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Protective Role of Flavonoid on Histological Architecture of Kidney and Enzymatic Functions of Liver in Heat-Stressed Male Mice

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Abstract: The current study of the evaluation of renal and hepatic function of male mice exposed to the stressed environment condition. In the experiment design, twenty-four male mice have been divided into three groups: the control group drenched normal saline, the stressed group drenched normal saline and kept for 3 weeks, and the flavonoid group drenched flavonoid 25 mg/kg b.w. for 3 weeks. After 24 hours of flavonoid administration, synthesized mice with kitamine were subjected for blood draining to measurement serum MDA, GPx, AST, and ALT as well as to collection the kidney specimens for histology. The result of serum antioxidant enzyme MDA and GPx among groups of experiment showed highly significant effect between stressed group under heat stress and control. The decrement of serum MDA in the flavonoid group showed a significant effect when compared with the stressed group, while there was a slightly significant difference between the control and flavonoid groups showed significant decreased serum GPx of stressed group, while increase in serum GPx of flavonoid group were seen compared to stressed group, and slightly significant between control and flavonoid group. The result of hepatic function referred to effect of stressed on liver significant elevation in serum AST and ALT of stressed in comparison to other groups. Histopathalogical effects of stressed environment on renal tissues showed influx of the inflammatory cells to the renal tissues and epithelial degeneration appears. Also, hemorrhage, edema, fatty degeneration and accumulation of inflammatory cells were observed. Flavonoid administration to the adult male mice showed decreased effects of stressed on renal tissues through reduction inflammatory cells, edema, hemorrhage and epithelial cell degeneration when compared with the stressed group. In conclusion, the experiment referred to the effects of stressed environmental conditions on cellular activity through effects on cellular enzymes, cell membrane regulation, and metabolism.

Keywords: Antioxidants, Environmental conditions, Malondialdehyde, Glutathione peroxidase, Liver function, Iraq.

Introduction

Stressed environmental conditions have various impacts to tissues functions of different body organs through an imbalance in the antioxidant systems glutathione and MDA and upregulation of the hepatic enzymes ALT and AST. These results refer to the downregulation of the antioxidant system and the upregulation of serum hepatic enzymes (Chen et al., 2023; Ding et al., 2023; Hu et al., 2023). Stressed environmental conditions cause liver injury, which is the most common complication in animals and leads to disturbances in liver function and metabolism due to increased cellular reactive oxygen species (ROS) that disrupt cell enzyme function and cellular oxidative stress. These mechanisms refer to effects on mitochondrial function and disturbances in the cellular antioxidant system and apoptotic pathway that cause apoptosis and autophagy in hepatic tissues showing elevation to pro-inflammatory cytokines and lipid peroxidation (Cheng et al., 2019; Emami et al., 2020; Ji et al., 2024; Kabiri-Arani et al., 2024; Rahmani et al., 2024). Stressed environment causes heat shock protein stimulation to protect cellular damage from oxidative stress, on the other hand, the relationship between cellular metabolism energy and hypothalamus pituitary adrenal axis to regulation of cellular environment refers to the role of oxidative stress through enhanced reactive oxygen species and inflammatory responses that cause cellular hepatic damage (Balakrishnan et al., 2023; Kizir et al., 2024; Madkour et al., 2024; Yang et al., 2024).

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Renal function regulation of the cellular plasma in the body, a stressed environment leads to decreased renal plasma due to decreased renal blood flow through stimulation of the renin angiotensin aldosterone system (RAS); these mechanisms cause vasoconstriction of renal vessels (Hansson et al., 2020; Wesseling et al., 2020; Chapman et al., 2021; Rebez et al., 2023). Stressed environments affect cellar function through increased free radicals resulting from cellular oxidative stress, which leads to downregulation of the antioxidant system and upregulation of the apoptotic pathway, leading to renal cell apoptosis and enhanced cytokine levels with inflammatory reactions causing renal damage (Imbabi et al., 2023; Ke et al., 2024; Wang et al., 2024). In addition, the effects of heat stress on blood platelets due to a reduction plasma fibrinogen and platelet aggregation (Ke et al., 2024). Histopathological analysis of renal tissues showed cellular influx of neutrophils, basophils, and lymphocytes; cellular aggregation led to edema, hemorrhage, and inflammation. Beside this, fatty degeneration of renal epithelial tubules and chronic exposure to heat stress lead to renal failure caused by necrosis and degeneration of renal tubules (Chen et al., 2020; Chapman et al 2021).

