Archives of Razi Institute, Vol. 77, No. 2 (2022) 553-563

DOI: 10.22092/ARI.2021.356810.1917

Original Article

Effect of Caraway Seed Extract on the Blood Biochemistry and Antioxidant Capacity among the Hyperoxidative Stress-Induced Rats

Salah Najim, A[1 *], Bahry Al_Sadoon, M[2], Salem Sheet, M[1]

1. Department of Chemistry, Education College for Girls, Mosul University, Mosul, Iraq
2. Department of Chemistry, College of Science, Mosul University, Mosul, Iraq

Received 22 November 2021; Accepted 4 December 2021
Corresponding Author: nasserafad23@yahoo.com

Abstract

Carum carvi (Carium) or caraway is traditionally used for the treatment of several metabolic and non-metabolic disorders. In the current study, extracted oil, flavonoids, and alkaloids from the Carium were used to evaluate the effects of these components on blood lipid profile and heart regeneration from oxidative damages caused by hydrogen peroxide consumption. A total of 50 male BALB/c mice were used in this study with a body weight of 23-32 g. The animals were randomly divided into 5 groups (n=10). Group 1: The animals in this group were considered the control group and fed with a normal diet. Group 2: Hyperoxidative stress was induced in this group by giving hydrogen peroxide at a concentration of 1% into the drinking water for 6 weeks. After this period, they did not receive any treatments and only received saline solution by intraperitoneal (IP) injection once a day for 4 weeks. Group 3: Hyperoxidative stress was induced by hydrogen peroxide at a concentration of 1% for 6 weeks. All the animals in this group received 1.25 mg/kg body weight (B.W.) extracted oil from Caraway seeds for 4 weeks by IP injection once a day each week. Group 4: Hyperoxidative stress was induced by hydrogen peroxide at a concentration of 1% for 6 weeks. All the animals in this group received 61.28 mg/kg B.W. extracted flavonoids from Caraway seeds for 4 weeks by IP injection once a day each week. Group 5: Hyperoxidative stress was induced by hydrogen peroxide at a concentration of 1% for 6 weeks. All the animals in this group received 7.8 mg/kg B.W. extracted alkaloids from Caraway seeds for 4 weeks by IP injection once a day each week. The levels of glutathione and malondialdehyde were estimated in the liver and kidneys in the animals with cardiovascular disorders induced by hydrogen peroxide at a concentration of 1%. The results of the current study showed that the alkaloids had the greatest effect in reducing harmful total cholesterol and a complete recovery of the heart and aorta from atherosclerotic lesions through viewing the tissue sections.

Keywords: Cardiovascular disease, GC, Glutathione, High-density lipoprotein cholesterol, HPLC, Low-density lipoprotein cholesterol, Malondialdehyde, TG, Total cholesterol, Very low-density lipoprotein cholesterol

1. Introduction

The progress of modern science that is increasingly rapid and sophisticated today should not rule out herbal medicine. In addition, there is still a lack of knowledge and information about various types of plants that can be used as herbal remedies for certain disorders and be developed into formulations (1). *Carum carvi* (Carium) or caraway is an aromatic plant belonging to the Apiaceae family and is one of the oldest cultivated plants in Asia, Africa, and Europe (Figure 1) (2). Caraway grows best in sunny places and in soil rich in organic matter, which reaches the height of 30-80 cm. Caraway is used in the treatment of numerous diseases similar to any medicinal plant and is widely employed as traditional medicine or in foods as a cooking spice (3).

Figure 1. Caraway plant (2)

The results of experimental studies have reported various benefits of caraway, including anti-ulcer, antispasmodic, pain killer, anti-dyspepsia, anti-hyperglycemic, anti-inflammatory, anti-hyperlipidemic, and anti-oxidant (4). According to the European Herbal Union Study, caraway has been traditionally used to relieve symptoms of digestive disorders, such as bloating and flatulence. Caraway seeds are also used to flavor rye bread, treat digestive disorders, and fight worms (5). Linalool, carvacrol, anethole, flavonoids, and other polyphenol compounds are the most important components of caraway (6). Caraway is considered one of the best plants in the production of essential oils, which are widely employed in biological activities, including anti-inflammatory, antioxidant, antibacterial, antifungal, antiviral, and antimutagenic (7-9). The antioxidant, antimicrobial, and anti-aflatoxin effects of caraway, along with its reputation as a spice, encourage its use as a natural preserving agent in addition to being an antioxidant (10).

Biomarkers are beneficial biological tools used to identify high-risk individuals through rapid and accurate disease diagnosis; nevertheless, they might also determine treatment plans and prognosis. Moreover, biomarkers provide powerful and dynamic approaches to understanding the spectrum of some diseases with applications in observational and analytic epidemiology and haphazard clinical trials. In this regard, it is advised to use some biomarkers for the assessment of myocardial damages (11).

Cardiovascular diseases are considered among the main causes of death in most developed countries (12). One of the most common heart diseases is atherosclerosis, which is the main underlying cause of acute cardiovascular diseases, such as stroke or myocardial infarction (13). This disease is reported as one of the first diseases related to dyslipidemia. Several studies have recently highlighted the importance of the immune component of atherosclerosis (14). In addition, people with existing cardiovascular diseases, of any origin, are at risk of acute and fatal cardiovascular events, such as heart attack and stroke. The common factor in such events is the formation of a blood clot that can block the blood vessels leading to the death of the heart muscle or neurons (15).

Cardiovascular diseases are acute myocardial infarction, stroke, and thrombosis, which are the main causes of death worldwide (16). Cigarette smoking is a major contributor to cardiovascular diseases as a result of damaging blood vessels caused by the regular inhalation of a mixture of harmful chemicals, including those in gaseous form (17). Cardiovascular diseases are directly related to lipoprotein metabolism and indirectly to glycemic status (18-20).

To the current knowledge, it is well documented that caraway has several components, such as essential oils, flavonoids, and alkaloids. These ingredients have some antioxidant and anti-inflammatory characteristics. Therefore, the current study aimed to investigate the effects of caraway extracted essential oils, flavonoids,

and alkaloids to cure hyperoxidative stress induced by hydrogen peroxide on mouse liver, heart, kidney, and blood lipid profile.

