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Effects of the Anthocyanin Compound (Cyanidin-3-Glucoside) on Some Histological and Physiological Parameters Related to the Heart in Male Rats Exposed to Oxidative Stress

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ABSTRACT

The increasing incidence of heart disease due to an unhealthy diet rich in fats has encouraged the use of plant extracts, which have shown efficiency in improving body immunity and promoting human health. The current study was designed to investigate the effect of anthocyanin cyanidin-3-glucoside on some physiological and histological parameters related to the heart in white male rats exposed to oxidative stress with hydrogen peroxide. The study included 48 adult male white rats with a weight range of 200-300 g, and an ages range of 8-12 weeks. The rats were randomly divided into six groups of eight rats per group. Group 1 was considered a negative control group supplied with water and the basal diet for 30 days. Group 2 was a positive control group in which the rats were given drinking water containing hydrogen peroxide at a concentration of 1%. The third group orally received cyanidin-3-glucoside at a concentration of 50 mg/kg. The fourth group received both cyanidin-3-glucoside compounds at a concentration of 70 mg/kg and drinking water containing hydrogen peroxide at a concentration of 1%. The fifth group was dosed orally with a cyanidin-3-glucoside only at a concentration of 50 mg/kg, and the sixth group was dosed orally with a cyanidin-3-glucoside at a concentration of 70 mg/kg. At the end of the experiment, the animals were anesthetized, then blood samples were collected from the heart directly to obtain serum for measuring the levels of troponin, lactate dehydrogenase (LDH), and creatine kinase (CK-MB). The results showed a significant increase in troponin, LDH, and CK-MB levels in the positive control group compared to the negative control group. However, there was a significant decrease in the level of these enzymes in the third and fourth groups, compared to the positive control group. The fifth and sixth groups demonstrated a significant decrease, compared to the positive control group. However, they revealed a nonsignificant difference in the levels of these parameters, compared to the negative control group. The obtained results indicated that the cyanidin-3-glucoside compound positively prevented heart muscle damage caused by oxidative stress.

Keywords: Anthocyanin compound, Heart, Hydrogen peroxide, Male rats, Oxidative stress, Physiological parameter

INTRODUCTION

The composition of diet plays a key role in the initiation and development of cardiovascular diseases and also acts as an important factor in lifestyle to prevent these and other diseases. Cardiovascular diseases (CVD) are disorders that affect the heart and blood vessels and represent the main cause of disease and mortality worldwide (Libby et al., 2011; Bokov et al., 2022; Hafsan et al., 2022). Data from epidemiological and clinical studies have shown a negative relationship between the development of CVD and diets rich in fruits and vegetables (Tang et al., 2017; Zhao et al., 2017; Ansari et al., 2022).

Numerous reports have indicated that fruits and vegetables rich in flavonoids contribute to cardiovascular health as these compounds can exhibit anti-inflammatory, anticoagulant, and antioxidant activities through complex mechanisms (Cassidy et al., 2011; Tang et al., 2017; Zhao et al., 2017). Flavonoids can interact with cell membranes, which leads to changes in their structure and physical and chemical properties (Oteiza et al., 2005). This can alter cell function, interfere with and modulate the activities of enzymes and transcription factors, and affect gene expression (Krga et al., 2016; Krga et al., 2018; Huldani et al., 2022).

Epidemiological evidence suggests that dietary intake of flavonoid-rich foods is associated with a lower incidence of CVD (Hooper et al., 2008; Dohadwala and Vita, 2009; Zadeh et al., 2022). An imbalance of oxidative stress and cellular reduction is believed to cause endothelial dysfunction (Paravicin and Touyz, 2006). Therefore, the protective properties of flavonoids for the cardiovascular system are mainly related to their antioxidant activities (Perez-Vizcaino et

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al., 2006; Perez-Vizcaino et al., 2009) directly by scavenging free radicals or indirectly as inducers of antioxidant enzymes (Schewe et al., 2008).

Flavonoids include most of the biologically active molecules found in fruits and vegetables, such as anthocyanins, which are water-soluble pigments responsible for giving the red, blue, and purple color to fruits, flowers, seeds, and vegetables (Khaki et al., 2010; Khoo et al., 2017; Zainab and Qasim, 2021). Anthocyanin is one of the natural and effective colors in reducing the danger of free radicals. It is a natural alternative to industrial antioxidants, which raised many doubts about its health safety (Yang et al., 2011).

Anthocyanins have been widely used in food manufacturing. Studies have focused on biological activities and their health effects through medical applications since they are important sources of antioxidants, besides having a high inhibitory ability against microorganisms, which increase the duration of food preservation (Pazmino-Duran et al., 2001; Kuntz et al., 2014; Martin et al., 2017). Numerous studies have also been conducted on its health effects on humans in reducing cardiovascular diseases and anti-carcinogen factors and inflammation (Cassidy et al., 2011). In addition to having good color ability due to its high stability in storage conditions, it has been used as a safe and effective food coloring (Strack and Wray, 1994).

Due to an unhealthy diet rich in fats, there has been an increase in the incidence of CVD among individuals. On the other hand, there has been a growing interest in using plant extracts to improve the body immunity and human health since they contain phytochemical compounds in high concentrations, especially anthocyanin pigment. With this in mind, the current study aimed to evaluate the ability of an anthocyanin type (cyanidin-3-glucoside) to reduce the oxidative stress induced by hydrogen peroxide at a concentration of 1% in adult male albino rats.