Methodology

The experiment has been conducted healthy twenty four male mice weighted 34 ±2 gm aged 2 month. A total of 24 adult male mice were randomly divided into three equal groups (8 mice/ group) were intubated daily by using gavage and handled for three weeks. Control group were intubated normal saline and kept at 22 ±1, heat-stressed group were drenched normal saline and kept at 32 ±1 for 3 weeks, flavonoid group were intubated flavonoid 25 mg/kg b.w. daily and kept at 32 ±1 for 3 weeks. After end of experiment animals synthesized with kitamine 100 mg/kg b.w. and xylazine 10 mg/kg b.w. serum collected from centrifuged blood to estimate serum (MDA, GPx, ALT, and AST) and took kidney sample for histopathological examination, and kept at 10% formalin.

Statistical analysis

The result of the experiment was analyzed by graph pad prism program compression performed using one-way ANOVA to detect significant differences between values of study groups at $p< 0.05$ (Gharban, 2023).

Result

The result of serum antioxidant enzyme MDA and GPx among groups of experiment showed highly significant ($p<0.05$) effect between stressed group under heat stress and control. The decrement of serum MDA in flavonoid group showed a significant ($p<0.05$) effect when compared with the stressed group, while there was a slightly significant ($p< 0.05$) difference between the control and Flavonoid groups figure 1. In the figure 2 showed significant decreased serum GPx of stressed group when compared with control, while significant increase of serum GPx of flavonoid group when compared with stressed group, and slightly significant between control and flavonoid group. The result of hepatic function referred to effect of stressed on liver (Figures 3 and 4) significant elevation in serum AST and ALT in stressed group compared to others. Histopathalogical effects of stressed environment on renal tissues (Figure 5) showed influx of the inflammatory cells to the renal tissues and epithelial degeneration appears compared to others (Figure 5C) so that, hemorrhage, edema, fatty degeneration and accumulation of inflammatory cells when compared to control. Flavonoid administration 25 mg/kg b.w. to the adult male mice showed decreased effects of stressed on renal tissues through reduction inflammatory cells, edema, hemorrhage and epithelial cell degeneration compared to stress group (Figure 5 Q).

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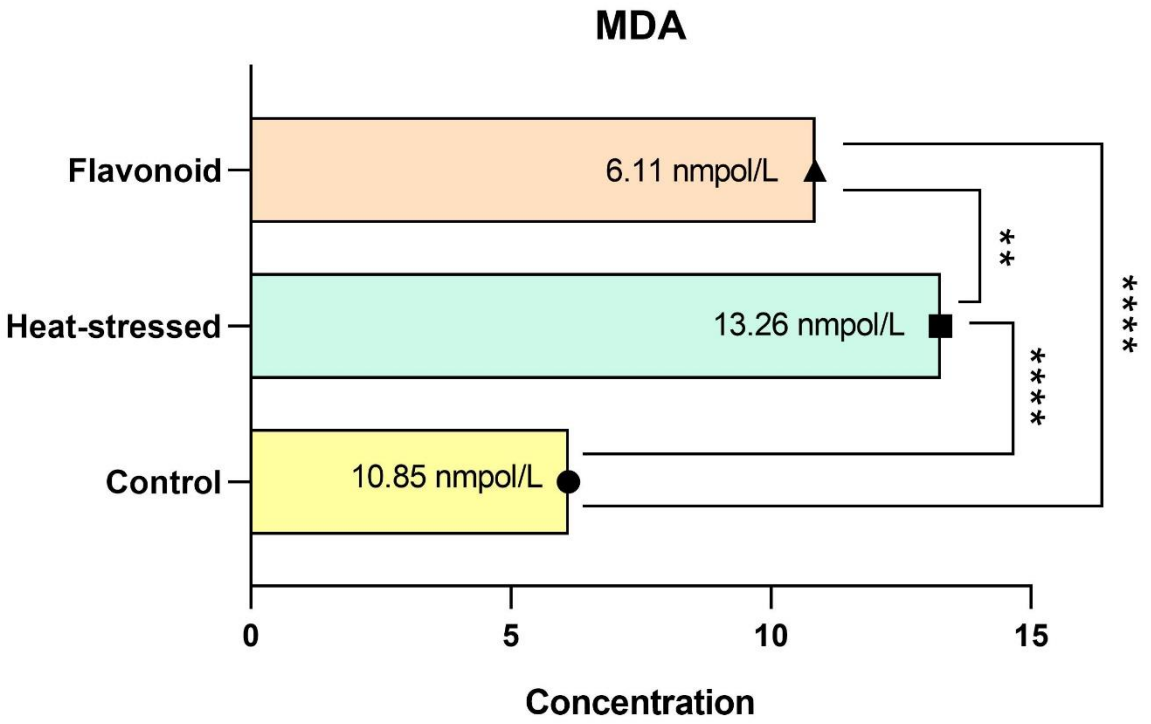

