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The Effectiveness of Hawthorn Fruits in Improving Biochemical Changes in Hepatic Rats

LOBNA SAAD MOHAMMED ABD ELMEGED, Ph.D.*,** and ZARAH I. ALZAHRANI, Ph.D.***

The Department of Nutrition, Al-Baha University, AlMakhwa, Saudi Arabia, Department of Nutrition and Food Sciences, Faculty of Home Economics, Menoufia University, Shibin El Kom, Menofia Governorate 6131567, Egypt** and Department of Chemistry, Al-Baha University, AlMakhwa, Saudi Arabia****

Abstract

Background: The largest internal organ of the human body, the liver produces the most vital chemicals required for survival. Hawthorn fruits are considered one of the plants that most help remove hepatotoxicity, and not only that but also improve the functional state of the liver, as we will notice from the present research.

Aim of Study: Know the effectiveness of hawthorn fruits in improving biochemical changes in hepatic rats.

Material and Methods: Twenty-four male albino mice, specifically Sprague-Dawley breed, were utilized in the present investigation. Each group comprised six mice, & all mice were provided with a basal diet for one week before the start of the research. For twenty-eight days, the initial main group sample of control negative normal mice (C–ve) was provided with only the basal diet. Rats comprising the 2nd main group (n=18) were injected with Ccl4. This the primary group was further separated into 3 subgroups, one of which was administered a basal diet without any kind of therapy, serving as the control positive group (C+ve). Two group of this subgroup were fed a basal diet added with varying concentrations of hawthorn fruits (10% & 15%). The findings indicated that group four consisting of hepatic mice fed fifteen percent hawthorn fruits, exhibited superior serum high-density lipoprotein cholesterol levels in comparison to the control group (–). Additionally, group four (15% hawthorn fruit).

Results: Serum ALP & GPT, had a non-significant variance in GPT activity when compared to the group of healthy mice. The optimal therapy, as determined by the CAT to GPX ratio, was identified for group 4.

Conclusion: The fruits of the hawthorn plant are considered one of the plants that have a therapeutic and preventive effect on many diseases, especially liver diseases. The reason for this is that hawthorn fruits have a significant number of flavonoids & phenolic compounds.

Correspondence to: Dr. Lobna S. Mohammed Abd Elmeged,
E-Mail: Lobna@bu.edu.sa

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Introduction

THE largest internal organ in the human body, the liver, is an essential chemical factory that performs vital functions for survival. It receives all substances, toxins, and nutrients ingested by the digestive tract. Liver injury or dysfunction is a significant public health concern that poses obstacles for drug regulatory agencies, the pharmaceutical industry, & health care professionals alike. The liver is an essential organ that regulates a wide range of physiological processes; its activity is intricately connected to various critical functions, including secretion, metabolism, & storage. The substance can both exogenous (toxic compounds) and detoxify endogenous (waste metabolites) substances present in organisms, as well as synthesize beneficial agents. A significant portion of the toxins generated during the process of digestion are promptly conveyed to the liver, where they are either stored, resynthesized into alternative forms, or transported to other anatomical sites as required **[1]**. One of the body's vital organs, the liver, is the primary location for increased metabolism and excretion. Therefore, it performs and regulates the body's homeostasis in a superior way. Virtually all biochemical pathways that contribute to reproduction, nutrient provision, energy generation, and disease resistance involve it **[2]**. We classify hepatotoxic carbon tetrachloride (CC14) as a haloalkane. The hepatotoxicity has been the subject of thorough investigation, & its proposed mechanism entails an initial reductive dechlorination of carbon tetrachloride (CCU) to produce a trichloromethyl radical (+CC13). This radical then initiates membrane lipid peroxidation, which ultimately results in damage to the liver. Research has shown that the liver damage caused by CC14 can be significantly mitigated or prevented by pre-treating animals with a variety of antioxidants. Cyclic reticulum and mitochondrial

cytochrome P-450 metabolize carbon tetrachloride, The maximal concentration of the poison in the liver occurs within three hours of administration. After twenty-four hours, the level drops to the point where there is no CC14 remaining in the liver. Hepatic enzymes released into the serum correlate with the occurrence of necrosis. Intraperitoneal administration of CC14 at a dose varying from 0.1 to 3ml/kg can induce hepatotoxicity **[2]**. Global cultivation is underway for Hawthorn (Crataegus), a botanical specimen belonging to the Rosaceae family. It is renowned for its medicinal and culinary properties, earning the moniker "nutritious fruit" for the abundance of bioactive compounds it contains. It is included in the composition of functional meals, dietary supplements, and medicinal products. Hawthorn has significant medicinal and nutritional benefits because it contains vitamins, minerals, pectin, amino acids, vitamin C, epicatechol, and choline. Numerous investigations have demonstrated that hawthorn not only improves digestion but also has antioxidant, anti-inflammatory, anti-cancer, & anti-cardiovascular disease characteristics. This is due to the presence of bioactive polyphenol constituents **[3]**. The potential benefits of hawthorn fruit's elevated antioxidant content include reductions in inflammation, enhancement of skin health, cholesterol levels, and aiding in digestion. However, it may interact negatively with specific cardiovascular medications **[4]**. Hawthorn berry is an excellent source of polyphenols, which are potent plant-based antioxidant compounds. At high concentrations, unstable molecules known as free radicals can cause damage to the body. Antioxidants assist in their neutralization. Substances can produce free radicals. Additionally, increased levels of these substances may occur due to environmental factors like cigarette smoke and air pollution. As a result of their antioxidant activity, polyphenols have a variety of health benefits, including a reduced risk of developing certain malignancies **[5]**.