MATERIALS AND METHODS

Experimental animals

Ethical approval

This study was confirmed by the ethical committee of the University of Al-Qadisiyah, Iraq. The authors followed the rules related to the rights of animals during the study. In the present experiment, 48 male Albino rats of the *Rattus norvegicus* strain were used. The rats were within the age range of 8-12 weeks and had a weight range of 200-300 g. They were placed in plastic cages; each cage had a metal cover, a clamp fitted with a water bottle, and a place to put food. The cage floor was covered with sawdust, which was replaced periodically to maintain the cleanliness of the rats while cleaning the litter of cages was done three times a day. The high-protein ration was used to feed the rats freely. The animals were subjected to controlled laboratory conditions for water, ventilation, and lighting for 12 hours of light and 12 hours of dark under temperature (26±2) for 30 days.

Study design

In the current study, 48 male adult white rats were used, randomly divided into six groups and two replicates for each group (Four rats in each replicate). The first group (G1) was a negative control group that received water and food *ad libitum* for 30 days. The rats in the second group (G2), the positive control group, received the rations but drinking water containing hydrogen peroxide at the concentration of 1% using special drinking bottles. The third group (G3) received drinking water containing hydrogen peroxide at a concentration of 1% and Cyanidin-3-glucoside at a concentration of 50 mg/kg (Chayati et al., 2019). The fourth group (G4) took orally drinking water containing hydrogen peroxide at a concentration of 1% and Cyanidin-3- glucoside at a concentration of 70 mg/kg (Chayati et al., 2019). The fifth group (G5) was given Cyanidin-3-glucoside orally at a concentration of 50 mg/kg. Finally, the rats in the sixth group (G6) received Cyanidin-3-glucoside compound at the concentration of 70 mg/kg.

At the end of the experiment, the animals were anesthetized using chloroform, and then blood samples were taken immediately from the heart directly through a sterile 2-ml syringe; then it was placed in clean test tubes free of anticoagulant and left for 15-20 minutes at laboratory temperature. Therefore, the samples were centrifuged at 3000 rpm for 15 minutes the serum. The serum was kept at -20°C to measure enzyme levels.

RESULTS

Troponin level

Regarding troponin changes, the results of the current study indicated a significant increase in the G2-positive group treated with 1% hydrogen peroxide compared to the G1-negative control group ($p < 0.05$; Table 1). Moreover, there was a significant decrease in G3, compared to the G2-positive group, G1-negative control, and other experimental groups ($p < 0.05$). On the other hand, G4 showed a significant decrease, compared to G2, G1, and G5 ($p < 0.05$). A significant decrease was also observed in the G5 in comparison with the positive control group ($p < 0.05$), while no difference was observed when compared to the negative control ($p > 0.05$). In G6, there was a significant decrease in

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troponin level compared to the positive control group ($p < 0.05$), and there was no significant difference when compared to G1 and G5 ($p > 0.05$).

Table 1. The effect of Cyanidin-3-glucoside on the levels of troponin, creatine phosphokinase, and lactate dehydrogenase enzymes in male rats exposed to oxidative stress

Groups \ Parameters	LDH (U / I)	CK-MB (ng / ML)	Troponin (ng / ML)
G1	209.4 ± 21.2^{bc}	2.76 ± 0.73^{b}	3.67 ± 0.73^{b}
G2	277.7 ± 18.5^{a}	4.43 ± 1.55^{a}	4.1 ± 0.18^{a}
G3	211.4 ± 45.1^{bc}	3.07 ± 0.74^{b}	2.34 ± 1.02^{d}
G4	234.2 ± 54.2^{b}	1.72 ± 0.60^{c}	2.73 ± 0.56^{c}
G5	198.0 ± 22.5^{bc}	3.05 ± 0.51^{b}	3.12 ± 0.45^{b}
G6	183.7 ± 41.3^{c}	3.17 ± 0.70^{b}	3.01 ± 0.77^{bc}
L.S.D	42.51	0.835	0.31

The values represent the mean ± standard error. LDH: Lactate dehydrogenase, CK-MB: Creatine kinase, G1: A negative control group in which they received water and food *ad libitum*, G2: A positive control group that received the drinking water containing hydrogen peroxide at the concentration of 1%. G3: Received drinking water containing hydrogen peroxide at a concentration of 1% and Cyanidin-3-glucoside at a concentration of 50 mg/kg, G4: Received drinking water containing hydrogen peroxide at a concentration of 1% and Cyanidin-3- glucoside at a concentration of 70 mg/kg, G5: Received Cyanidin-3-glucoside at the concentration of 50 mg/kg, G6: Received Cyanidin-3-glucoside compound at the concentration of 70 mg/kg. Different letters within the same column indicate significant differences at the probability level $p < 0.05$.

Creatine kinase level

As can be seen in Table 1, there was a significant increase in the level of creatine kinase (CK-MB) in G2, compared to G1 and other groups ($p < 0.05$). The rats in G3 did not differ significantly from those in G1, G5, and G6 ($p > 0.05$) and recorded a significant decrease when compared to G2 ($p < 0.05$). There was a significant decrease in the level of creatine kinase (CK-MB) in G4 when compared to other groups ($p < 0.05$). Regarding G5, no significant was observed compared to G1, G3, and G6 ($p < 0.05$), while a significant decrease was recorded when compared to G2 ($p < 0.05$), and there was a significant increase ($p < 0.05$) in the level of CK-MB, compared to the fourth group treated with hydrogen peroxide and C3G dye at a concentration of 70 mg/kg. The rats in G6 did not differ from those in G1 and G3 in terms of CK-MB level ($p > 0.05$), while there was a significant decrease in the level of CK-MB level in compared to G2 ($p < 0.05$).