Figure 1: Effect of stress on serum MDA

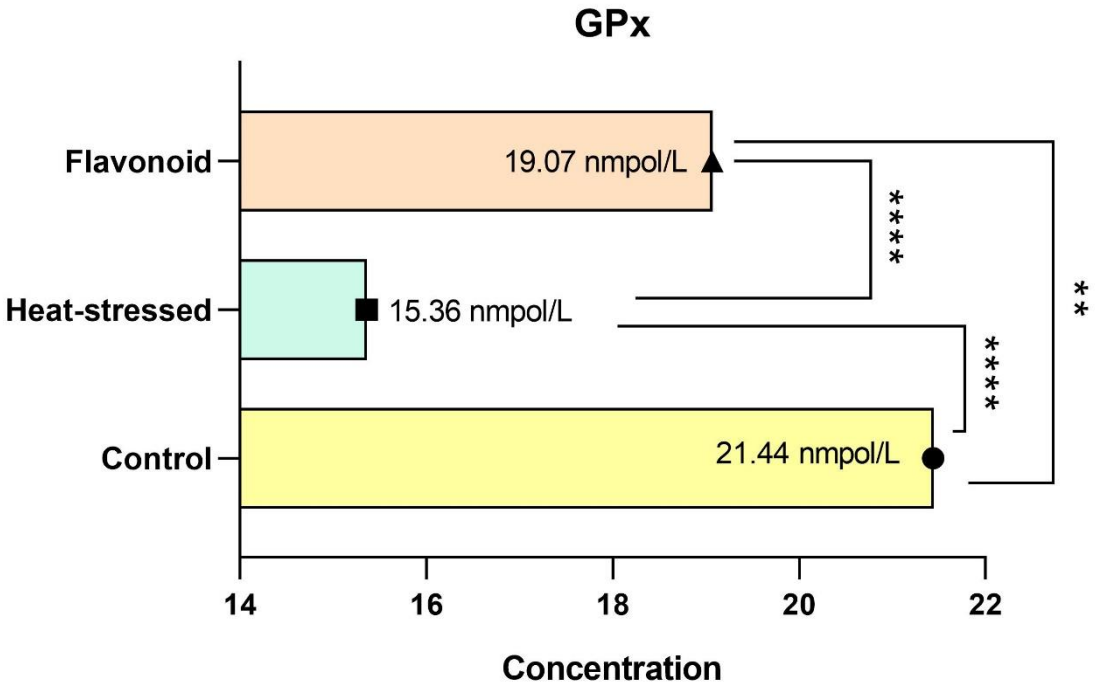

Figure 2: Effect of stress on serum GPx

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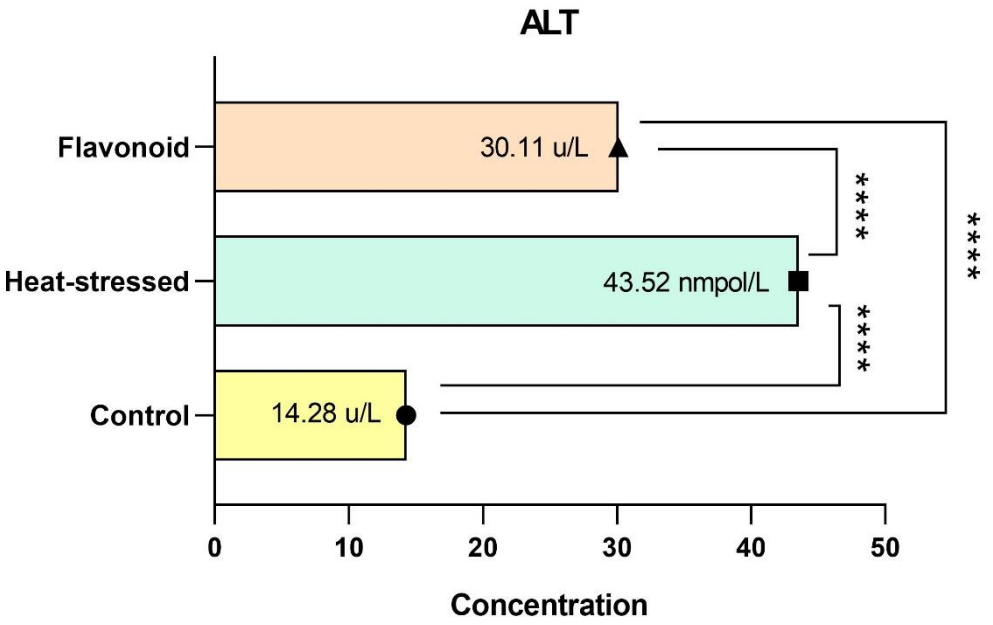