2. Materials and Methods

Caraway seeds were obtained from the local markets in the city of Mosul, Iraq.

2.1. Isolation and Diagnosis of Natural Products of *Carum Crive. L*

2.1.1. Separation of Oil from Caraway Seeds

In this study, fatty acids and volatile oils were isolated from caraway seeds by soaking (400 g) caraway seed powder in petroleum ether (60-80) for 3 days, after which the soaked plant was placed in a Soxhlet extraction device for 3 days. Using the same solvent, after 3 days, the oil extract was obtained with the solvent, then the solvent was evaporated by a rotary evaporator.

2.2. Diagnosis of Fatty Acids in the Produced Oil Using Gas Chromatography

2.2.1. Gas Chromatography Technique

The fatty acids of the isolated oil from the seeds of the caraway plant were determined using a GC device, which used a flame ionized detector (FID).

Chromatographic analysis of the sample: The fatty acid compounds were analyzed using GC-2010 (Shimadzu, Japan) where the FID was used and a capillary column type (SE-30) with the lengths of 30 m × 0.25 mm was employed according to the conditions provided in table 1. The fatty acids composition in caraway oil is presented in table 2. Figure 2 depicted the standard Gas chromatography GC and chromatograms of caraway oil fatty acids.

Table 1. Conditions used in the analysis of the sample

No.	Parameters	Temperature
1	Injection area temperature	28°C
2	Detector temperature	33°C
3	Separator column temperature	(120-290°C)10°C/min
4	Gas flow rate	100 Kpa

Table 2. Some fatty acids and their percentage in caraway oil

No	Name	Con (%)
1	Oleic	19.5
2	Palmitic	7.2
3	Stearic	3.9
4	Linoleic	16.7
5	Lenolenic	0.7
6	Myristic	3.4
7	Arachidic acid	2.8
8	Pentadecanoic	1.7

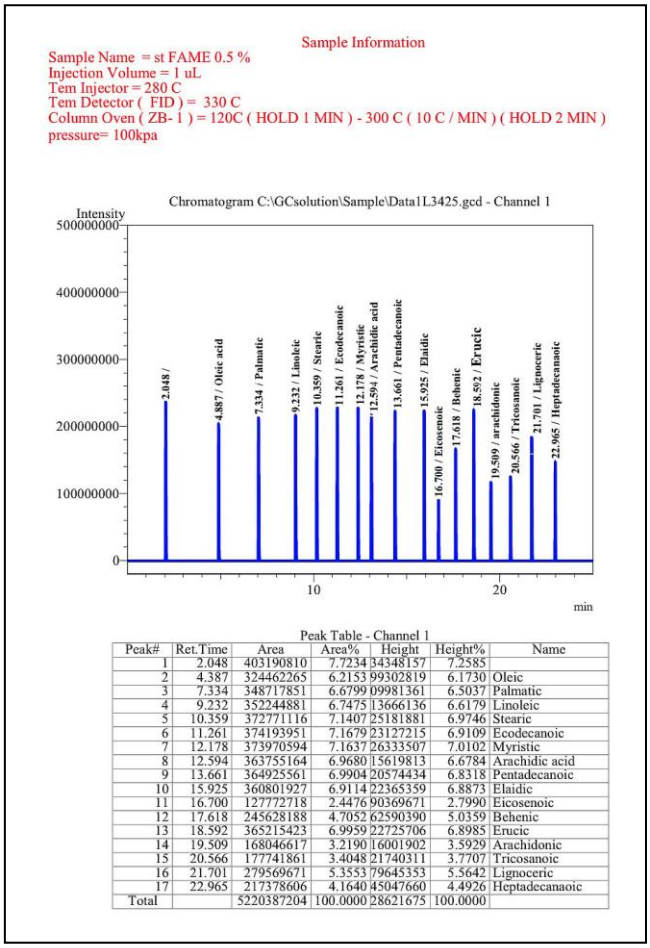

Figure 2. Standard gas chromatography chromatograms of fatty acids and their retention time

2.3. Separation of Flavonoids from Caraway

After isolating oil from the caraway plant powder, the remaining tissue (bagasse) was collected and exposed to the air for whole 3 days to get rid of petroleum ether. The resulting extract represented the

extract of flavonoids (which were flavonoids dissolved in ethanol). This extract was taken to the rotary evaporator to be concentrated and completely disposed of the ethanol; afterward, the obtained material was collected and placed in a tight-fitting tube and kept refrigerated until the subsequent tests (21).

2.4. Identification of Flavonoids Using High-Performance Liquid Chromatography Technology

The quantification of individual phenolic compounds was performed by reverse-phase high-performance liquid chromatography (HPLC) analysis (SYKAMN HPLC chromatography system equipped with an ultraviolet-detector, Chemstation, Zorbax Eclipse Plus-C18-OSD 0.25 cm column, 4.6 mm column) at 30°C. The graduated rinsing method, using eluent A (methanol) and eluent B (1% formic acid in water (v/v)), was carried out as follows: 0-130 min, 40% B; 14-20 min, 50% B. The flow rate was 0.7 mL/min. The volume of injected samples was 100 µL and standards were 100 µL, and this was performed automatically using the automatic sampler. Spectra were acquired at 280 nm.

The flavonoid concentration is tabulated in table 3. The HPLC chromatogram for the analysis of the caraway flavonoids is depicted in figure 3. The external titration curve for Apigenin, Qurcetine, Keamferol, P-Coumaric, Catechine, Caffeic Acid, and Gallic Acid are presented in figures 4-10.