Aim of study:

The purpose of this research is to know the efficiency of hawthorn fruits in improving biochemical changes in hepatic rats.

Material and Methods

Material:

The experiment was conducted in the animal house of the Faculty of Home Economics, Menoufia University, June 2023.

Preparation fruits of Hawthorn (Crataegus species): Fruits of hawthorn were acquired from the Jeddah, Saudi Arabia, local market as a dried, the hawthorn fruits were pulverized and milled.

Experimental animals: In the experiment, we employed (24) male albino Sprague Dawley rats that weighed 150 plus or minus 10 grams each.

Carbon tetra chloride (Ccl4): A ten percent liquid solution of CCl4 was procured from El-Gomhoryia Company for Drugs, Equipments, & Chemical Industries, located in Cairo, Egypt **[6]**. Reported that the material in concern was dispensed in white plastic bottles, with each container holding one liter, and was classified as a toxic chemical risking liver poisoning. At the same time, it is mixed with paraffin oil procured from the pharmacy to achieve this throughout the induction process.

Methods:

Biological experiment:

Basal diet composition of rats:

The basal diet comprised the following components: Five percent cellulose, ten percent maize oil, 0.25 percent choline chloride, one percent vitamin mixture, 0.35 percent methionine, & four percent salt mixture **[7]**. MgSO4. 2H2O (204 milligrams), CaCO3 (600 milligrams), K2HPO4 (645 milligrams), CaHPO4. 2H2O (150 milligrams), ZnCl2 (0.5 milligrams), Fe(C6H5O7) 26H2O (55 milligrams), NaCl (334 milligrams), CuSO4. 5H2O (0.06 milligrams), MnSO4. 4H2O (10 milligrams), as well as Kl (1.6 milligrams) comprised the basal diet utilized in the experiment **[8]**. The standard test diet included all of the following: Vitamin E (ten international units), Thiamin (0.50 milligrams), Calcium panthothenic acid (0.40 milligrams), Vitamin A (200 international units), Vitamin K (0.50 international units), Pyridoxine (1.00 milligrams), Niacin (4.00 milligrams), Para-amino-benzoic acid (0.02 milligrams), Vitamin D (100 international units), Choline chloride (two hundred milligrams), Folic acid (0.02 milligrams), Inositol (twenty-four milligrams), and Vitamin B12 (two grams) **[9]**.

Table (1): Demonstrations the components of the fundamental & experimental diets.

Component (g)	Basal diet	5% Hawthorn	10% Hawthorn	15% Hawthorn
Evaluate substances	–	5	10	15
Casein	20	20	20	20
Corn oil	4.7	4.7	4.7	4.7
Mineral mix	3.5	3.5	3.5	3.5
Vitamin mix	1	1	1	1
Cellulose	5	5	5	5
Cholin chloride	2	2	2	2
Sucrose	10	10	10	10
Corn starch	Up to 100	Up to 100	Up to 100	Up to 100

Design of experiments & animal groups:

The Science Research Ethics Committee of the Faculty of Home Economics accepted the research protocol #11-SREC-06-2024.

• At the age of fourteen to sixteen weeks, 24 male Sprague-Dawley albino rats at maturity weighed 150±10g. The animals were housed in strain-free metallic coverings secured to plastic enclosures,

and stringent hygiene protocols were adhered to. To facilitate adjusting, a basal-style diet was supplied to the rodents for a duration of 7 days prior to the commencement of the experiment. We utilized specialized non-scattering feeding containers to administer diets to the rodents, thereby preventing food loss and contamination. Ad libitum water was supplied through a narrow-mouthed container equipped with a metallic tube securely fastened to its mouth using a rubber tube Previously, we exposed the organisms to a twelve-hour light and twelve-hour dark cycle for seven days to acclimate them to the experimental protocol. We separated the rats into five groups of six. The rodent classes consisted of the following:

- Group one: Six normal rats were provided with a basal diet (negative control).
- Group two: Six hepatic rats consuming a basal diet (positive control).
- Group three: Six hepatic rats consumed a basal diet comprising + 10% Hawthorn fruits.
- Group four: Six hepatic rats consumed a basal diet comprising + 15% Hawthorn fruits.

