Uttar Pradesh Journal of Zoology

Volume 46, Issue 1, Page 155-170, 2025; Article no.UPJOZ.4516
ISSN: 0256-971X (P)

Buckthorn Leaves and Fruits: A Comparative Study of Their Hepatoprotective Effects in Tetrachloride-Induced Liver Disorders in Rats

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

DOI: https://doi.org/10.56557/upjoz/2025/v46i14751

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://prh.mbimph.com/review-history/4516

Original Research Article

Received: 05/11/2024
Accepted: 07/01/2025
Published: 11/01/2025

ABSTRACT

An overdose of carbon tetrachloride by injection leads to liver damage and massive hepatocellular necrosis, whereas sea buckthorn leaves and fruits have hepatoprotective properties. The aim of this study was to compare the hepatoprotective effects of sea buckthorn leaves and fruits in hepatotoxic rats induced by chlorocarbon. The experiment was carried out in an animal enclosure.

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Cite as: *Abbas, Rasha Khalid, and Lobna Saad Mohammed Abd Elmeged. 2025. "Buckthorn Leaves and Fruits: A Comparative Study of Their Hepatoprotective Effects in Tetrachloride-Induced Liver Disorders in Rats". UTTAR PRADESH JOURNAL OF ZOOLOGY 46 (1):155-70. https://doi.org/10.56557/upjoz/2025/v46i14751.*

Before the start of the experiment, all rats were given a basic diet for one week. The rats were then divided into six groups, each group comprising six rats. The 1st group received only a basic diet for twenty-eight days and served as the rats' normal negative control (C -ve). The other groups of rats (thirty in total) were administered carbon tetrachloride. The groups were divided into five groups, with four groups receiving BL (5% and 10%) and BF (5% and 10%) and one group acting as a control group that suffered from the disease but did not follow the experimental diet. In contrast to the control group (+), all liver values of the rats given different diets showed significant mean reductions. Group "4" (hepatotoxic rats fed ten percent BL) had the highest FI, BWG and ARR compared to the control group (+). For ALP, insignificant differences were found between groups "4" and "6". Mathematically, the best management considering the serum albumin has been documented for group"4" (rats fed on 10% BL) in comparison with control (+) group. Research results indicate its positive effect on the liver and improvement in the condition of liver tissue. It is important to recognise that research on sea buckthorn is still ongoing and further investigation is needed to validate its potential therapeutic applications and determine the appropriate dosages.

Keywords: Flavonoid; antioxidant; anti-inflammatory; acetaminophen; hepatotoxicity.

1. INTRODUCTION

The liver is an essential organ that supports nearly all the body's other organs. In addition, it is the primary organ responsible on storing, enzymatic metabolism, secretion, detoxification, and removal of medications and other exogenous products. (Mahmoud & Mudawi, 2020) and (Naz, & Mushtaq. 2020). Liver damage is primarily caused by toxic substances, infections, autoimmune diseases and excessive alcohol consumption. (Ji et al*.,* 2020). In the metabolism of carbohydrates, the liver participates in a variety of functions, such as gluconeogenesis, which involves the production of glucose from glycerol, lactate, or specific aa`. and glycogenesis is the process of transforming glucose into glycogen, while glycogenolysis is the process of changing glucose from glycogen (Liu et al., 2012). The immune system (IS) composed of a highly & complex interactive cell network & their products. The system demonstrates. (Reichlin, 1993). distinct features: "memory" & exquisite specificity. A subset of immune cells identifies & reacts to the various external stimuli and cases might have during their lifetime. The immune system is modulated by helper suppressor cells & their soluble products. It maintains intimate communication with other systems in body, such as neuroendocrine system, & is controlled by these systems. Buckthorn Fruits (BF) are pea-sized, berry-like that begin as red and convert to black in late summer to early fall. They additionally have antioxidant and anti-inflammatory characteristics, as well as a variety of nutrients that have been demonstrated to have health advantages for humans. Antioxidants are present in Buckthorn Leaves (BL) leaves, helping in protecting your cells from the damage triggered by free radicals. This damage may result in the development of serious illnesses, including tumors, cardiovascular diseases stroke, and liver diseases. Consuming buckthorn leaves could decrease your susceptibility to potentially fatal illnesses (Cai et al., 2022; Tanwar et al., 2017). The fermentation liquid of buckthorn fruits was found to be protective against an alcoholic liver disorder and to regulate the composition of the gastrointestinal microbiota. Buckthorn fruits are a third-generation functional fruit that is utilized in Tibetan and Uygur medicine. The extract of buckthorn has been demonstrated to possess activity against tumors of the liver, and recent investigations have demonstrated that it contains a variety of efficient chemical elements.5 The hepatocytes are protected from free radical injury by the natural phenols of sea buckthorn, which eliminate peroxide free radicals generated by lipids throughout liver metabolism. Its flavonoids show antioxidant properties, which reduce hypertension, optimize hepatic fat decomposition, and reduce elevated blood lipid concentrations. (Becker et al., 2014; Kumar et al., 2019). To prevent the excessive accumulation of free radicals in the liver and to protect hepatocytes from damage, terpenoids stimulate the production of metallothioneins in liver tissues that contain a potent free radical scavenging capacity.8 Investigations have suggested that triterpenoids may protect against alcoholic liver illness by controlling E. coli numbers, bifidobacteria and Lactobacillus acidophilus in microbiota of the intestinal tract, thus enhancing the imbalance (Snedecor & Cochran, 1967). The application of modern fermentation engineering offers a new pathway

