps the reason for reduced calcium reabsorption and excessive excretion of vitamins and minerals. The congestion of blood in the lungs might suggest increased shunting of blood to the lungs to extract oxygen for metabolism, or it could result from the increased respiratory rate. However, little information is available about the lungs. The biochemical analysis could not reveal any insight into the lungs; hence microscopy is the best option. The degeneration and necrosis of neurons in the brain (Mohamed et al., 2015; Shahri, 2020) could cause behaviour and sleep rhythm changes affecting several standard motor and sensory controls.

Furthermore, dead and abnormal sperm cells in the testis (Razooqi et al., 2019) and decreased hierarchical follicle number in the ovary (Pu et al. 2019a) will affect reproduction. Immune system compromise results from damage in the spleen and the lymphocytes. Muscle colour affects the overall customer appeal to meat products, which heat stress has ruined.

Although we extracted these effects from several reports, it translates to one Japanese quail exposed to heat stress. Thus, depending on the intensity and duration of the heat, if one could study all the organs in an exposed quail, several organs would be affected simultaneously. An investigator could only focus on one organ at a time, and the limited resources could not allow a detailed study of some organs, hence the need for more studies in this area of research.

However, dietary strategies help mitigate the effect of heat stress in Japanese quail. For example, Erişir et al. (2018) suggested that grape seed has high tocopherols content and was able to reduce malondialdehyde (MDA), aspartate transferase (AST) and alanine transferase (ALT) levels in heat-stressed quails. In Fig. 4, we showed some phytochemicals that directly fight the reactive oxygen species; details of phytochemicals used to mitigate heat stress are provided in the results section.

Studying microscopic changes will elucidate underlying physiological and functional derangements caused by heat stress. For example, histochemical staining of the brain will elaborate on the neurons involved in the behavioural changes seen in Japanese quail exposed to heat stress (Soares et al., 2019). But no immunohistochemical study of the brain was identified by this scoping review.

A detailed ultrastructural study of the blood-gas barrier will elucidate the evaporative cooling mechanisms and pathological changes in the lungs of the Japanese quail during heat exposure. However, no histological record on the Japanese quail lungs was found in this review, except for the lung congestion reported (Mohamed et al., 2015). The statement was unclear whether the lung congestion was seen at gross or light microscopy level, and no micrographs were provided. Furthermore, the lungs receive a large volume of direct hot air during exposure because of its involvement in evaporative cooling; hence will require an additional strategy to cool the air.

Limitations of the scoping review

This scoping review was limited to full texts that were written in the English language. It is anticipated that valuable information was excluded from a full text written in Portuguese (Porto & Fontenele-Neto, 2020). The search query was developed in English, which by default might not identify records in which the title, abstract and full text were not in English, as such valuable records might not be identified. In addition, some records might not be indexed in any of the databases and grey literature sources that were searched; hence could be missed. A valuable paper (Mohamed et al., 2015) was found while searching the references of the full texts retrieved for second-level screening, which was not identified by database searches.

The findings of this study were limited to gross and light microscopic observations, two studies reported immunohistochemical analysis (De Moraes et al., 2021; Turk et al., 2015), but no ultrastructural result was seen in any of the records.

Conclusions

Heat stress threatened the Japanese quail's welfare and survival. Microscopic findings include cellular death (necrosis) in vital organs—liver, kidney, brain, testis, ovary, spleen and pituitary gland—affecting the normal functioning of the organs. In addition, the review identified some baseline information which could guide future research related to Japanese quail and heat stress. It means there is a shortage of microscopic information on the effects of heat stress on Japanese quail organs.

Abbreviations

ALT	Alanine transferase
AST	Aspartate transferase
CAT	Catalase
COX-2	Cyclooxygenase 2
GSH-Px	Glutathione peroxidase
H/L	Heterophil/lymphocyte ratio
HO-1	Haem-oxygenase 1
HSP	Heat shock proteins
IκBα	Nuclear factor of kappa light polypeptide gene enhancer in B cells alpha
MDA	Malondialdehyde
NF-κB	Nuclear factor kappaB
Nrf2	Nuclear factor (erythroid-derived) like 2
OSF	Open science framework
PHA-P	Phytohaemagglutinin-P
ROS	Reactive oxygen species
SOD	Superoxide dismutase
SRBC	Sheep red blood cell
TNF-α	Tumor necrosis factor alpha
UCP	Uncoupling protein

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41936-023-00331-z.

Additional file 1. Appendices of the scoping review.

Acknowledgements

The Authors acknowledged the financial support of NRF, South Africa and TETFUND, Nigeria, which made the study possible.

Author contributions

AA and DR contribute equally to conceptualising the idea and conduct of the review and all authors have read and approved the final manuscript.

Funding

No funding was received.

Availability of data and materials

The data are available from the corresponding author upon request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Received: 19 January 2023 Accepted: 27 February 2023
Published online: 05 March 2023

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