Figure 3: Effect of stress on serum ALT

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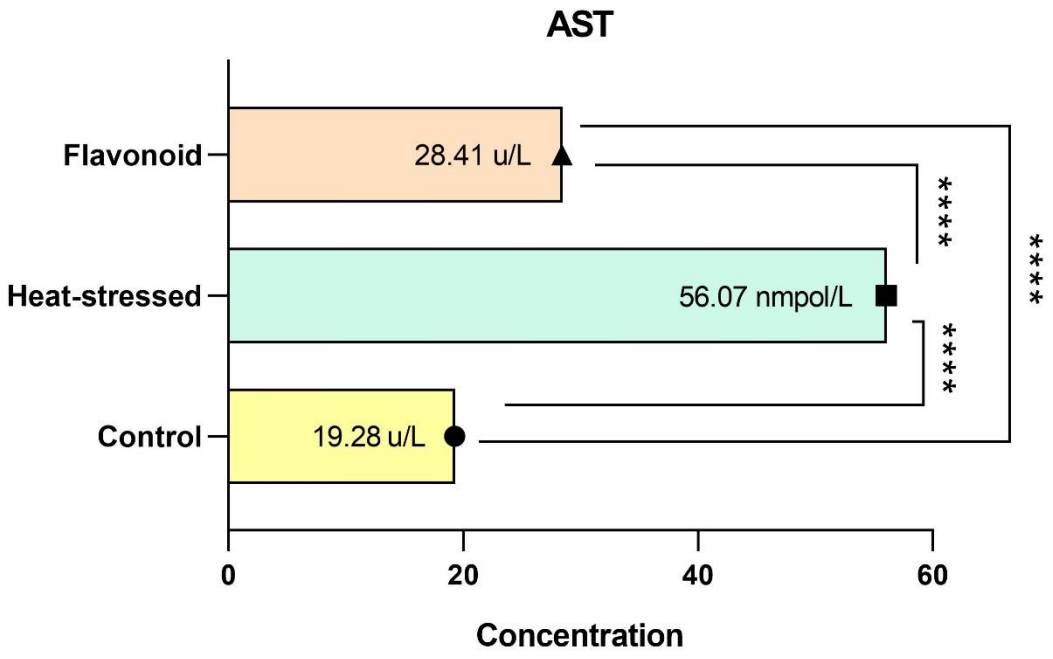

Figure 4: Effect of stress on serum AST

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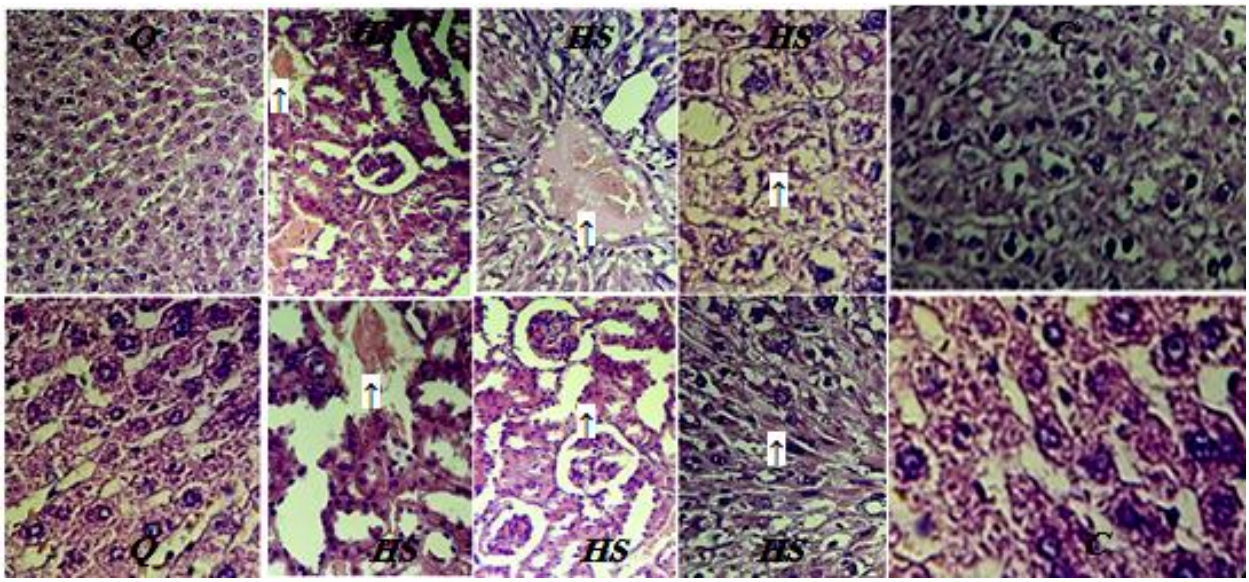