for marketing buckthorn leaves, which are distinguished by their high acidity and low sugar content. The fermentation broth is the subject of very little research, despite the fact that research on buckthorn currently focusses on its chemical elements and pharmacologically active components. Consequently, we developed a mice model of alcoholic liver illness and administered buckthorn fermentation liquid (SFL) to the rats. We assessed the degree of liver damage and determined lipid metabolism indexes. Additionally, we followed alterations in antioxidant enzyme activity to identify the protective impact of SFL on alcoholic liver illness and the regulation of the gastrointestinal microbiota association to manage alcoholic liver disease. The objective was to enhance the utilization rate of buckthorn and to establish a scientific basis for the investigation of SFL as a functional food (Singh et al., 2019).

The antioxidant enzyme activity has been enhanced and MDA levels were reduced through the oral administration of flavonoids and buckthorn powder. The messenger RNA concentrations of nuclear factor NF-E2-related factor (nrf2) in the hepatopancreas and muscle were markedly elevated by sea buckthorn powder and sea buckthorn flavonoids according to antioxidant molecular markers. Furthermore, Nrf2-regulated messenger RNA expression concentrations of downstream antioxidant-related genes (gr, cat, gpx, and sod) had additionally increased. The mRNA expression concentration of proinflammatory cytokines, involving interleukin-1β, interleukin-6, and nuclear factor-κB (nf-κb), have been decreased in the immune aspects. Conversely, the expressions of anti-inflammatory cytokines, involving growth factor-β (tgf-β) and interleukin-10, have been increased in the head kidney and spleen tissues following the oral intake of sea buckthorn. Following giving sea buckthorn flavonoids, the ratio of n-3 polyunsaturated fatty acid (PUFA)/n-6 PUFA within muscle fatty acid composition was significantly greater than that of the glucose group (P-value < 0.05). (Wang et al., 2011). buckthornit has important health functions and medicinal value, and enjoys the reputation of ‘green gold buckthorn has a high content and rich variety of flavonoids. Because it contains these abundant flavonoids, buckthorn has the functions of depressing blood pressure, blood glucose, and blood lipids and improving oxidation resistance. (Smith et al., 2019). A study in broiler has shown that buckthorn leaf flavonoids enhance antioxidant capacity under heat stress conditions by increasing the activity of total antioxidant capacity (T-AOC) and copper-zinc superoxide dismutase and decreasing malondialdehyde (MDA) contents.24 Within human peripheral blood mononuclear cells, buckthorn flavonoids also inhibit inflammatory responses through modulating cytokine secretion and inflammatory cytokine secretion. In addition, studies have shown that the ratio of unsaturated fatty acids to saturated fatty a` in the muscle of broilers was elevated by buckthorn flavonoids (0.1%). (Tulsawani et al., 2013). The antioxidant and immune characteristic of rats were substantially improved by oral ingestion of buckthorn flavonoids and fruits buckthorn powder, which thus mitigated the negative consequences of a high-carbohydrate diet on growth. buckthorn exhibited its potential as a novel immune enhancer by modulating the expression of pathway-related genes and enzyme activity in crucial metabolic and immune organs. These findings establish a solid theoretical foundation for utilizing buckthorn (Zeli Gao et al., 2014).