Lactate dehydrogenase level

Table 1 shows the results of the lactate dehydrogenase (LDH) enzyme in the six groups of this experiment. Accordingly, there was a significant increase in G2, compared to all groups ($p < 0.05$), while no significant difference was observed in G3 when compared with G1, G4, and G5 ($p > 0.05$). A significant decrease in LDH level was recorded in G3 when compared to G2 ($p < 0.05$). Moreover, G4 recorded a significant decrease in the level of LDH enzyme compared to G2 ($p < 0.05$); however, no significant difference was recorded when compared to G1, G3 and G5 ($p > 0.05$). As for G5 there was a significant decrease, compared to G2 ($p < 0.05$), while no significant difference was indicated compared to G1, G3, and G4 ($p > 0.05$). The results indicated a significant decrease when comparing G6 with G2 G3, and ($p < 0.05$), although no significant difference was shown in the level of the enzyme when comparing G1 with G5 ($p > 0.05$).

Histological changes in heart

The tissue sections of G1 taken from the heart showed normal cardiac muscle fibers with elongated nuclei and regular transverse layout Figure 1. As G2 was treated with 1% hydrogen peroxide, the histological sections of the heart showed clear pathological changes. The expanded space between the muscle cells, bleeding, and congestion are illustrated in Figure 2. The cardiac tissue section of G3 and G4 treated with C3G compound at a concentration of 50 mg/kg and 70 mg/kg and hydrogen peroxide 1%, respectively, showed a significant improvement in tissue with the spaces between the muscle cells figures 3 and 4. The tissue sections of the heart taken from G5 and G6 treated with C3G compound at a concentration of 50 mg/kg, and 70 mg/kg indicated the normal cardiac tissue in figures 5 and 6.

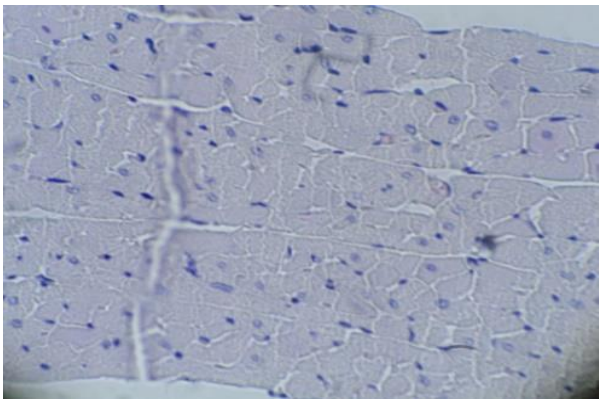

Figure 1. Normal heart tissue of a healthy rat. 40X (H&E)

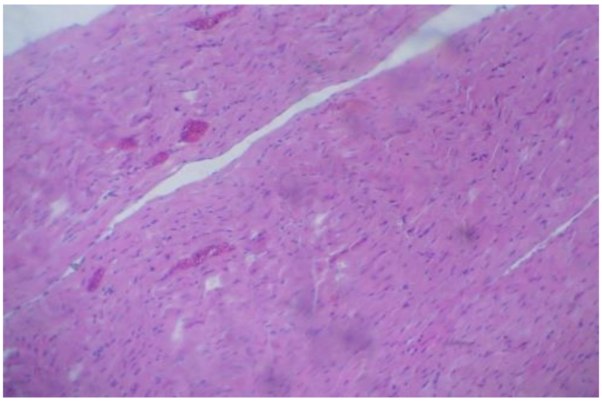

Figure 2. The heart tissue of a rat treated with 1% hydrogen peroxide. The congestion hemorrhage, and an expansion of the space between muscle cells are shown. 40X

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(H&E)

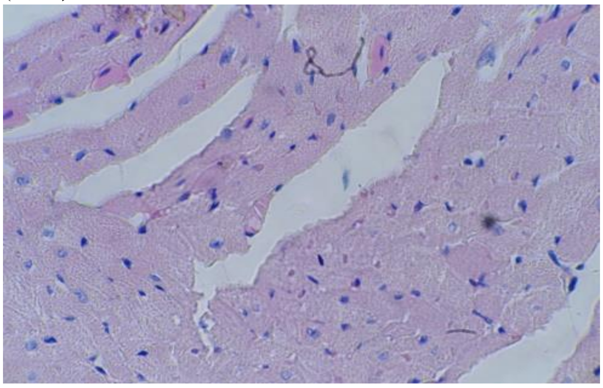

Figure 3. The heart tissue of a rat treated with Cyanidin-3-glucoside at a concentration of 50 mg/kg and hydrogen peroxide. The expansion of the space between muscle cells is obvious. 40X (H&E)

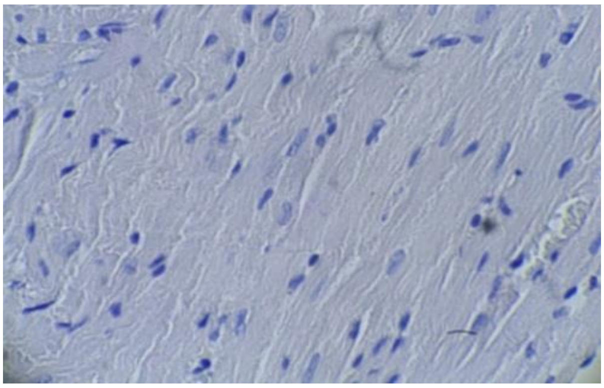

Figure 4. The heart tissue of a rat treated with Cyanidin-3-glucoside at a concentration of 70% mg/kg and hydrogen peroxide. The expansion of the space between the muscle cells is obvious. 40X (H&E)