Biological evaluation:

We documented daily feed consumption and weekly body weight measurements throughout the twenty-eight-day experimental period. The body weight gain (B.W.G. percent), food efficiency ratio (F.E.R.), as well as organ weight, were ascertained in accordance with the methodology outlined via [10].

Blood sampling:

At the end of the twenty-eight-day trial, we sacrificed the mice under anesthesia and ether. We gathered blood samples in a sterile, dry centrifuge tube using the retro-orbital method. After clotting the blood samples at room temperature for twenty minutes, we centrifuged them at 1500 revolutions per minute for fifteen minutes. Until biochemical analysis, serum samples were obtained by a dry, sterile hypodermic infusion into Wisserman tubes, frozen at –10ºC in the refrigerator, and preserved. Following this, the liver, spleen, heart, lungs, & kidneys of the mice were extracted, rinsed in saline solution, desiccated, & weighed. The procedures followed were in line with the guidelines provided by [11].

Biochemical analysis:

Quantification of Lipids in Serum:

TG: Triglycerides were determined by enzymatic calorimetry in accordance with [12].

TC: Primary application of TC measurement, as described by [13].

High-density lipoprotein-cholesterol: Magnesium ions & Phosphotungstic acid, which precipitate lipoproteins other than the high-density lipoprotein fraction, can be used to measure cholesterol in the supernatant using a method like that employed for TC, according to [14].

Very low-density lipoproteins & low-density lipoproteins - cholesterol: The methodology established by [15]. was applied to the quantification of low-density lipoproteins (LDL) and very low-density lipoproteins (VLDL).

Total Lipids: According to [16]. The colorimetric approach was used to determine the amount of total lipids.

Estimation of liver functions:

Estimation of Alanine transferase (ALT): The approach proposed by [17]. Was used for the analysis necessary to establish the ALT. Pyruvate & L-Glutamate are produced as a byproduct of the reaction that ALT catalyzes, which involves the amino group transfer from L-alanine to a-ketoglutarate.

Estimation of AST: The approach developed by [18]. Was utilized throughout the process of determining the (AST).

Serum antioxidation enzyme activity: The serum samples were subjected to a ten-minute centrifugation at four degrees Celsius at 7000 x g. Following separation, the enzymes superoxidase dismutase (SOD), CAT, & glutathione peroxidase (GSII-Px) were determined. The estimation of antioxidant enzyme activity was conducted in accordance with the methodology outlined by Oyanagui (1984). The activity of (GPX) glutathione peroxidase enzyme was assessed using the methodology outlined by Paglia & Valentine in 1967. The methodology utilized for determining the activity of (CAT) antioxidant enzyme catalase was outlined by [19].

Complete Blood Count (CBC) Test:

WBC count, Hemoglobin level, red blood cell count, and WBC platelet count were all components of the complete Blood Count test [20]. state that the outcomes of complete Blood Count are produced by pneumatic & highly automated electronic analyzers utilizing aperture-impedance and/or laser beam cell measurement & counting described by [21].

Statistical analysis: One-way classification was employed to compute statistical analyses. In accordance with [22]. Analysis of variance (ANOVA) as well as least significant variance (LSD) are utilized.

HPLC identification of phenolic compounds:

The high-performance liquid chromatography analysis was carried out utilizing an Agilent 1260 series instrument. Using a Zorbax Eclipse Plus C8 column (4.6 millimeters x 250 millimeters i.d., five micrometers), the separation was accomplished. At a flow rate of 0.9 milliliters per minute, the mobile phase comprised water (A) & 0.05 percent trifluoroacetic acid in acetonitrile (B). We sequentially

programmed the mobile phase in the following linear-gradient fashion: 0 minutes (eighty-two percent A); 0–1 minute (eighty-two percent A); 1–11 minutes (seventy-five percent A); 11–18 minutes (sixty percent A); 18–22 minutes (eighty-two percent A); and 22–24 minutes (82 percent A). We observed the multiwavelength detector at 280 nanometers. We injected a volume of 5 l into each of the sample solutions. We maintained the temperature of the column at forty degrees Celsius.

Chemical analysis was performed on raw materials according to the **[23].**

The contents of moisture, protein, fat, crude fiber, & ash of lemongrass, Cratagaeus leaves, & fruits were determined. Total carbohydrates were calculated by the difference.

Results

The purpose of this investigation to know the efficacy of hawthorn fruits in improving biochemical changes in hepatic rats.