1.1 Hypothesis

H0: Buckthorn leaves and Fruits do not im-proves the functional status of the liver in hepatotoxic rats.
HA: Buckthorn leaves and Fruits im-proves the functional status of the liver in hepatotoxic rats.

2. MATERIALS AND METHODOLOGY

2.1 Test Substances and Chemicals

Buckthorn leaves and fruits: have been purchased from a local market in (Jeddah, KSA).

Experiraental animals: Thirty (36) male albino Sprague Dawley rats, each weighed 150±10grams, have been utilized for the purpose of the research.

Used chemicals: Ccl4 has been acquired as a ten percent liquid solution from El-Gomhoryia Company for Chemical Industries in Cairo, Egypt. It arrived in white plastic bottles, each containing one liter, as a dangerous chemical compound for hepatic poisoning, regarding Passmore & Eastwood (1986).

2.2 Study Design

An experimental animal study was conducted over nine days. The rats were split at random across six groups (n= six per group) following:

Group (1): Rats received a fundamental diet and normal rats control(-)
Group (2): Rats with liver toxicity received a basal diet Control (+)
Group (3): Rats with liver toxicity nourished by a basal diet+ 5%Buckthorn Leaves (BL).
Group (4): Rats with liver toxicity nourished by a basal diet+10% Buckthorn Leaves (BL)
Group (5): Rats with liver toxicity nourished by a basal diet+ 5%Buckthorn Fruits (BF)
Group (6): Rats with liver toxicity nourished by a basal diet+ 10%Buckthorn Fruits (BF)

All rats were sacrificed by ether anesthesia on the ninth day of the experiment. Therefore, the blood samples have been collected in a dry, clean centrifuge tube by inferior vena cava process. Afterward, they were clotted after 20 minutes at room temperature and 15 minutes of cenrifugation at 1500 rpm. Moreover, serum samples have been obtained by a dry clean syringe, poured into Wasserman tubes, and frozen at mince ten degrees Celsius before biochemical examination. Furthermore, the rat's liver was then removed and washed in a saline solution before dried and weighted.

The following formula was used to measure the relative liver weight:

$$\text{Relative liver weight} = \frac{liver\ organ\ weight}{\text{final body weight}} \text{ X } 100$$

2.3 Biological Assessment

Weight of rats was measured at the beginning and end of the trial, and their daily feed intake (FI) was recorded. The experimental diets were subjected to a biological evaluation at the conclusion of the study to assess body weight gain (BWG%) and feed efficiency ratio (FER), as previously documented (Chapman et al*.,* 1959).

2.4 Biochemical Analysis

Chemical kits were used to assess serum glucose in accordance with (Trinder, 1969*).* Triglycerides were carried out using the techniques mentioned in (Fassati et al*.,* 1982). Total cholesterol has been calculated utilizing the (Allain et al., 1974) technique. The concentration of high-density lipoprotein has been detected by the methods of (Lopez et al*.,* 1977). The following equation was utilized for determining both Low-Density Lipoprotein (LDL) & Very Low- Density Lipoprotein (VLDL): LDL-Cholesterol = Total Cholesterol - HDL-c + VLDL. VLDL-c = (triglycerides /5) (Lee et al*.,* 1996). The alkaline phosphatase (ALP) concentration has been calculated by using the technique of (FCC et al 1983), alanine aminotransferase (ALT) levels have been estimated by utilizing the technique of (Yound et al*.,* 1975), & aspartate aminotransferase transferase levels have been estimated by using the method of (Henry et al*.,* 1974). While serum creatinine, urea, & uric acid have been calculated by using the technique of (Schmit, 1964; While et al*.,* 1970; Malhotra et al*.,* 2003).

HPLC identification of phenolic compounds: HPLC analysis has been performed with an Agilent 1260 series. The separation applied a Zorbax Eclipse Plus C8 column (4.6-millimeter x 250-millimeter i.d., 5 micrometers). The mobile phase included water (A) and 0.05% trifluoroacetic a in acetonitrile (B) at a flow rate of 0.9 milliliter per minutes. The mobile phase has been progressively programmed in a linear gradient as detailed below: zero minute (eighty-two percent A); zero to one minute (82% A); one to eleven minute (75% A); eleven to eighteen minute (60% A); eighteen to twenty-two minute (82% A); twenty-two to twenty-four minute (82% A). The multi-wavelength detector has been detected at 280 nanometers. The volume of injection for every sample solution was five micrometers. The column temperature maintained at forty degrees Celsius A.O.A.C. (2000).