Figure 2: Renal histology in study mice

Discussion

The result of the experiment confirm to the effects of stressed environmental condition on the physiological function of liver and kidney, the result of serum antioxidant record effects of heat stress on lipid peroxidation due to significant increase of serum MDA in stressed group when compared with the control group, while significant decrease in serum GPx when compared with the control group, these result referred to the effects of stressed environment condition on the antioxidant system and apoptotic pathway lead to influx of free radicals causes cellular oxidative stress through enhancement in reactive oxygen species, these material effect on mitochondrial metabolism regulation and causes apoptosis to the renal and hepatic cells (Malyar, et al., 2020; Delkhosh, et al., 2021; Aderao, et al., 2023; Chinko, and Umeh, 2023; Mbepera, et al., 2023; He, et al., 2024; Li, et al., 2024). So, the study showed the effects of stress on the function of hepatic and renal cells through an increase in serum ALT and AST. The result referred to a significant effect of the stressed group when compared with the control group of serum ALT and AST. These findings confirm the role of the stressed environment on cellular function through a downregulation of antioxidants, an upregulation of lipid peroxidation, and an increase in free radicals and oxygen species that effect cell membrane function and lead to the efflux of enzymes out of the cell (Malyar et al., 2021; Zhang et al., 2022; Ding et al., 2023; Rahmani et al., 2024; Yang et al., 2024).

On the other hand, the result of the experiment recorded the role of Flavonoid on cellular function regulation to decrease the effect of oxidative stress and free radicals result from a stressed environment through downregulation of lipid peroxidation reduction serum MDA and upregulation of glutathione peroxidase. These mechanisms ensure the effect of Flavonoid on cellular mechanism through a decrease oxygen species and free radicals that cause disturbances in cellular function. The experiment result was a decrease in serum MDA of the Flavonoid treatment group when compared with the stressed group and an increase in serum GPx of the Flavonoid group when compared with the stressed group. The result referred to the administration of Flavonoid as an antioxidant and cellular protective role (Alsharidah et al., 2021 ; Khalifa et al., 2021; Almatroodi et al., 2021; Ghonim, 2023; Abd El-Hamid et al., 2024; Manoharan et al., 2024). In addition, the role of Flavonoid treatment in regulating cellular activity through regulation of ALT and AST cellular enzymes refers to the effect of Flavonoid on cellular function and enzyme regulation through reduction of free radicals and oxygen species that disrupt cell membrane function. The experiment result showed a significant effect of Flavonoid on oxidative stress through downregulation of serum ALT and AST when compared with the stressed group. These results confirm the effects of flavonoid on cellular mechanism regulation and protection from oxidative stress and reactive oxygen species (Ghonim et al., 2023; Caglar et al., 2024; Hafez et al., 2024; Raghunandhakumar et al., 2024). The result of the renal histopathologic section showed

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effects of heat stress on renal tissue through a significant influx of inflammatory cells, hemorrhage, edema, and degeneration of tubule epithelial cells. These referred to disrupting balance between the antioxidant system and oxidants that lead to increased lipid peroxidation, free radicals, and reactive oxygen species that cause disturbances in the apoptotic pathway that resulted in the degeneration and accumulation of inflammatory cells (Hansson et al., 2020; Khalil et al., 2020; Chapman et al., 2021). Admiration of Flavonoid 25 mg/kg b.w. daily for three weeks reduced the effects of heat stress on renal tissues through decreased inflammatory cells and degeneration when compared with the control group. These mechanisms referred to the effects of Flavonoid on regulation of the cellular antioxidant system and the apoptotic pathway that decreased inflammatory cell influx and degeneration (Alsharidah et al., 2021; Ashour et al., 2021).

Conclusion

The result of the experiment referred to the effects of stressed environmental conditions on cellular activity through effects on cellular enzymes, cell membrane regulation, and metabolism. That results in the effect of heat stress on lipid peroxidation, hepatic function, and renal function through effects on serum MDA, GPX, ALT, and AST, so it effects on histopathological examination of renal tissues influx of inflammatory cells and degeneration, while administration of flavonoid reduces the effects of the stressed environment condition through stimulating the antioxidant system and regulating the apoptotic pathway, leading to decreased lipid peroxidation and degeneration through reduction of inflammatory cells.

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