Chemical results:

Approximate chemical composition of Hawthorn (Crataegus) fruits:

Table (2) presents the chemical composition of Hawthorn (Cratagaeus fruits). The results indicated that the moisture, fat, protein, fiber, carbohydrates, ash, & energy value contents of Hawthornas dry weight (D/W) were 29.32, 6.27, 2.60, 3.22, 11.54 and 57.45 Kcal/100g, respectively. The contents of Hawthornas included moisture, ash, protein, lipids, fiber, and carbohydrates.

Table (2): Approximate chemical composition of Hawthorn.

Samples	Moisture (%)	Approximate chemical composition (%)				Total carbohydrates
		Ash	Protein	Lipids	Fiber	
Hawthorn Cratagaeus fruits	29.32	6.27	2.60	2.60	3.22	57.54

Total content of polyphenols compounds of the Hawthorn (Cratagaeus) fruits:

The total number of twenty various phenolic compounds were evaluated in fruits of Hawthorn 19 of them existed, while 1 were absent. Total phenolic compounds reached as high as (24726.03ppm). By focusing on the major phenolic compound, it was found that the highest content was recorded for chlorogenic acid (18627.55 ppm), Gallic acid (3449.39 ppm) & Catechin (975.97ppm).

Table (3): The total content of polyphenols compounds in Hawthorn (Cratagaeus) fruits.

		Area	Conc. (µg/ml)	Conc. (µg/g)
1	Gallic acid	1949.85	172.47	3449.39
2	Chlorogenic acid	7177.83	931.38	18627.55
3	Catechin	226.19	48.80	975.97
4	Methyl gallate	23.35	1.18	23.53
5	Coffeic acid	170.67	13.21	264.14
6	Syringic acid	93.06	6.81	136.12
7	Pyro catechol	20.32	2.93	58.59
8	Rutin	220.23	32.49	649.72
9	Ellagic acid	21.81	2.18	43.58
10	Coumaric acid	194.69	6.93	138.58
11	Vanillin	0.00	0.00	0.00
12	Ferulic acid	305.49	17.75	354.93
13	Naringenin	11.78	1.08	21.53
14	Rosmarinic acid	10.87	1.17	23.31
15	Daidzein	2.14	0.12	2.40
16	Querectin	16.51	2.23	44.57
17	Cinnamic acid	18.33	0.33	6.56
18	Kaempferol	7.05	0.44	8.90
19	Hesperetin	61.27	3.01	60.24

Biological effects:

Impact of distinct levels of hawthorn fruits on feed intake (FI) & feed efficiency ratio, body weight gain,of hepatointoxicated mice:

Table (4) presents the average value of BWG (g/day/rat) in hepatic mice fed different diets. The mean value of BWG in group 2 was significantly less than in group 1, at 0.11±0.02 and 0.75±0.11, correspondingly, indicating a significant distinction. In comparison to group 2, the mean values of all hepatic mice fed different diets did not differ significantly. 0.33±0.02 & 0.65±0.01 were the respective values. The group that consumed 15% hawthorn fruits (hepatic mice) achieved the highest body weight gain% value in comparison to group 2.

Table (4) provides the average feed intake (g/day/rat) of hepatic mice given variable diets. The information indicated that group 2 had a lesser mean value of F.I. than group 1, at 11.5±0.1 & 15.75±0.2, respectively, indicating a significant variance of 37% in the increase of group 1 over group 2. The mean values of All-hepatotoxicated mice on different diets differed significantly from those in group 2, except for group 4. Group 4, which consisted of hepatic mice fed fifteen percent hawthorn fruits, achieved the highest numerical F.I. in comparison to the control group.

Table (4) displays the average FER values of hepatic rats fed various diets. The information indicates that group 2 had a decrease mean value of FER than group 1, with 0.010±0.001 & 0.048±0.04, correspondingly. This distinction is statistically significant, with group 1 experiencing a 380% decrease in FER compared to group 2. All hepatic mice fed on

different diets saw a significant decline in mean values compared to group 2. The values for hawthorn fruits at ten percent and fifteen percent are 0.11± 0.02 and 0.042±0.04, respectively. These findings are from *[3]*. Researchers documented a gradual reduction in body weight in mice fed hawthorn fruits.

Table (4): Impact of various levels of hawthorn fruits on body weight gain, feed intake (FI) & feed efficiency ratio of hepatointoxicated mice.

Parameters Groups	BWG (g/day/rat)		FI (g/day/rat)		FER	
	Mean ± SD	% Change of control (+)	Mean ± SD	% Change of control (+)	Mean ± SD	% Change of control (+)
(l) Control -Ve	0.753a±0.01	+581.8	15.75a±0.2	37	0.048a±0.04	380
(2) Control +Ve	0.11d±0.002	+00.00	11.50c±0.1	00.00	0.010d±0.001	00.00
(3) 10 % hawthorn fruits	0.33c±0.02	+200	13.3d±0.2	15.7	0.0ld±0.02	110
(4) 15 % hawthorn fruits	0.65b±0.01	+490.9	15.5a±0.03	34.8	0.042c±0.04	320
LSD	0.197		0.264		0.002	

All results are expressed as mean ± SD (standard deviation of the mean).