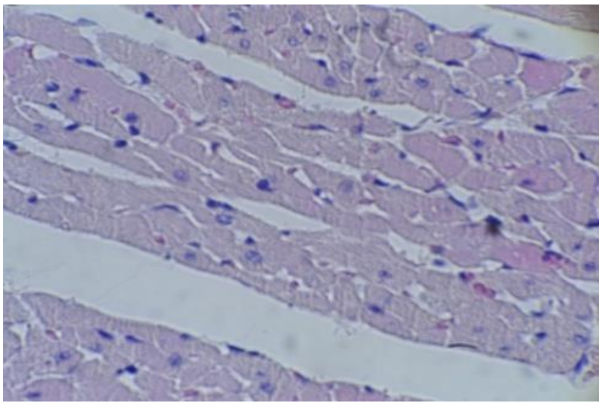

Figure 5. The heart tissue of a rat treated with Cyanidin-3-glucoside at a concentration of 50% mg/kg. 40X (H&E)

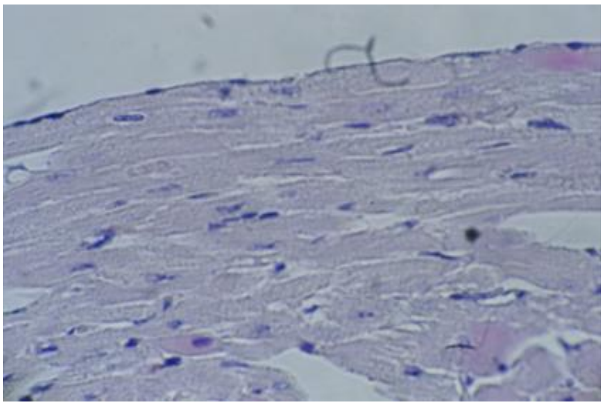

Figure 6. The heart tissue of a rat treated with Cyanidin-3-glucoside at a concentration of 70% mg/kg. 40X (H&E)

DISCUSSION

Troponin, CK-MB, and LDH are the enzymes related to cardiac activity. The increased level of each enzyme in the positive control group treated with hydrogen peroxide at a concentration of 1% could be evidence of damage to the heart muscle due to oxidative stress caused by free radicals. This risk may increase or develop into cardiomyopathy and heart failure later (Nimse and Pal, 2015). Membrane damage and leakage of Troponin, CK-MB, and LDH into cardiac tissue induced by hydrogen peroxide are prominent signs of experimentally induced myocardial infarction (Padmanabhan and Prince, 2006).

There was a significant decrease in the levels of CK-MB, Troponin, and LDH in the G3 and G4 groups compared to the positive control group. This could support reflect the positive role of Cyanidin-3-glucoside in terms of the ability to protect the heart and resist stress. Treatment with cyanidin extracted from red cabbage protected the heart through what was observed in the percentage of heart weight, a decrease in the level of CK-MB, troponin, and LDH an improvement in the levels of the antioxidant enzymes Superoxide Dismutase Catalase. In a study conducted by (Li et al., 2018), rats treated with cyanidin at a concentration of 5 mg/kg for five days before treatment with (LPS) for 18 hours showed a significant reduction of 30.4% and 30.6% in the levels of CK-MB and LDH, respectively.

Another study showed an improvement in cardiac function by treatment with cyanidin in rats that induced heart failure with doxorubicin (Petroni et al., 2017). Several reports have also indicated a protective role of cyanide against oxidative stress that induces myocardial and endothelial cell damage (Serraino et al., 2003; Qian et al., 2018).

Previous studies reported that the natural food component (cyanidin) plays an important role in the pre-death effect of oxidative cells in the heart muscle (Akhlaghi and Bandy, 2012), and they also reported that flavonoids reduced heart damage (Elberry et al., 2010; Hao et al., 2013). In another study by Mahmmoud (2013) on the profile of lipids and oxidative stress in animals treated with a high-calorie diet and with different concentrations (2.5%, 5%, 10%) of two types of blackberries, namely *Morus albal* and *Morus nigra* 4four weeks, they noticed a decrease in the levels of Nitric Oxide (NO) and Malondialdehyde (MDA) in *Morus albal* (10%, 5%) and *Morus nigra* group (2.5%, 5%, 10%). These fruits also increased the total antioxidant capacity at all used concentrations. The same results were obtained for fats.

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Compared to the control group, there was a significant decrease in total cholesterol, triglycerides, LDL, and VLDL and an increase in HDL in plasma. Consuming blackberries, which are rich in natural antioxidants, can prevent the risk of developing vascular diseases and reduce lipids and oxidative stress.

In a study by Sankhari et al. (2012), it was found that animals using an atherosclerosis-inducing diet plus red cabbage extract (rich in anthocyanins) showed a decrease in GSH, an increase in HDL-C and a decrease in liver enzymes (alanine transaminase and aspartate aminotransferase), compared to the group of animals in which atherosclerosis was induced arteries.

As for the G5 and G6 groups, there was a significant decrease in the levels of CK-MB, LDH, and troponin enzymes, compared with the positive control group. As an antioxidant, cyanidin, which can remove destructive molecules generated in the body (free radicals), destroys cell membranes and causes DNA changes and cell death. Cyanidin acts as an anti-inflammatory agent and helps protect the heart against disease (Ischizawa et al., 2011). Therefore, flavonoid cyanidin reduces damage to cardiac muscle cells and maintains the function of mitochondria, thus preventing heart muscle failure. Moreover, this substance can strengthen the immune system by supporting the main enzymes in the metabolic pathways in cells and removing free radicals that affect them (Faddah et al., 2013).