Table 3. Flavonoid concentration in the extracted sample

No	Name	Con (ppm)
1	Apigenin	20.6
2	Qurcetine	36.8
3	Keamferol	41.3
4	P-coumaric	26.9
5	Catechine	17.2
6	Caffeic Acid	9.2
7	Gallic Acid	10.8

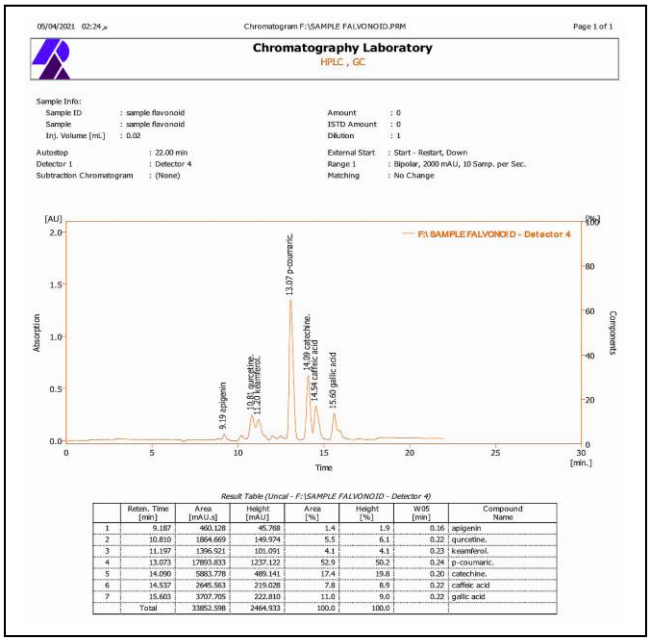

Figure 3. HPLC chromatogram for the analysis of the extracted sample (flavonoids)