* Values in each column with different letters are significantly different (p<0.05).

* One way ANOVA test used.

Impact of distinct levels of hawthorn fruits on triglycerides, Low density lipoprotein cholesterol, total cholesterol, high density lipoprotein cholesterol, & very low-density lipoproteins cholesterol of hepatic mice:

Table (5) displays the average serum concentration (T.C.) in milligrams per deciliter for hepatic mice fed various diets. The data indicates that group 2 had a higher mean value of (T.C.) than group 1, with respective values of 278±0.4 & 145±0.3. This variation represents a significant percentage reduction of -47.8% for group 1 in comparison to group 2. All hepatic mice fed various diets saw a significant reduction in mean values compared to group 2. The values for hawthorn fruits containing ten percent and fifteen percent hawthorn were 152.3±0.2 & 149±0.5mg/dL, respectively. The respective percentages of decline were -45.3 and -46.3. In comparison to group 2, group 4, consisting of hepatic mice fed fifteen percent hawthorn fruits, exhibited the highest serum concentration (T.C.).

Table (5) also presents the average serum triglyceride value (milligrams/deciliter) in hepatic rats fed various plant extracts. Group 2 exhibited a higher average triglyceride value than group 1, indicating a statistically significant variance of 46.06 percent for group 1 compared to group 2. The mean values of all hepatic mice that were fed diets containing varying concentrations of hawthorn fruits decreased significantly when compared to group 2. We documented the optimal treatment for group four.

The average level of serum high-density lipoprotein c (mg/dL) of hepatic mice on various diets is presented in Table (5). The data revealed that group 2 had a lower mean value of HDL c than group 1, measuring 25.3±0.2 versus 51.8±0.2, respectively. This discrepancy indicates a significant percentage increase of 104.7 percent for group 1 compared to group 2. All hepatic mice, fed various diets, significantly increased their mean values compared to group 2. The groups experienced increases of +57.3, +83, correspondingly. In comparison to the control group, group 4, consisting of hepatic mice fed fifteen percent hawthorn fruits, exhibited the highest serum HDL c levels.

Table (5) shows the mean value of serum LDL-c (milligram/deciliter) in hepatic mice fed various diets. According to the data, the control (+) group had a higher mean value of LDL c than group 1, measuring 216.7±0.3 vs. 74±1. This difference was statistically significant, with group 1 losing -65.8% compared to group 2. All hepatic mice fed various diets showed a significant decrease in mean values compared to group 2. Group 4 mice are comparable to the healthy cohort.

Table (5) presents the average serum VLDL c concentration (mg/dL) of hepatic mice on various diets. The information revealed that group 2 had a higher mean value of (V.L.D.L.c) than group 1, at 36.1±0.1 & 19.5±0.5, respectively. This variation indicated a significant 45.9 percent reduction for group 1 in comparison to group 2. For the ten percent and fifteen percent hawthorn fruit groups, the percentage reductions were –32.1 and 38.5%, respectively. With respect to serum (V.L.D.L.c), group 4 (15 percent hawthorn fruit) exhibited the most effective treatment.

Table (5): Effect of different levels of hawthorn fruits on high density lipoprotein cholesterol, total cholesterol, triglycerides, Low density lipoprotein cholesterol, and very low density lipoproteins cholesterol of hepatic mice.

	TC (mg/dL)	TG (mg/dL)	HDLc. (mg/dL)	VLDLc. (mg/dL)	LDLc. (mg/dL)
(1) Control - ve	145a±0.3	97.4a±0.1	51.8a±0.2	19.5f±0.5	74a±0.1
Change of control (+) group%	–47.8	–46.07	104.7	–46.6	–96.6
(2) Control + ve	278.1d±0.4	180.6d±0.4	25.3d±0.2	36.1a±0.1	216c±0.3
Change of control (+) group%	00.00	00.00	00.00	00.00	00.00
(3) 10% hawthorn fruits	152.3c±0.2	122.3c±0.2	39.8c±0.2	24.5b±0.2	88b±0.4
Change of control (+) group%	–45.3	–32.3	57.3	–32.2	–95.9
(4) 15% hawthorn fruits	149.b1c±0.5	1108b±0.2	46.3b±0.4	22.2c±0.1	74.4a±0.2
Change of control (+) group%	–46.4	–38.7	83	–38.5	–96.6
LSD	0.689	0.370	0.889	459	0.469

All results are expressed as mean ± SD (standard deviation of the mean).
* Values in each column with different letters are significantly different ($p<0.05$).
* One way ANOVA test used.