2.5 Statistical Analysis

The data have been investigated utilizing a completely randomized factorial design (SAS Users Guide, 1988) upon detection of a significant main effect; means have been separated utilizing the student-Newman-Keuls method. Variations among therapies (P-value equal 0.05 or less) have been deemed significant utilizing the Costat Program. The biological data have been examined with one-way ANOVA.

3. RESULTS

3.1 Chemical Results

This investigation aimed to know comparative hepatoprotective effect between buckthorn leaves and fruits in hepatotoxic rats induced by carbon tetra chloride. The results of the current study were presented as follows:

3.2 Total Phenolics Content (TPC) and Some of the Flavonoid's Compounds

Table 1 evaluated the total phenolics and phenolic compounds of buckthorn leaves and fruits. The data was indicated a high total phenolics content (TPC) of buckthorn leaves and fruits (1.821.2, 3.052.91 mg/1000g) respectively. Analysis of some phenolic compounds demonstrated buckthorn leaves and fruits contain a vital phenolic compound like, catechin, quercetin, chlorogenic acid, caffeic acid, apigenin and ferulic. Agreement with the outcomes, Espindola, et al*.,* (2019) discovered that caffeic acid's powerful antioxidant action is one of the mechanisms by which it acts in HCC, preventing the production of ROS and decreasing the oxidative stress that is prevalent in this disorder. The found outcomes were in agreement with the outcomes discovered by Ay et al*.,* (2021) who stated that Quercetin is a naturally occurring flavonoid that is prevalent in fruits and vegetables. Quercetin's therapeutic potential for the prevention and management of various illnesses, such as tumor, cardiovascular disease, and neurodegenerativ conditions, is increasingly supported by an increasing body of evidence. In a variety of cellular and animal models, in addition to in humans, quercetin was demonstrated to perform antioxidant, anti-inflammatory, and anticancer activities by regulating the signaling pathways and gene expression included in these processes.

Table 1 clearly shows that compared to buckthorn leaves and fruits has higher total phenolic and flavonoid components. More catechin, quercetin, apigenin, caffeic a`, and ferulic a` were also detected in buckthorn fruits than within buckthorn leaves.

3.3 Biological Effects

Effect of Buckthorn Leaves and Fruits on feed intake (FI) (gram per day per rat), body weight gain (gram per day per rat) & feed efficiency ratio of hepatotoxic rats Table 2 discovered that the mean value of (FI) of control (+) group was lesser than control (-) group, being 7.50 ±0.50 and 14.50 ± 1.20 (gram per day per rat) , respectively demonstrating significant differences with percent of rise +93.33% of control (-) group if comparing with control (+) group. The mean values of FI were significantly increased in all hepatotoxic rats that were nourished on a variety of experimental BL (five percent and ten percent) and BF (five percent and ten percent) diets. The range of FI values was from 8.60 gram per day per rat to 12.80 gram per day per rat. Mathematically, the best FI has been documented for groups "4" (hepatotoxic rats nourished on ten percent BL) if comparing with control (+) group.

Table 2 showed the mean value of body weight gain of hepatotoxic rats nourished on several diets. It might be noticed that the mean value of BWG of control (+) group was lesser than control (-) group being 0.0129 ±0.001 and 0.3348 ± 0.092 (g/day/rat), respectively showing significant differences with percent of rise +2495.35% of control (-) group if comparing with control (+) group. hepatotoxic rat nourished on different experimental BL (5% and 10%) and BF (5% and 10%) diets demonstrated significant rise within mean values of BWG ranged from (0.0243 g/day/rat to 0.1728 g/day/rat). Groups ”3", "6" revealed insignificant variances among them. Rats from groups "2" & "5" indicated insignificant variances among them. The best BWG has been noted for group "4" (hepatotoxic rats nourished on ten percent BL) if comparing with control (+) group.

Table 2 demonstrated the mean value of feed efficiency ratio of hepatotoxic rats fed on different diets. Data showed that the mean value of feed efficiency ratio of control (+) group was lesser than control (r) group, being 0.0017 ± 0.0001 and 0.0231 ±0.0035, respectively demonstrated significant variances with percent of rise +1258.82 % of control (-) group if comparing with control (+) group. All hepatotoxic rats fed on several experimental BL (five percent and ten percent and BF (five percent and ten percent) diets showed significant rise in FER ranged from (0.0028 to 0.0135). Groups "2" and "5" illustrated insignificant variances among them. The best FER has been documented for group "4" ((hepatotoxic rats nourished on ten percent BL) if comparing with control (+) group. The outcomes of Table 2 are in parallel with that found by Ciesarova et al., (2020) he found that hepatointoxication decreased FI, BWG and FER while feeding rats on diets containing some plants other that used in present work corrected the above changes.