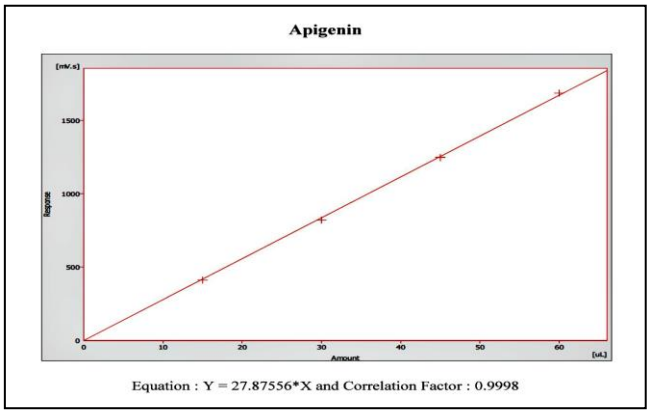

Figure 4. External titration curve of pure apigenin

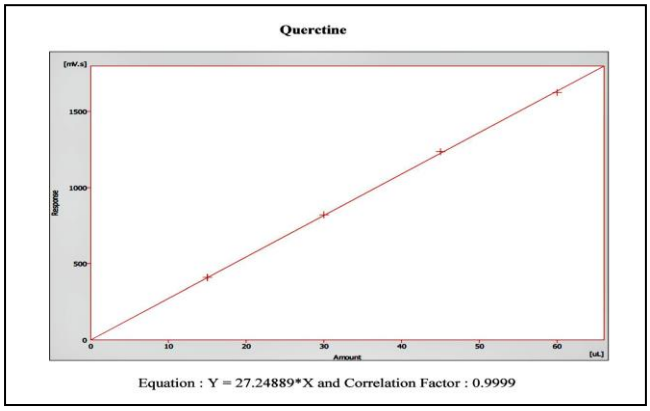

Figure 5. External titration curve of pure kerosene

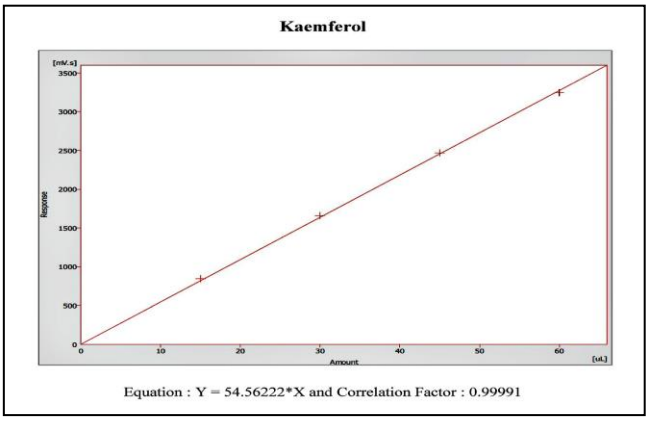

Figure 6. External titration curve of pure camperol

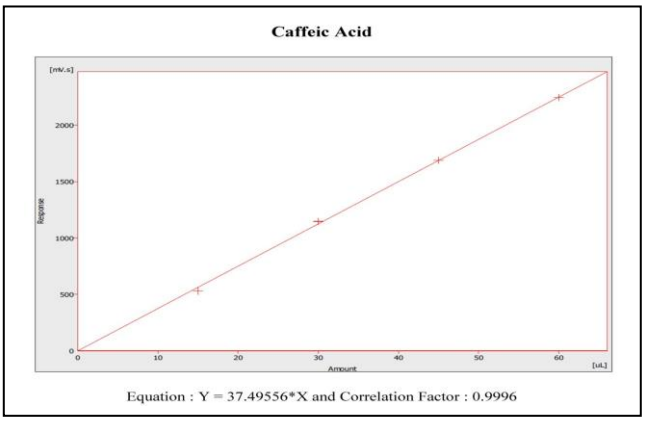

Figure 9. External titration curve of pure caffeic acid

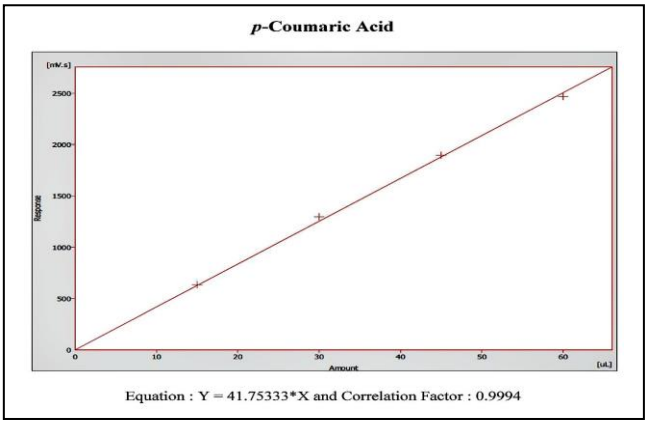

Figure 7. External titration curve of pure p-coumaric acid

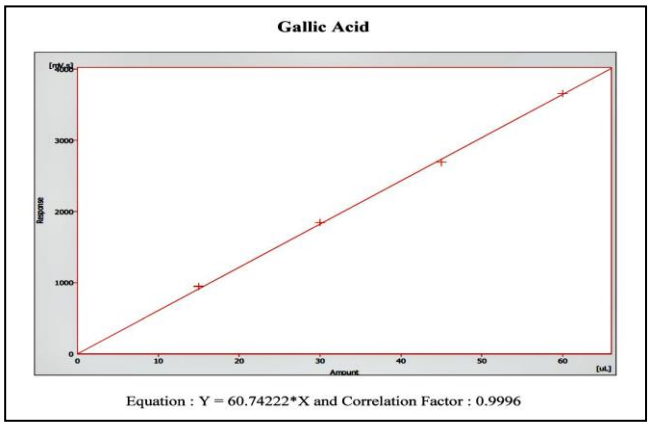

Figure 10. External titration curve of pure gallic acid

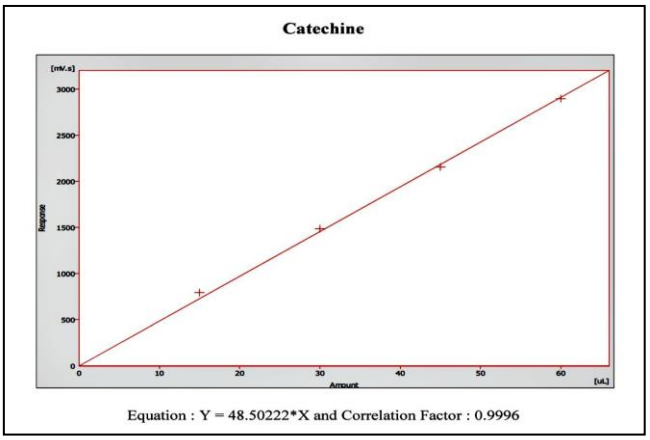

Figure 8. External calibration curve for pure cation

2.5. Isolation of Alkaloids from Caraway Plant

2.5.1. Isolation of Alkaloids from *Carum Crive. L Carum carvi*

The alkaloids were isolated by collecting the remaining caraway seeds produced after isolating both the oil and the flavonoids. They were dried on the air for a whole day to completely get rid of the remaining ethanol; subsequently, the bagasse was soaked with distilled water for 2 days, after which the soaked bagasse and the remaining soaking water were placed in the Soxhlet extraction device for a while. For 3 days, using distilled water, the resulting solution was placed in a lyophilizer, and then it was frozen to reduce its

volume and the water was disposed of to obtain the final extract in the form of a dry powder that was kept in a tightly sealed tube until the animals were dosed later (22).

2.6. Animals

A total of 50 adult male Wistar rats were used in this study. Their body weight ranged at 250-350 g. The animals were obtained from the College of Veterinary Medicine, University of Mosul, Iraq. The samples were randomly divided into 5 groups (n=10), and they had ad-libitum access to food and water during the experiments. The animals were kept for about 2 weeks for adaptation before starting the experiment. The experiment duration was 12 weeks. The housing condition was as follows: 12:12 light-dark cycle, environmental temperature of 24°C, and humidity of 55%.

2.7. Study Design

Group 1: The animals in this group were considered the control group. They were fed a normal diet. Group 2: Cardiovascular disorder was induced in this group by giving hydrogen peroxide at a concentration of 1% in the drinking water for 6 weeks. After this period, they did not receive any treatments. They only received saline solution by intraperitoneal (IP) injection once a day for 4 weeks. Group 3: Cardiovascular disorder was induced by hydrogen peroxide at a concentration of 1% for 6 weeks. All the animals in this group received 1.25 mg/kg body weight (B.W.) extracted oil from Caraway seeds for 4 weeks by IP injection once a day each week. Group 4: Cardiovascular disorder was induced by hydrogen peroxide at a concentration of 1% for 6 weeks. All the animals in this group received 61.28 mg/kg B.W. extracted flavonoids from Caraway seeds for 4 weeks by IP injection once a day each week. Group 5: Cardiovascular disorder was induced by hydrogen peroxide at a concentration of 1% for 6 weeks. All the animals in this group received 7.8 mg/kg B.W. extracted alkaloids from Caraway seeds for 4 weeks by IP injection once a day each week.

2.8. Blood Sampling and Lipid Profile Evaluation

At the end of the experimental procedure, all the animals were anesthetized and the blood samples were obtained via heart puncture. Afterward, the serum samples were used for blood biochemical assays. The study included the estimation of total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol through the application of a ready-made kit (BIOLABO, France), which is one of the approved enzymatic methods (23). The level of glutathione in the liver and kidneys was also estimated as in the modified Mann method (24); in addition, the level of malondialdehyde (MDA) in the liver and kidney tissues was measured using the method used by researchers (25).

2.9. Histological Examination of Tissue Samples

After euthanasia, the tissue samples were gathered and preserved in 10% formalin solution till the preparation of histological sections. Several tissue sections were prepared according to Lee and Luna (16). Tissue samples taken from organs and specimens were fixed by 10% formalin-buffered for 48 h at room temperature. After the procedures of fixation, the tissues were dehydrated in alcohol, cleared in two stages of xyline, and implanted in liquid-paraffin for 2 h at a 56-degree temperature. The tissue was cut at 5 μm by microtome for sectioning. In the end, tissue sections were dewaxed, stained with Hematoxylin and Eosin, and studied using 4x, 10x, and 40x objective of light microscopy.

2.10. Statistical Analysis

The data were normally distributed according to the Kolmogorov-Smirnov test. The collected data were analyzed in SPSS software (version 18) using the one-way analysis of variance, followed by the Dunnett's test. A *P*-value of < 0.05 was considered statistically significant.

3. Results and Discussion

The rats were injected with these substances at doses of 1.25, 61.28, and 7.8 mg/kg B.W., respectively. Intraperitoneal injection of oil, flavonoids, and alkaloids extracted from caraway led to a significant decrease ($P<0.05$) in the levels of total cholesterol, triglycerides, LDL cholesterol, and very LDL cholesterol. However, a significant increase ($P<0.05$) in the level of HDL was recorded in the animals receiving

extracted oil, flavonoids, and alkaloids from caraway, compared to non-treated rats in group 2 (Table 4). The recorded decrease in the level of LDL was due to the ability of these caraway extracts, in comparison to a reduction in the oxidation of apo B-100 (26).