A study by Cara et al. (2017) demonstrated the high antioxidant capacity of gooseberry and gon-berry, which is consistent with studies showing that gooseberry contains high levels of anthocyanins and has antioxidant activity (Zheng and Wang, 2003; Grace et al., 2014; Isaak et al., 2015). Numerous reports have shown that antioxidant compounds, including anthocyanins, protect cells from apoptosis caused by oxidative stress through several mechanisms, including induction of autoinflammatory, inhibition of mitochondrial dysfunction, and activation of antioxidant enzymes. (Angeloni et al., 2007; Lv and Zhou, 2012; Kim et al., 2014; Lei et al., 2015).

Histological changes in heart

The tissue sections in G2 (positive control) showed an expansion in the space between muscle cells, blood bleeding, and clear congestion. Results reflect the negative cardiac tissue changes due to oxidative stress and species generation (Argun et al., 2015). Studies have indicated that free radicals of active oxygen species such as hydroxyl, hydrogen peroxide, and superoxide radicals lead to nucleolytic and programmed death (Kalivendi et al., 2001; Wang et al., 2004).

The generation of oxidative stress by hydrogen peroxide through drinking water leads to a significant increase in the activity of AST, ALT, and CK enzymes, in addition to damaging body tissues, including endothelial cells of vessels and cardiac muscle (Tao et al., 2006). The pathological changes in the tissue of the heart may be due to the fact that hydrogen peroxide can break down cell walls, which leads to the release of many chemicals that work to attract inflammatory cells to the area of injury (Zhu et al., 2018).

The tissue sections of the heart, which were taken from the third and fourth groups, showed significant improvement and residual negative effects in the tissues. This could be evidence of the recovery state after the tissue was exposed to hydrogen peroxide, as it is known that flavonoid intake is associated with a reduction of damage and muscle recovery (Hollinger et al., 2015). Rahman et al. (2007) indicated that flavonoids, such as anthocyanins and quercetin could activate the defense mechanism in cardiac cells. Flavonoids are effective in scavenging free radicals, reactive oxygen species (ROS), and reducing oxidative stress as well as their role in preventing the biosynthesis of enzyme proteins that contribute to reactions of oxidation–reduction where gene expression activates the synthesis of active proteins of cardiac muscle fibers to replace damaged proteins, are indicated.

A study by Li et al. (2018) showed the role of cyanidin in inhibiting oxidative stress resulting from treatment with the endotoxin LPS, where histological analyzes of myocardial tissues of the treated groups showed a significant increase in protein nitration. The quantitative estimation of the mentioned study showed an increase of 5.6 times, and treatment with cyanidin affected the decrease in LPS-induced protein nitrate by 26.6%. They also examined the state of intracellular oxidation and reduction by determining the amount of oxidized glutathione and reduced glutathione in myocardial tissues, where the endotoxin caused an increase in the level of oxidized glutathione up to 47.3% and also reduced the level of reduced glutathione up to 36.9%, the oxidized glutathione increased by 17.3% and reduced glutathione increased by 22.2%.

CONCLUSION

The treatment with H2o2 has led to oxidative stress in the heart tissue through indicators of cardiac parameters and histological changes. The treatment with C3G could positively affect the biochemical parameters and heart tissues induced by oxidative stress with hydrogen peroxide. C3G did not negatively affect the general health or the heart of the animals used in the study. This can be inferred in particular by the results in the two groups subjected to compound treatment. The results showed the effectiveness of C3G as an antioxidant through its ability to scavenge free radicals and protect cells from oxidative stress.

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DECLARATIONS

Competing interests

The authors confirm that they do not have any conflicts of interest.

Authors' contribution

Aseel Najah Sabour designed the study and critically revised the manuscript. Huda Yasser Aliwi brought the experimental animals and dosed them with the materials throughout the experiment. Aseel Najah and Huda Yasser performed the process of drawing blood from animals, as well as the process of dissection. Huda participated in the biochemical tests for blood serum and writing. Both authors checked and approved the final version of the manuscript for publishing in the present journal.

Ethical considerations

Ethical issues (including plagiarism, consent to publish, misconduct, data fabrication and/or falsification, double publication and/or submission, and redundancy) have been checked by the authors.

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REFERENCES

Akhlaghi M and Bandy B (2012). Preconditioning and acute effects of flavonoids in protecting cardiomyocytes from oxidative cell death. Oxidative Medicine and Cellular Longevity, 2012: 782321. DOI: https://www.doi.org/10.1155/2012/782321

Angeloni C, Spencer JPE, Leoncini E, Biagi PL, and Hrelia S (2007). Role of quercetin and its *in vivo* metabolites in protecting H9c2 cells against oxidative stress. Biochimie, 89(1): 73-82. DOI: https://www.doi.org/10.1016/j.biochi.2006.09.006

Ansari MJ, Jasim SA, Taban TZ, Bokov DO, Shalaby MN, Al-Gazally ME, Kzar HH, Qasim MT, Mustafa YF, and Khatami M (2022). Anticancer drug-loading capacity of green synthesized porous magnetic iron nanocarrier and cytotoxic effects against human cancer cell line. *Journal* of Cluster Science, 34: 467-477. DOI: https://www.doi.org/10.1007/s10876-022-02235-4

Argun M, Üzüm K, Sönmez MF, Özyurt A, Karabulut D, Soyersarıca Z, Çilenk KT, Unalmış S, Pamukcu Ö, Baykan A, et al. (2015). Cardioprotective effect of metformin against doxorubicin cardiotoxicity in rats. The Anatolian Journal of Cardiology, 16(4): 234-241. DOI: https://www.doi.org/10.5152/akd.2015.6185

Cara KI, Jay CP, Heather B, Karmin O, and Yaw LS (2017). Lingonberry anthocyanins protect cardiac cells from oxidative-stress-induced apoptosis. Canadian Journal of Physiology and Pharmacology, 95(8): 904-910. DOI: https://www.doi.org/10.1139/cjpp-2016-0667