Effect of various levels of hawthorn fruits on kidney function of hepatic mice:

Table (6) presents the average serum urea concentration (in milligrams per deciliter) of hepatic mice that were provided with different diets. The data revealed that group 2 had a higher mean value of uric acid than group 1, at 48.1±0.1 vs. 22.6±0.1 mg/dL, respectively. This variation was statistically significant, as group 1 had a reduction of -53.02% compared to group 2. All hepatic rodents fed different diets saw a significant decrease in mean values compared to group (2). In comparison to group (2), group 4 (with fifteen percent hawthorn fruit) demonstrated the most efficient therapy. There is potential for the utilized plants to rectify the renal dysfunction in mice induced by CC14 injection.

Concerning serum creatinin, it was noted that group 2 had a mean value of 1.4±0.5 for creatinin & group 1 had a mean value of 0.76±0.1 for serum creatinin. This distinction was statistically significant, as group 1 had a decline of –45.7% in comparison to group 2. The mean values of all hepatic rodents that were fed various diets declined significantly in comparison to group (2).

Additionally, it was noted that group 2 had a greater mean value of U.A. than group 1, at 7.9±0.1 vs. 3.1±0.1 milligrams per deciliter, respectively. This discrepancy was statistically significant, as group 1 had a –60.7% reduction in U.A. compared to group 2. The mean values of all hepatic rodents that were fed various diets decreased significantly in comparison to group (2). Serum U.A. levels in the group of four percent hawthorn fruits were found to be superior to those in the control (2) group.

Table (6): Impact of different levels of hawthorn fruits on urea, uric acid Creatinine in serum of hepatic rat.

Parameters Groups	Urea (U/L)		Uric acid (U/L)		Creatinine (U/L)	
	Mean ± SD	% Change of control (+)	Mean ± SD	% Change of control (+)	Mean ± SD	% Change of control (+)
(l) Control -Ve	22.6r±0.1	–53.02	3.1c±0.1	–60.8	0.76b±0.01	–45.7
(2) Control +Ve	48.1a±0.15	±00.0 0	7.9a±0.1	00.00	1.4a±0.05	00.00
(3) 10% hawthorn fruits	40.1b±0.1	–16.6	4.7b±0.01	–40.5	0.78d±0.21	–44.3
(4) 15% hawthorn fruits	27.8°±0.2	-42.2	4.1d±0.1	–48.1	0.85c±0.1	–39.3
LSD	0.872		0.120		0.390	

All results are expressed as mean ± SD (standard deviation of the mean).
* Values in each column with different letters are significantly different ($p<0.05$).
* One way ANOVA test used.

Impact of various levels of hawthorn fruits on liver function of hepatic mice:

Table (7) presents the average serum (GOT) (U/L) values of hepatic rats that were provided with different diets. It was observed that group 2 had a higher average value of (GOT) (AST) than group 1, with respective values of 155±1 & 48±0.2. This variation indicates a significant distinction, as group 1 had a decrease of –69.03% in comparison to group 2. The mean values of all hepatic mice that were fed various diets reduced significantly in comparison to group 2.

Serum (U/L) (GPT) The analysis shown that group 2 had higher mean values of (GPT) and (ALT) than group 1, 75±1 & 35±0.2, respectively. This distinction was statistically significant, as group 1 had a –53.3 percent reduction in ALT levels compared to group 2. The mean values of all hepatic mice that were fed different diets declined significantly in comparison to group (2). The range of percentage decreases across all categories was from 31.9 to -43.9%. The most effective treatment, Group four percent hawthorn fruits, did not result in a statistically significant distinction in GPT activity when compared to the group of healthy rodents.

The analysis demonstrated that group 2 had a greater mean value of (ALP) than group 1, at 150±2 versus 111±1, correspondingly. This variation was statistically significant, as group 1 had a decline of twenty-six percent in comparison to group 2. The mean values of all hepatic mice that were fed different diets declined significantly in comparison to group (2). The optimal serum ALP therapy was identified for group four.

Table (7): Impact of various levels of hawthorn fruits on serum levels of AST, Alanine transaminase and alkaline phosphatase enzyme of hepatic mice.

Parameters Groups	AST (U/L)		ALT (U/L)		ALP (U/L)	
	Mean ± SD	% Change of control (+)	Mean ± SD	% Change of control (+)	Mean ± SD	% Change of control (+)
(l) Control -Ve	488a±0.2	–69.0	35g±0.1	–53.33	111f±l	–26
(2) Control +Ve	155d±l	+00.00	75a±1	00.00	150a±2	00.00
(3) 10% hawthorn fruits	74c±0.6	–52.3	51.07h±0.8	–31.9	138b±0.1	–8
(4) 15% hawthorn fruits	63.08b±0.1	–59.30	42.05c±0.4	–43.9	127e±0.22	–15.3
LSD	0.531		0.567		0.055	

All results are expressed as mean ± SD (standard deviation of the mean).
* Values in each column with different letters are significantly different (p<0.05).
* One way ANOVA test used.