The results obtained from group 2 showed that hyperoxidative stress cussed by hydrogen peroxide administration led to a significant decrease in the levels of glutathione (GSH); on the other hand, a significant increase was detected in the MDA levels in the liver and kidney ($P \leq 0.05$), compared to the healthy control group (Group 1). These results were consistent with those of a study conducted by Abd Al-Zahra, Ismael (27). This decrease in the content of GSH in group 2 was due to the increase in the content of free radicals as a result of treatment with hydrogen peroxide, which caused liver and kidney cells serious damage. A significant increase in the process of lipid peroxidation was observed due to the hyperoxidative stress cussed by hydrogen peroxide administration; consequently, it led to a depletion of glutathione. Moreover, the hyperoxidative stress might have affected the metabolism of glutathione as previously described by Al-Malki (28).

On the other hand, the significant increase ($P \leq 0.05$) that was detected in the MDA levels in the liver and kidney obtained from group 2 was attributed to an increase in the process of lipid peroxidation in the liver and kidneys as it has been known that MDA is a product of lipid peroxidation. This increase in the concentration of MDA is used as an indicator of damage to cell membranes (29). The recorded data from groups 3-5 showed a significant increase ($P<0.05$) in the level of glutathione in the liver and kidney tissues; nevertheless, a significant decrease ($P<0.05$) were recorded in the level of MDA in the liver and kidney tissues in animals belonging to the groups 3-5, as shown in table 5. The aforementioned separated active compounds have the ability to raise the concentration of glutathione. This ability is due to activating the function of the enzyme Gamma-Glutamyl Transpeptidase (30) or increasing the activity of glutathione reductase, which works to reduce the oxidized glutathione to the reduced form, using the enzymatic nicotinamide adenine dinucleotide phosphate (31).

Table 4. Effect of caraway extracted oil, flavonoids, and alkaloids on some biochemical parameters in the blood serum

Animals	Total cholesterol (mmol/liter)	TG (mmol/liter)	HDL (mmol/liter)	VLDL (mmol/liter)	LDL (mmol/liter)
Group 1	$8.75\pm0.19^{a, b}$	0.47 ± 0.03^{a}	1.24 ± 0.12^{a}	1.06 ± 0.07^{a}	2.48 ± 0.12^{a}
Group 2	2.08 ± 0.32^{c}	0.61 ± 0.38^{b}	0.65 ± 0.11^{b}	1.35 ± 0.08^{b}	3.35 ± 0.17^{b}
Group 3	0.63 ± 0.06^{d}	0.42 ± 0.05^{a}	0.86 ± 0.11^{c}	0.93 ± 0.11^{a}	1.90 ± 0.13^{c}
Group 4	0.75 ± 0.07^{d}	0.44 ± 0.02^{a}	0.80 ± 0.10^{c}	0.99 ± 0.04^{a}	1.94 ± 0.17^{c}
Group 5	0.90 ± 0.26^{e}	0.63 ± 0.04^{b}	0.86 ± 0.09^{c}	1.41 ± 0.09^{b}	2.36 ± 0.15^{a}

TG: Triglycerides; HDL: High-density lipoprotein; VLDL: Very low-density lipoprotein; LDL: Low-density lipoprotein
The vertically different letters indicate a significant difference at the probability level of $P \leq 0.05$ (mean±standard error).

Table 5. Effect of natural products of caraway seeds (oil, flavonoids, and alkaloids) on the liver and kidney tissues of rats with induced cardiovascular diseases, treated and untreated

Variables / Totals	MDA (unit/g wet tissue)		Glutathione (unit/g wet tissue)	
	Kidneys	Liver	Kidneys	Liver
Group 1	$0.09\pm0.01^{a, b}$	0.17 ± 0.01^{e}	0.25 ± 0.02^{a}	$0.64\pm0.11^{a, b}$
Group 2	0.18 ± 0.01^{e}	$0.31\pm 0.01^{c, d, e}$	0.14 ± 0.23^{b}	0.38 ± 0.09^{a}
Group 3	0.17 ± 0.01^{e}	$0.14\pm0.01^{d, e}$	0.53 ± 0.02^{a}	0.96 ± 0.09^{b}
Group 4	$0.13\pm0.03^{d, e}$	0.17 ± 0.01^{e}	1.26 ± 0.07^{b}	$0.77\pm0.06^{a, b}$
Group 5	$0.10\pm0.01^{c, d}$	0.25 ± 0.00^{f}	1.42 ± 0.28^{b}	0.82 ± 0.13^{b}

The vertically different letters indicate a significant difference at the probability level of $P \leq 0.05$ (mean±standard error).

The results of the histological evolutions in group 1 showed the normal structure of cardiac muscle cells (Figure 11), while histological examination of animals in group 2 revealed several changes and damages in the cardiac muscle cells (Figure 12). These changes were represented by coagulative necrosis of muscle cells, the presence of edema between muscle cells, and the infiltration of inflammatory cells in muscle tissues; this is due to the fact that hydrogen peroxide has the ability to break down cell walls, which helps release numerous chemical mediators, which in turn attract inflammatory cells to the area of damage (32).

The histological examination of the animals in group 1 showed the normal structure of the aorta. Figure 13 depicts the normal shape and regularity of the aortic lumen, in addition to the clarity of the three layers of the aortic wall consisting of the inner layer Tunica intima, the muscular middle layer Tunica media, and the outer layer Tunica adventitia. On the contrary, the histological examination of the animals in group 2 indicated the presence of histopathological changes, compared to the healthy control group. In the three layers of the aorta, in addition to the clear infiltration of inflammatory cells in them, the infiltration of foam cells in the muscle layer and the irregular shape and narrowing of the artery lumen are shown in figure 14. This is due to the disturbance of cellular metabolism as mentioned previously. Oxidative stress is one of the main factors that contribute to the occurrence of various diseases, including atherosclerosis, and heart diseases, such as heart failure (33).