Cassidy A, O'Reilly ÉJ, Kay C, Sampson L, Franz M, Forman J, Curhan G, and Rimm EB (2011). Habitual intake of flavonoid subclasses and incident hypertension in adults. The American Journal of Clinical Nutrition, 93(2): 338-347. DOI: https://www.doi.org/10.3945/ajcn.110.006783

Chayati I, Sunarti, Marsono Y, and Astuti M (2019). Purple corn anthocyanin extract improves oxidative stress of rats fed high fat diet via superoxide dismutase mechanism. International Journal of Science and Research, 8(8): 1057-1065. Available at: https://www.ijsr.net/get_abstract.php?paper_id=ART2020413

Bokov DO, Jalil AT, Alsultany FH, Mahmoud MZ, Suksatan W, Chupradit S, Qasim MT, and Nezhad PDK (2022). Ir-decorated gallium nitride nanotubes as a chemical sensor for recognition of mesalamine drug: A DFT study. Molecular Simulation, 48(5): 438-447. DOI: https://www.doi.org/10.1080/08927022.2021.2025234

Dohadwala MM and Vita JA (2009). Grapes and cardiovascular disease. The Journal of Nutrition, 139(9): S1788-S1793. DOI: https://www.doi.org/10.3945/jn.109.107474

Elberry AA, Abdel-Naim AB, Abdel-Sattar EA, Nagy AA, Mosli HA, Mohamadin AM, and Ashour OM (2010). Cranberry (Vaccinium macrocarpon) protects against doxorubicin-induced cardiotoxicity in rats. Food and Cheimcal Toxicology, 48(5): 1178-1184. DOI: https://www.doi.org/10.1016/j.fct.2010.02.008

Faddah LM, Abdel Baky NA, Al-Rasheed NM, and Al-Rasheed NM (2013). Biochemical responses of nanosize titanium dioxide in the heart of rats following administration of idepenone and quercetin. African Journal of Pharmacy and Pharmacology, 7(38): 2639-2651. DOI: https://www.doi.org/10.5897/AJPP2013.3426

Grace MH, Esposito D, Dunlap KL, and Lila MA (2014). Comparative analysis of phenolic content and profile, antioxidant capacity, and anti-inflammatory bioactivity in wild alaskan and commercial vaccinium berries. Journal of Agriculture Food Chemistry, 62(18): 4007-4017. DOI: https://www.doi.org/10.1021/jf403810y

Hafsan H, Bokov D, Abdelbasset WK, Kadhim MM, Suksatan W, Majdi H, Widjaja G, Jalil AT, Qasim MT, and Balvardi M (2022). Dietary Dracocephalum kotschyi essential oil improved growth, haematology, immunity and resistance to Aeromonas hydrophila in rainbow trout (Oncorhynchus mykiss). Aquaculture Research, 53(8): 3164-3175. DOI: https://www.doi.org/10.1111/are.15829

Hao E, Lang F, Chen Y, Zhang H, Cong X, Shen X, and Su G (2013). Resveratrol alleviates endotoxin-induced myocardial toxicity via the Nrf2 transcription factor. PLOS One, 8(7): e69452. DOI: https://www.doi.org/10.1371/journal.pone.0069452

Hollinger K, Shanely RA, Quindry JC, and Selsby J (2015). Long-term quercetin dietary enrichment decreases muscle injury in mdx mice. Clinical Nutrition, 34(3): 515-522. DOI: https://www.doi.org/10.1016/j.clnu.2014.06.008

Hooper L, Kroon PA, Rimm EB, Cohn JS, Harvey I, Le Cornu KA, Ryder JJ, Hall WL, and Cassidy A (2008). Flavonoids, flavonoid-rich foods, and cardiovascular risk: Ameta-analysis of randomized controlled trials. The American Journal of Clinical Nutrition, 88(1): 38-50. DOI: https://www.doi.org/10.1093/ajcn/88.1.38

Huldani H, Jasim SA, Bokov DO, Abdelbasset WK, Shalaby MN, Thangavelu L, MargianaR, and Qasim MT (2022). Application of extracellular vesicles derived from mesenchymal stem cells as potential therapeutic tools in autoimmune and rheumatic diseases. International Immunopharmacology, 106: 108634. DOI: https://www.doi.org/10.1016/j.intimp.2022.108634

Isaak CK, Petkau JC, Karmin O, Debnath SC, and Siow YL (2015). Manitoba lingonberry (Vaccinium vitisidaea) bioactivities in ischemia-reperfusion injury. Journal of Agricultural *and* Food Chemistry, 63(23): 5660-5669. DOI: https://www.doi.org/10.1021/acs.jafc.5b00797

Ischizawa K, Yoshizumi M, Kawai Y, Terao J, Kihira Y, Ikeda Y, Tomita S, Minakuchi K, Tsuchiya K, and Tamaki T (2011). Pharmacology in health food: Metabolism of quercetin *in vivo* and its protective effect against arteriosclerosis. Journal of Pharmacological Sciences, 115(4): 466-470. DOI: https://www.doi.org/10.1254/jphs.10r38fm

Kalivendi WSV, Kotamraju S, Zhaao H, Joseph J, and Kalyanaraman B (2001). Doxorubicin-induced apoptosis is associated with increased transcription of endothelial nitric-oxide synthase. Journal of Biological Chemistry, 276(50): 47266-47277. DOI: https://www.doi.org/10.1074/jbc.M106829200

Khaki AA, Khaki A, Ahmadi-Ashtiani HR, Rastegar H, Rezazadeh S, Babazadeh D, Zahedi A, and Ghanbari Z (2010). Treatment effects of ginger rhizome & extract of carrot seed on diabetic nephropathy in rat. Journal of Medicinal Plants, 9(6): 75-80. Available at: https://jmp.ir/article-1-516-en.pdf