Table 1. Total flavonoid and phenolic compounds of buckthorn leaves and fruits

Component	Buckthorn Leaves (BL)	Buckthorn Fruits (BF)
Total phenolics and Flavonoids (mg /1000g)	1.821.2	3.052.91
Phenolic and Flavonoids Compounds (mg/1000g)		
Catechin	632.61	2031.98
Syringic acid	8.22	ND*
Caffeic acid	ND*	151.97
Chlorogenic acid	394.02	ND*
Coumaric	45.47	40.19
Myricetin	15.51	ND*
Quercetin	519.44	697.09
Cinnamic	35.69	ND*
Resveratrol	55.02	ND*
Ferulic	71.33	79.09
Rosemarinic acid	43.89	ND*
Apigenin	ND*	52.59

**ND: Not detecte*

3.4 Effect of Buckthorn Leaves and Fruits on Relative Organs Weight % (Kidneys, Heart, and Liver) of Hepatotoxic Rats

Table 3 and showed the mean value of liver relative weight (%) of hepatotoxic rats nourished on several diets. It might be observed that the mean value of liver relative weight of control (+) group was greater than control (-) group, being 4.45 ± 0.015 & 2.75 ±0.11, respectively with significant differences illustrating percent of reduction -38.20% of control (-) group when comparing with control (+) group. All hepatic rats fed on various experimental BL (5% and 10%) and BF (5% and 10%) diets showed percent of decreases in liver relative weight ranged from (-16.63% to 28.76%) if comparing with control (+) groups. Moreover, rats from groups "4" & "6" demonstrated insignificant variances among them.

Table 3 showed the mean value of kidneys relative weight (%) of hepatotoxic rats nourished on variant diets. It might be showed that the mean value of kidneys relative weight (%) of control (+) group was greater than control (-) group, being 1.15 ± 0.04 & 0.69 ± 0.01, correspondingly demonstrating a significant variance with percent of reduction - 40.00% of control (-) group if comparing with control (+) group. All hepatotoxic rats nourished on various experimental BL (5% and 10%) and BF (5% and 10%) diets demonstrated significant variances in percent of reduction in kidneys relative weight (%) if comparing with control (+) group ranging from (-4.35 % to -28.69.04 %). Insignificant variances have been noticed among groups 3 and 4. The best kidneys relative weight (%) has been documented for group "4" (hepatotoxic rats nourished on 10% BL) if comparing with control (+) group.

Table 3 indicated the mean value of heart relative weight (%) of hepatotoxic rats nourished on variant diets. It might be observed that the mean value of heart relative weight (%) of control (+) group was greater than control (-). group, being 0.80 ±0.01 & 0.40 ± 0.001, correspondingly demonstrating a significant variance with percent of reduction - 50.00 % of control (-) group as comparing with control (+) group. All hepatic rats nourished on various experimental BL (5% and 10%) and BF (5% and 10%) diets demonstrated significant variances in percent of reduction in heart relative weight (%) as comparing with control (+) group ranging of (-5.00 % to -40.00%). Numerically, the best heart relative weight (%) has been documented for groups "4" hepatotoxic rats nourished on ten percent BL) if comparing with control (+) group.

The outcomes of Tables 3 are in agreement with Ranard et al*.,* (2018) observed that the relative weight of vital organs and hematological variables didn't alter as a result of sub-acute oral ingestion of the extract of buckthorn fruits at a dosage of more than 1000 milligram per kilogram. These outcomes are in harmony with Gutzeit et al*,. (*2008) who revealed that the internal organs relative weight of buckthorn Leaves extracts treated groups have significant reduction as comparing with control positive group.