Impact of distinctive levels of hawthorn fruits on serum antioxidation enzyme activity of hepatic mice:

The data in Table (8) represent the average serum SOD (U/mL) levels of hepatic mice that were provided with various diets. It was observed that group 2 had a lesser mean value of SOD than group 1, at 8.3±0.3 versus 40.6±0.4. This distinction was statistically significant, with group 1 exhibiting a 389.16% rise in SOD compared to group 2. The mean values of all hepatic mice that were fed various diets increased significantly in comparison to group (2). The treatment group containing fifteen percent hawthorn fruits demonstrated the greatest SOD value when compared to group 2.

Regarding GPX (U/mL), it was observed that group 2 had a mean value of 44.6±0.4 for GPX and 17.2±0.2 for GPX in group 1. This distinction was statistically significant, with group 1 having a 159.3% rise in GPX compared to group 2. The mean values of all hepatic mice that were fed various diets increased significantly in comparison to group (2). The corresponding percentages of rise were 91.9% and 129.7%. Based on the GPX ratio, group 4 (with fifteen percent of hawthorn fruits) exhibited the most efficient therapy.

The average CAT value of group 2 was 27.5±0.2, while that of group 1 was 82±0.1. This distinction was statistically significant, as group 1 had a 198% enhance in CAT values compared to group 2. The average values of all hepatic mice that were fed various diets increased significantly in comparison to group (2). Compared to group (2), group 4 (15 percent hawthorn fruit) demonstrated the most effective treatment as measured by the CAT.

Table (8): Effect of different levels of hawthorn fruits on serum antioxidation enzyme activities.

Parameters Groups	SOD (U/L)		GPX (ng/mL)		CAT (mmol/l)	
	Mean ± SD	% Change of control (+)	Mean ± SD	% Change of control (+)	Mean ± SD	% Change of control (+)
(l) Control -Ve	40.6a±0.4	398.2	44.6a±0.4	159.3	82.1a±0.4	198.6
(2) Control +Ve	8.3d±0.0.3	+00.0 0	17.2d±0.3	00.00	27.5d±0.3	00.00
(3) 10% hawthorn fruits	32.5c±0.2	291.6	33c±0.2	91.9	69.7c±0.2	153.5
(4) 15% hawthorn fruits	35.2b±0.3	324.1	39.5b±0.3	129.7	79.4b±0.3	188.7
LSD	0.455		0.436		0.451	

All results are expressed as mean ± SD (standard deviation of the mean).
* Values in each column with different letters are significantly different (p<0.05).
* One way ANOVA test used.

Discussion

The largest internal organ in the human body, the liver, is an essential chemical factory that performs vital functions for survival. It receives all substances, toxins, and nutrients ingested by the digestive tract. Liver injury or dysfunction is a significant public health concern that poses obstacles for drug regulatory agencies, the pharmaceutical industry, & health care professionals alike. The liver is an essential organ that regulates a wide range of physiological processes; its activity is intricately connected to various critical functions, including secretion, metabolism, & storage. The substance can both exogenous (toxic compounds) and detoxify endogenous (waste metabolites) substances present in organisms, as well as synthesize beneficial agents. A significant portion of the toxins generated during the process of digestion are promptly conveyed to the liver, where they are either stored, resynthesized into alternative forms, or transported to other anatomical sites as required *[1]*.

Hawthorn fruits decrease postprandial lipid levels in humans, according to research *[24]*. Serum lipids were significantly impacted by hawthorn fruits, which reduced cholesterol levels *[25]* agreed with the findings of *[26]*. The researchers reported that mice, given a daily concentration of 150mg/kg b.w. of hawthorn fruit extract for fifteen days, demonstrated a significant defense against the induced reduction in serum cholesterol *[27]*. Researchers reported a reduction in serum TG levels when they added five percent hawthorn fruit to the diet of hypercholesterolemic rats. Table 5's findings corroborate those of *[28]*. which indicate that hawthorn fruits decrease low-density lipoprotein (bad cholesterol) and cholesterol levels. Hawthorn fruit has been demonstrated in numerous human studies conducted over the last few decades to reduce LDL (bad cholesterol) levels & increase elevation high-density lipoprotein (good cholesterol) levels. Hawthorn fruit extracts of dichloromethane (MK.D.) & ethyl acetate (MICE) decreased plasma total cholesterol, body weight gain, and triglyceride levels in a statistically significant manner. Researchers have established a correlation between the antiobesity and antihyperlipidemic properties of this extract and the carbazole alkaloids, specifically Mahanimbine. Oral administration thirty mg/kg/day) reduced body weight gain and plasma total cholesterol and triglyceride levels significantly. The findings of this study indicate that hawthorn fruits have remarkable pharmacological potential for obesity prevention *[29]*.