Khoo HE, Azlan A, Tang ST, and Lim SM (2017). Anthocyanidins and anthocyanins: Colored pigments as food, pharmaceutical ingredients, and the potential health benefits. Food & Nutrition Research, 61(1): 1361779. DOI: https://www.doi.org/10.1080/16546628.2017.1361779

Kim D, Kim B, Shin H, Kwon HJ, and Park E (2014). The protective effect of hispidin against hydrogen peroxide-induced apoptosis in H9c2 cardiomyoblast cells through Akt/GSK-3ß and ERK1/2 signaling pathway. Experimental Cell Research, 327(2): 264-275. DOI: https://www.doi.org/10.1016/j.yexcr.2014.07.037

Krga I, Milenkovic D, Morand C, and Monfoulet LE (2016). An update on the role of nutrigenomic modulations in mediating the cardiovascular protective effect of fruit polyphenols. Food & Function, 7(9): 3656-3676. DOI: https://www.doi.org/10.1039/c6fo00596a

Krga I, Tamaian R, Mercier S, Boby C, Monfoulet LE, Glibetic M, Morand C, and Milenkovic D (2018). Anthocyanins and their gut metabolites attenuate monocyte adhesion and transendothelial migration through nutrigenomic mechanisms regulating endothelial cell permeability. Free Radical Biology and Medicine, 124: 364-379. DOI: https://www.doi.org/10.1016/j.freeradbiomed.2018.06.027

Kuntz S, Kunz C, Herrmann J, Borsch CH, Abel G, Fröhling B, Dietrich H, and Rudloff S (2014). Anthocyanins from fruit juices improve the antioxidant status of healthy young female volunteers without affecting anti-inflammatory parameters: Results from the randomised, double-blind, placebo-controlled, crossover ANTHONIA (ANTHOcyanins in Nutrition Investigation Alliance) study. British Journal of Nutrition, 112(6): 925-936. DOI: https://www.doi.org/10.1017/S0007114514001482

Lei SW, Cui G, Leung GPH, Luk SCW, Hoi MPM, Wang L, Mahady GB, and Lee AMY (2015). Icaritin protects against oxidative stress-induced injury in cardiac H9c2 cells via Akt/Nrf2/HO-1 and calcium signalling pathways. Journal of Functional Foods, 18(Part A): 213-223. DOI: https://www.doi.org/10.1016/j.jff.2015.06.054

Li F, Lang F, Wang Y, Zhai C, Zhang C, Zhang L, and Hao E (2018). Cyanidin ameliorates endotoxin-induced myocardial toxicity by modulating inflammation and oxidative stress through mitochondria and other factors. Food and Chemical Toxicology, 120: 104-111. DOI: https://www.doi.org/10.1016/j. fct.2018.05.053

Libby P, Ridker PM, and Hansson GK (2011). Progress and challenges in translating the biology of atherosclerosis. Nature, 473: 317-325. DOI: https://www.doi.org/10.1038/nature10146

Lv XC and Zhou HY (2012). Resveratrol protects H9c2 embryonic rat heart derived cells from oxidative stress by inducing autophagy: Role of p38 mitogen-activated protein kinase. Canadian Journal of Physiology and Pharmacology, 90(5): 655-662. DOI: https://www.doi.org/10.1139/y2012-051

Mahmmoud MY (2013). Natural antioxidants effect of mulberry fruits (Morus nigra and Morus alba L.) on lipids profile and oxidative stress in hypercholestrolemic rats. Pakistan Journal of Nutrition, 12(7): 665-672. DOI: https://www.doi.org/10.3923/pjn.2013.665.672

Martin J, Kuskoski EM, Navas MJ, and Asuero AG (2017). Antioxidant capacity of anthocyanin pigments. In: J. Justino (Editor), Flavonoids—From Biosynthesis to Human Health. Science, Technology and Medicine Open Access Publisher., Rijeka, Croatia. Chapter 11, pp. 205-255. Available at: https://b2n.ir/r38243

Nimse SB and Pal D (2015). Free radicals, natural antioxidants, and their reaction mechanisms. Royal Society of Chemistry Advances, 5(35): 27986-28006. DOI: https://www.doi.org/10.1039/C4RA13315C

Oteiza PI, Erlejman AG, Verstraeten SV, Keen CL, and Fraga CG (2005). Flavonoid-membrane interactions: A protective role of flavonoids at the membrane surface?. Journal of Immunology Research, 12: 592035. DOI: https://www.doi.org/10.1080/10446670410001722168

Padmanabhan M and Prince PSM (2006). Preventive effect of S-allylcysteine on lipid peroxides and antioxidants in normal and isoproterenol-induced cardiotoxicity in rats: A histopathological study. Toxicology, 224(1-2): 128-137. DOI: https://www.doi.org/10.1016/j.tox.2006.04.039

Paravicini TM and Touyz RM (2006). Redox signaling in hypertension. Cardiovascular Research, 71(2): 247-258. DOI: https://www.doi.org/10.1016/j.cardiores.2006.05.001

Pazmiño-Durán AE, Giusti MM, Wrolstad RE, and Glória BA (2001). Anthocyanins from oxalis triangularis as potential food colorants. Food Chemistry, 75(2): 211-216. DOI: https://www.doi.org/10.1016/S0308-8146(01)00201-1

Perez-Vizcaino F, Duarte J, Jimenez R, Santos-Buelga C, and Osuna A (2009). Antihypertensive effects of the flavonoid qurecetin. Pharmacological Reports, 61(1): 67-75. DOI: https://www.doi.org/10.1016/s1734-1140(09)70008-8