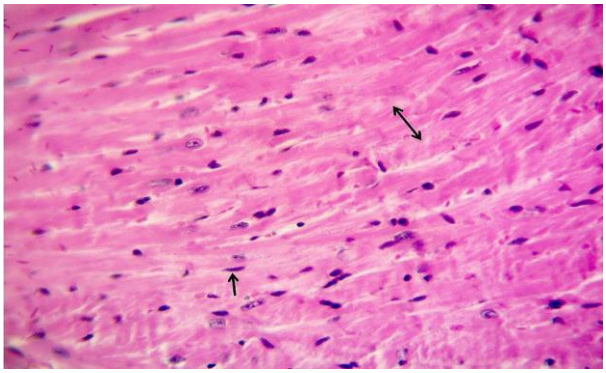

Figure 11. Histological section of a rat from the healthy control group showing the normal histological features of the heart tissue represented by the cardiomyocytes (↔) (Hematoxylin and eosin tincture, 400x)

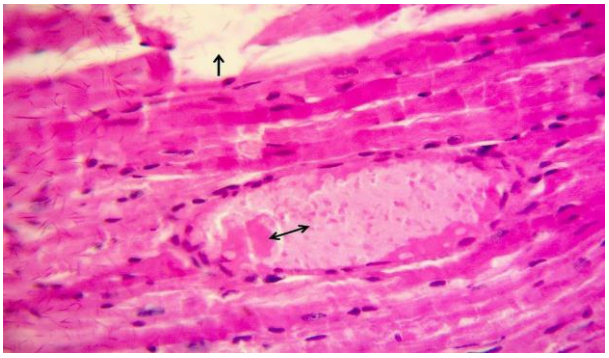

Figure 12. Histological section of the heart of a rat from a group with untreated induced cardiovascular disease showing the presence of Zenker's necrosis in the cardiac muscle fibers, the presence of recent thrombus in the blood vessel of the myocardium (↔), and the presence of edema between the myocardial fibers (←) (Hematoxylin and eosin stain, 400x)

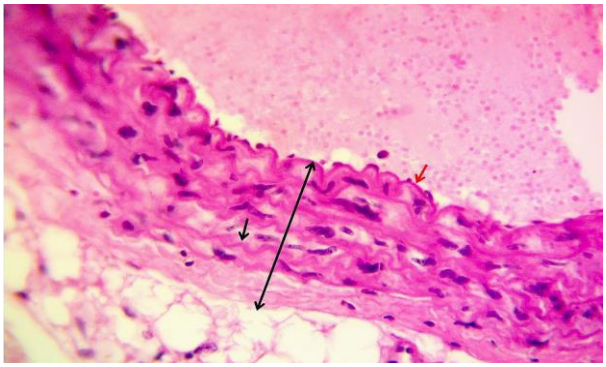

Figure 13. Histological section of the aorta of a rat from the healthy control group showing the normal histological features of aortic layers (↔), endothelial cells (←), cells, and smooth muscle fibers (←) (Hematoxylin and eosin stain, 400x)

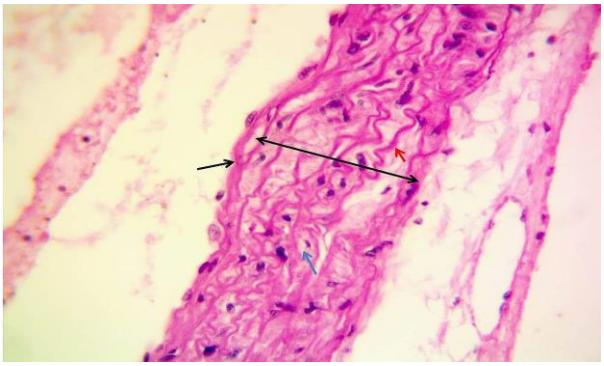

Figure 14. Histological section of the aorta of a rat from a group with untreated induced cardiovascular diseases showing the presence of atherosclerosis lesions in the inner and middle layers of the tunica (↔), represented by thickening of the inner tunica and its protrusion into the lumen (←) and the presence of foam cells (←) enlargement and irregularity of smooth muscle fibers (←) (Hematoxylin and eosin tincture, 400x)

The treatment of animals in groups 3-5, which were affected by hydrogen peroxide, with the natural products of caraway seeds for 4 weeks led to the healing or symmetry of the tissues of the heart and aorta. The animals suffering from heart and blood vessel disorders returned to the normal state or the natural approach, especially the animals treated with alkaloids, compared to group 2, as shown in figures 15-20.

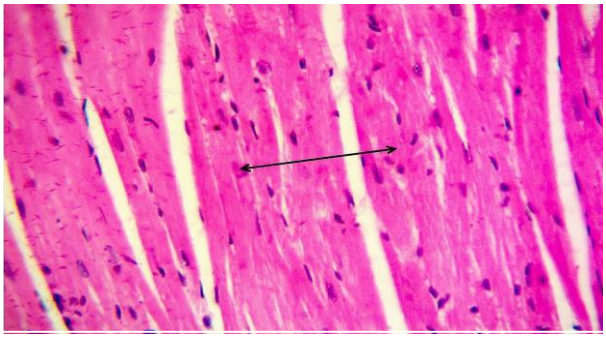

Figure 15. Histological section of the heart of a rat from the group treated with alkaloids (G) showing the normal histological features of the heart tissue represented by the cardiac muscle (↔) (Hematoxylin and eosin tincture, 400x)

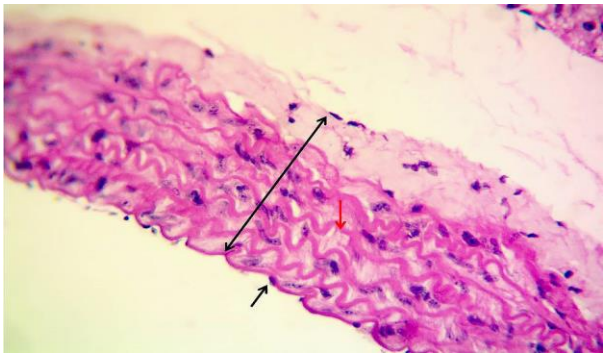

Figure 16. Histological section of the aorta of a rat from the alkaloid-treated group (G) showing the normal histological features of aortic layers (↔), endothelial cells (←), cells, and smooth muscle fibers (←) (Hematoxylin and eosin tincture, 400x)