According to human studies, hawthorn fruits have substantial impacts on urea and creatinine levels *[30]*. According to *[31]*. The structure of hawthorn fruits inhibits glomerular hyperfiltration. Similarly, *[32]*. Determined that a 500mg/kg body weight hawthorn in diuretic decreased body weight without proximal function, Na+ excretion, or uric acid excretion.

The outcomes presented in Table (7) are consistent with the results reported by *[31]*. Regarding the efficacy of the ethanolic extract derived from hawthorn fruits. In a study conducted by *[32]*. Hawthorn leaves administered orally to rats overloaded with iron for 31 days prior to the experimental condition. The rats received hawthorn leaves at a concentration of fifty milligrams per kilogram of b.w. daily. *[33]*. The avoidance & management of nonalcoholic fatty liver illness in rodents induced by a high-fat diet can be achieved through the extraction of hawthorn fruits. The mechanism by which this occurs is by enhancing the ability to resist oxidation. According to a study by *[34]*. Hawthorn possesses hepatic protective properties against CCl4. Additionally, the researchers found that hawthorn inhibits platelet-derived growth factor-stimulated hepatic stellate cell migration & CC14-induced liver fibrosis in mice.

The findings presented in Table (8) are consistent with those reported by *[5]*. Induced a significant rise in the activities of hepatic & kidney SOD, GPx, and CAT in comparison to rodents treated with iron overload. The fruit of the hawthorn plant was discovered to contain a significant quantity of flavonoids & phenolic compounds. These compounds potentially contain free radicals and being of natural origin, could serve as an example for the development of novel biologically active compounds with iron-chelating capabilities.

Recommendations:

1- It is suggested to use hawthorn fruits for hepatic patients to improve liver function.
2- Various levels of hawthorn fruits, may be suggested for lowering ow-density lipoprotein levels.

Conclusion:

The fruits of the hawthorn plant are considered one of the plants that have a therapeutic and preventive effect on many diseases, especially liver diseases. The reason for this is that hawthorn fruits have a significant number of flavonoids & phenolic compounds, which were discovered to possess high levels of free radical activity. These natural molecules can potentially serve as a basis for the development of novel biologically active substances.

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فعالية ثمار الزعرور فى تحسين التغيرات البيوكيميائية فى الفئران المصابة بالالتهاب الكبدى

الكبد هو أكبر عضو داخلى فى جسم الإنسان، وينتج أهم المواد الكيميائية اللازمة للبقاء على قيد الحياة. وتعتبر ثمار الزعرور من أكثر النباتات التى تساعد فى إزالة السمية الكبدية، وليس ذلك فحسب، بل تعمل أيضًا على تحسين الحالة الوظيفية للكبد، كما سنلاحظ من البحث الحالى والذى يهدف الى معرفة فعالية ثمار الزعرور فى تحسين التغيرات البيوكيميائية فى الفئران الى تم حقنها برابع كلوريد الكربون، تم استخدام أربعة وعشرين فأر ذكور من سلالة ألبينو، وتم تقسيم الفئران الى اربع مجاميع تتألف كل مجموعة من ستة فئران، وتم تغذية جميع الفئران بنظام غذائى أساسى لمدة أسبوع واحد قبل التجربة وتتكون المجموعة الأولى من ست فئران طبيعية تم تغذيتها على الوجبة الأساسية والمجموعة الضابطة السالبة والمجموعة الثانية وهى تتكون من ست فئران تم حقنها برابع كلوريد الكربون وتتغذى على الوجبة الأساسية دون علاج وتعتبر المجموعة الضابطة الموجبة، والمجموعة الثالثة التى تتكون من ست فئران تم حقنها برابع كلوريد الكربون وتغذت على الوجبة الأساسية +١٠٪ من ثمار نبات الزعرور والمجموعة الرابعة وتتكون من ست فئران تم حقنها برابع كلوريد الكربون وتغذت على الوجبة الأساسية +١٥٪ من ثمار نبات الزعرور واستمرت التجربة ٢٨ يوم وبعدها تم ذبح الفئران و اخذ عينات الدم لعمل التحاليل البيوكيميائية . اظهرت النتائج مستويات عالية من الكوليسترول عالى الكثافة (HDL) لدى المجموعة الثالثة والرابعة وذلك عند مقارنتها بالمجموعة الضابطة السالبة، بالإضافة إلى ذلك، أظهرت المجموعة الرابعة (١٥٪ من ثمار الزعرور) تباينًا فى نشاط GPT عند مقارنتها بالمجموعة الضابطة السالبة. لذا تعتبر ثمار نبات الزعرور من النباتات التى لها تأثير علاجى ووقائى على العديد من الأمراض، وخاصة أمراض الكبد. والسبب فى ذلك أن ثمار الزعرور تحتوى على عدد كبير من الفلافونويدات والمركبات الفينولية.