Perez-Vizcaino F, Duarte J, and Andriantsitohaina R (2006). Endothelial function and cardiovascular disease: Effects of quercetin and wine polyphenols. Free Radical Research, 40(10): 1054-1065. DOI: https://www.doi.org/10.1080/10715760600823128

Petroni K, Trinei M, Fornari M, Calvenzani V, Marinelli A, Micheli LA, Pilu R, Matros A, Mock HP, Tonelli C, et al (2017). Dietary cyanidin 3-glucoside from purple corn ameliorates doxorubicin-induced cardiotoxicity in mice. Nutrition, Metabolism & Cardiovascular Diseases, 27(5): 462-469. DOI: https://www.doi.org/10.1016/j.numecd.2017.02.002

Qian P, Yan LJ, Li YQ, Yang HT, Duan HY, Wu JT, Fan XW, and Wang SL (2018). Cyanidin ameliorates cisplatin- induced cardiotoxicity via inhibition of ROS-mediated apoptosis. Experimental and Therapeutic *Medicine,* 15(2): 1959-1965. DOI: https://www.doi.org/10.3892/etm.2017.5617

Rahman AM, Yusuf SW, and Ewer MS (2007). Anthracycline-induced cardiotoxicity and the cardiac-sparing effect of liposomal formulation. International Journal of Nanomedicine, 2(4): 567-583.

Sankhari JM, Thounaojam MC, Jadeja RN, Devkar RV, and Ramachandran AV (2012). Anthocyanin-rich red cabbage (*Brassica oleracea* L.) extract attenuates cardiac and hepatic oxidative stress in rats fed an atherogenic diet. Journal of the Science of Food and Agriculture, 92(8): 1688-1693. DOI: https://www.doi.org/10.1002/jsfa.5532

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Schewe T, Steffen Y, and Sies H (2008). How do dietary flavanols improve vascular function? A position paper. Archives of Biochemistry and Biophysics, 476(2): 102-106. DOI: https://www.doi.org/10.1016/j.abb.2008.03.004

Serraino I, Dugo L, Dugo P, Mondello L , Mazzon E, Dugo G, Caputi AP, and Cuzzocrea S (2003). Protective effects of cyanidin-3-O-glucoside from blackberry extract against peroxynitrite-induced endothelial dysfunction and vascular failure. Life Sciences, 73(9): 1097-1114. DOI: https://www.doi.org/10.1016/s0024-3205(03)00356-4

Strack D and Wray V (1994). The anthocyanins. In: J. B. Harborne (Editor), The flavonoids: Advances in research since1986. Chapman and Hall.

Tang GY, Meng X, Li Y, Zhao CN, Liu Q, and Li HB (2017). Effects of vegetables on cardiovascular diseases and related mechanisms. Nutrients, 9(8): 857. DOI: https://www.doi.org/10.3390/nu9080857

Tao L, Gao E, Hu A, Colettic C, Wang Y, Chirstopher TA, Lopez BL, Kocch W, and Ma XL (2006). Thioredoxin reduce post-ischemic myocardial apoptosis by reducing oxidative/ nitrative stress. British Journal of Pharmacology, 149(3): 311-318. DOI: https://www.doi.org/10.1038\sj.bjp.0706853

Wang S, Konorev EA, Kotamraju S, Joseph J, Kalivendi S, and Kalyanaraman B (2004). Doxorubicin induces apoptosis in normal and tumor cells via distinctly different mechanisms. intermediacy of H(2)O(2)- and p53-dependent pathways. Journal of Biological Chemistry, 279(24): 25535-25543. DOI: https://www.doi.org/10.1074/jbc.M400944200

Yang P, Ke HQ, Hong PZ, Zeng SK, and Cao WH (2011). Antioxidant activity of bigeye tuna (Thunnus Obesus) head protein hydroiysate prepared with alcalase. International Journal of Food Science & Technology, 46(12): 2460-2466. DOI: https://www.doi.org/10.1111/j.1365-2621.2011.02768.x

Zadeh FA, Bokov DO, Salahdin OD, Abdelbasset WK, Jawad MA, Kadhim MM, Qasim MT, Kzar HH, Al-Gazally ME, Mustafa YF et al. (2022). Cytotoxicity evaluation of environmentally friendly synthesis Copper/Zinc bimetallic nanoparticles on MCF-7 cancer cells. Rendiconti Lincei. Scienze Fisiche e Naturali, 33: 441-447. DOI: https://www.doi.org/10.1007/s12210-022-01064-x

Zainab MI and Qasim MT (2021). Hormonal profile of men during infertility. Biochemical and Cellular Archives, 21: 2895-2898. Available at: https://connectjournals.com/03896.2021.21.2895

Zhao CN, Meng X, Li Y, Li S, Liu Q, Tang GY, Li HB (2017). Fruits for prevention and treatment of cardiovascular diseases. Nutrients, 9(6): 598. DOI: https://www.doi.org/10.3390/nu9060598

Zheng W and Wang SY (2003). Oxygen radical absorbing capacity of phenolics in blueberries, cranberries, chokeberries, and lingonberries. Journal of Agricultural and Food Chemistry, 51(2): 502-509. DOI: https://www.doi.org/10.1021/jf020728u

Zhu W, Wang XR, Du SQ, Yan CQ, Yang N, Lin LL, Shi GX, and Liu CZ (2018). Anti-oxidative and anti-apoptoti effects of acupuncture: Role of Thioredoxin-1 in the hippocampus of vascular dementia rats. Neurosciense, 379: 281-291. DOI: https://www.doi.org/10.1016/j.neuroscience.2018.03.029

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