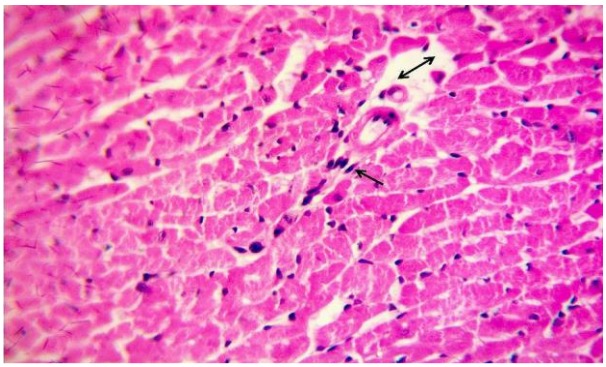

Figure 17. Histological section of the heart of a rat from the oil-treated group illustrating the presence of perivascular edema (↔), inflammatory cell infiltration (→), and Zenker's necrosis (Hematoxylin and eosin staining, 400x)

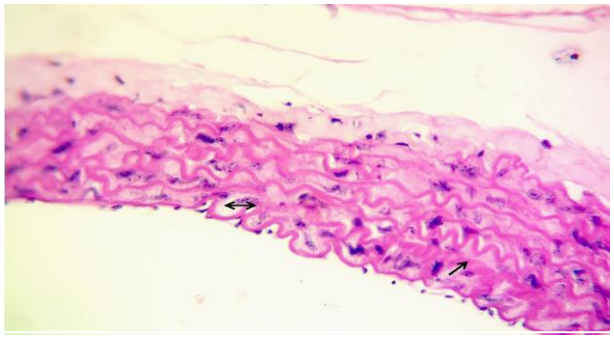

Figure 18. Histological section of the aorta of a rat from the oil-treated group showing the presence of foam cells in the tunica intima (↔), hypertrophy, and smooth muscle fibers (←) (Hematoxylin and eosin tincture, 400x)

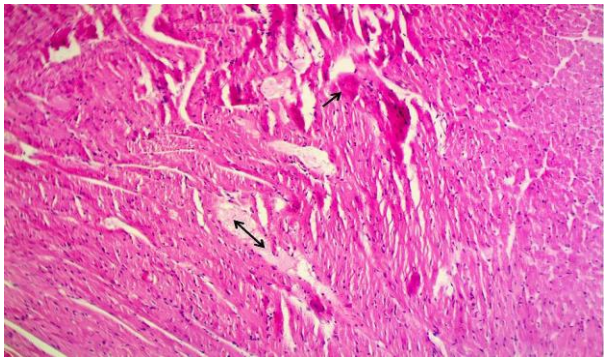

Figure 19. Histological section of the heart of a rat from the flavonoid-treated group showing the presence of edema between cardiomyocytes (↔) and Zenker's necrosis in cardiac muscle fibers (←) (Hematoxylin and eosin tincture, 400x)

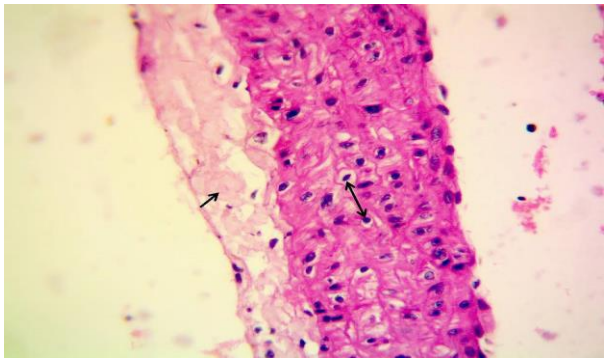

Figure 20. Histological section of the aorta of a rat from the flavonoid-treated group showing the presence of foam cells in the tunica media (↔) and the thickening of the tunica adventitia (←) (Hematoxylin and eosin stain, 400x)

The histological evaluations showed that the animals in group 5 after a 4-week treatment with alkaloids extracted from Carium usually returned to their normal state and showed normal appearance in the cardiac muscles similar to the healthy control animals (group 1). Nonetheless, the recovery rate was lower in the animals treated with oil than in those administered alkaloids. In group 3, the histological evaluations revealed a small percentage of Zenker's necrosis in the heart, infiltration of inflammatory cells, and presence of edema around the blood vessels, which was slightly less than its presence in group 2. These findings might have occurred due to the ability of the extracted components of Carium to activate or stimulate the Lysyloxidas enzyme, which works to repair damages in affected tissues by restoring links or bonding between the lysine units belonging to the elastin and collagen proteins found in the lining of the heart tissue and the aorta, and the formation of a compact network of lysine units (34).

In conclusion, the extracted components of Carium, especially the alkaloids containing quercetin, rutin, and camperol, increase the activity of the enzyme Hem oxygenase-1 which, is presented in smooth muscle cells of blood vessels and the heart, where this enzyme works to protect cells from hydrogen peroxide damage, thus increasing the healing rate of tissues exposed to hydrogen peroxide.

Authors' Contribution

Study concept and design: A. S. N.
Acquisition of data: A. S. N.
Analysis and interpretation of data: A. S. N.
Drafting of the manuscript: M. B. A. S.
Critical revision of the manuscript for important intellectual content: M. S. S.
Statistical analysis: M. S. S.
Administrative, technical, and material support: M. B. A. S.

Ethics

The Institutional Review Board at the Mosul University, Mosul, Iraq approved this study.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Solikhah TI, Solikhah GP, Kuncoroningrat RJ. Aloe vera and Virgin Coconut Oil (VCO) accelerate healing process in domestic cat (Felis domesticus) suffering from scabies. Iraqi J Vet Sci. 2021;35(4):699-704.
2. Johri R. Cuminum cyminum and Carum carvi: An update. Pharmacogn Rev. 2011;5(9):63.
3. Aćimović M, Oljača S, Tešević V, Todosijević M, Đisalov J. Evaluation of caraway essential oil from different production areas of Serbia. Hortic Sci. 2014;41(3):122-30.
4. Sachan AK, Das DR, Kumar M. Carum carvi-An important medicinal plant. J Chem Pharm Res. 2016;8(3):529-33.
5. Attokaran M. Natural food flavors and colorants: John Wiley & Sons; 2017.
6. Thippeswamy N, Naidu KA. Antioxidant potency of cumin varieties—cumin, black cumin and bitter cumin—on antioxidant systems. Eur Food Res Technol. 2005;220(5):472-6.
7. Camele I, Elshafie HS, Caputo L, De Feo V. Anti-quorum sensing and antimicrobial effect of mediterranean plant essential oils against phytopathogenic bacteria. Front Microbiol. 2019;10:2619.
8. Elshafie H, Caputo L, De Martino L, Gruľová D, Zheljazkov V, De Feo V, et al. Biological investigations of essential oils extracted from three Juniperus species and evaluation of their antimicrobial, antioxidant and cytotoxic activities. J Appl Microbiol. 2020;129(5):1261-71.
9. Raut JS, Karuppayil SM. A status review on the medicinal properties of essential oils. Ind Crops Prod. 2014;62:250-64.
10. Mahboubi M. Caraway as important medicinal plants in management of diseases. Nat Prod Bioprospec. 2019;9(1):1-11.
11. AlSaad KM, Al-Autaish HN, Ahmed JA. Evaluation of cardiac enzymes and acute phase response as biomarkers for rapid diagnosis of myocarditis in calves with FMD. Iraqi J Vet Sci. 2020;34(1):31-7.
12. Joint F. Fats and oils in human nutrition: report of a joint expert consultation. FAO Food and nutrition paper: FAO; 1994.

13. Herrington W, Lacey B, Sherliker P, Armitage J, Lewington S. Epidemiology of atherosclerosis and the potential to reduce the global burden of atherothrombotic disease. Circ Res. 2016;118(4):535-46.
14. Libby P, Ridker PM, Hansson GK, Atherothrombosis LTNo. Inflammation in atherosclerosis: from pathophysiology to practice. J Am Coll Cardiol. 2009;54(23):2129-38.
15. Robertson S, Miller MR. Ambient air pollution and thrombosis. Particle and fibre toxicology. 2018;15(1):1-16.
16. Martín Giménez VM, Kassuha DE, Manucha W. Nanomedicine applied to cardiovascular diseases: latest developments. Ther Adv Cardiovasc Dis. 2017;11(4):133-42.
17. Conklin DJ, Schick S, Blaha MJ, Carll A, DeFilippis A, Ganz P, et al. Cardiovascular injury induced by tobacco products: assessment of risk factors and biomarkers of harm. A Tobacco Centers of Regulatory Science compilation. Am J Physiol Heart Circ Physiol. 2019;316(4):801-27.
18. Al-Aalim AM, Hamad MA, AL-ledani AA. Some insights of novel COVID 19 virus: structure, pathogenicity and immunity aspects. Iraqi J Vet Sci. 2020;34(2):287-93.
19. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential effects of coronaviruses on the cardiovascular system: a review. JAMA Cardiol. 2020;5(7):831-40.
20. Mohammed IH, Kakey ES. Effect of Prosopis farcta extracts on some complications (hematology and lipid profiles) associated with alloxan induced diabetic rats. Iraqi J Vet Sci. 2020;34(1):45-50.
21. Kato H, Li W, Koike M, Wang Y, Koike K. Phenolic glycosides from Agrimonia pilosa. Phytochemistry. 2010;71(16):1925-9.
22. Sezgin AC, Artik N. Determination of saponin content in Turkish tahini halvah by using HPLC. Adv J Food Sci Technol. 2010;2(2):109-15.
23. Burtis CA, Ashwood ER, Bruns DE. Tietz textbook of clinical chemistry and molecular diagnostics-e-book: Elsevier Health Sciences; 2012.
24. James RC, Goodman DR, Harbison RD. Hepatic glutathione and hepatotoxicity: changes induced by selected narcotics. J Pharmacol Exp Ther. 1982;221(3):708-14.
25. Volken E, Nurperi G, Ahmet B. N-acetyl cystine reduces cerebral lipid peroxidation in a rat model of infantile hydrocephalus. J Neurol Sci. 2001:1302-10.
26. Keppler AF, Gariani RA, Lopes DG, Comasseto JV. Lithium butylchalcogenolate induced Michael-aldol tandem sequence: easy and rapid access to highly functionalized organochalcogenides and unsaturated compounds. Tetrahedron Lett. 2009;50(19):2181-4.
27. Abd Al-Zahra JI, Ismael DK, Al-Shawi NN. Preventive effects of different doses of pentoxyfilline against ccl4-induced liver toxicity in rats. Iraqi J Pharm Sci. 2009:39.
28. Al-Malki AL. Antioxidant properties of thymol and butylated hydroxytoluene in carbon tetrachloride–induced mice liver injury. J KAU: Sci. 2010;22(1):239-48.
29. Trivedi S, Lal N, Mahdi AA, Mittal M, Singh B, Pandey S. Evaluation of antioxidant enzymes activity and malondialdehyde levels in patients with chronic periodontitis and diabetes mellitus. J Periodontol. 2014;85(5):713-20.
30. Paolicchi A, Emdin M, Ghliozeni E, Ciancia E, Passino C, Popoff G, et al. Human atherosclerotic plaques contain gamma-glutamyl transpeptidase enzyme activity. Circulation. 2004;109(11):1440-.
31. Prieto A, Campos A, Cameán A, Vasconcelos V. Effects on growth and oxidative stress status of rice plants (Oryza sativa) exposed to two extracts of toxin-producing cyanobacteria (Aphanizomenon ovalisporum and Microcystis aeruginosa). Ecotoxicol Environ Saf. 2011;74(7):1973-80.
32. MA Al-Saidya A. Study of pathological and anti-hyperlipidemic offects of ginger Zingiber officinalae in rats exposed to oxidative stress. Iraqi J Vet Sci. 2010;24(2):103-8.
33. Mahmood DFD, Abderrazak A, El Hadri K, Simmet T, Rouis M. The thioredoxin system as a therapeutic target in human health and disease. Antioxid Redox Signal. 2013;19(11):1266-303.
34. Cai L, Xiong X, Kong X, Xie J. The role of the lysyl oxidases in tissue repair and remodeling: a concise review. Tissue Eng Regen Med. 2017;14(1):15-30.