Table 2. Effect of Buckthorn Leaves and Fruits on feed intake (gram per day per rat), body weight gain (gram per day per rat) & feed efficiency ratio of hepatotoxic rats

Parameters	Feed intake g/day/rat		Body weight gain g/day/rat		Feed efficiency ratio	
Groups	Mean± Standard Deviation	%Change of C(+)ve	Mean± Standard Deviation	%Change of C(+)ve	Mean± Standard Deviation	%Change of C(+)ve
GI: Control(-ve)	14.50[a]±1.20	+93.33	0.3348 [a] ±0.092	+2495.35	0.0231[8]±0.0035	+1258.8
G2: Control(+ve)	7.50 [g] ±0.50	—	0.0129 [f] ±0.001	—	0.0017[a]±0.0001	—
G3: 5% (BL)	10.00 [d] 0.02	+33.33	0.0937[c]±0.002	+626.36	0.009 [f] ±0.0004	+452.9
G4: 10% (BL)	12.80[b]±0.12	+70.67	0.1728[b]±0.020	+1239.53	0.0013[b]±0.0012	+694.1
G5: 5% (BF)	8.60 [f] ±0.04	+14.67	0.0243 [d]±0.003	+88.37	0.0028[c]±0.0012	+64.7
G6: 10% (BF)	11.90[c]±0.40	+58.67	0.0971[c]±0.001	+652.71	0.0082[d]±0.0007	+382.3
LSD:	**0.584**		**0.0439**		**0.0016**	

Values are expressed as mean ± S.D. Significance is represented at (p-value < 0.05) utilizing one way ANOVA test and LSD test.

Table 3. Impact of Buckthorn Leaves and Fruits on relative organs weight % (Heart , liver , and kidneys) of hepatotoxic rats

Parameters	Liver		Kidneys		Heart	
Groups	Mean± Standard Deviation	%Change of C(+)ve	Mean± Standard Deviation	%Change of C(+)ve	Mean± Standard Deviation	%Change of C(+)ve
GI: Control(-ve)	2.75 [a] ±0.11	-38.20	0.69 [e] ±0.01	-40.00	0.40[f] ±0.001	-50.00
G2: Control(+ve)	4.45[e]±0.015	—	1.1 [a] ±0.04	—	0.80[a]±0.01	—
G3: 5% (BL)	3.39[e]±0.012	-23.82	0.90[b]±0.04	-21.74	0.76[b]±0.025	-5.00
G4: 10% (BL)	3.24 [c] ±0.02	-27.19	0.85[c]±0.005	-26.09	0.58 [d] ±0.01	-27.50
G5: 5% (BF)	3.71 [d] ±0.20	-16.63	1.10[a]±0.006	-4.35	0.69[c] ±0.04	-13.75
G6: 10% (BF)	3.17 [b]±0.03	-28.76	0.82[d]±0.012	-28.69	0.48 [e] ±0.02	-40.00
LSD:	**0.099**		**0.024**		**0.020**	

Values which have different letters in each column differ significantly, whereas those with comparable letters completely or partially aren't significant

3.5 Impact of Buckthorn Leaves and Fruits on Alkaline Phosphatase, Alanine Aminotransferase and Serum Aspartate Aminotransferase (AST) U/L of Hepatointoxicated Rats

Data of Table 4 illustrated the mean value of serum aspartate aminotransferase U/L of hepatotoxic rats nourished on various diets. It might be observed that the mean value of (AST) of control (+) group was greater than control (-) group, being 250.00 ±1.80 & 99.00 ± 1.60 U/L, correspondingly, demonstrating a significant variance with percent of reduction -60.40 % of control (-) group when comparing with control (+) group. All hepatic rats fed on different experimental BL (five percent and ten percent) and BF (5% and 10%) diets revealed percent of decrease in mean values changed from (- 25.20 % to -38.80%) as comparing with cqntrol (+) group. Mathematically, the best heart relative weight (%) has been documented for groups "4" hepatotoxic rats nourished on 10% BL) if comparing with control (+) group.

Data of Table 4 demonstrated the mean value of serum alanine aminotransferase (unit per liters) of hepatotoxic rats nourished on variant diets. It might be detected that the mean value of (ALT) of control (+) group was greater than control (-) group, being 95.00 ±2.3 0 & 44.00 ± 1.80 unit per liters, respectively demonstrating a significant variance with percent of reduction -53.68 % of control (-) group if comparing with control (+) group. All hepatotoxic rats nourished on many experimental BL (5% and 10%) and BF (5% and 10%) diets revealed percent of decreases in mean values ranging from (-12.84% to -20.00%).

In comparison with control (+) group. Group "4 and 6 " noted the best management hepatotoxic rat fed on 10% BL and 10% BF) concerning ALT enzyme in comparison with control (+) group.

Data of Table 4 indicated the mean value of serum Alkaline phosphatase (ALP) (unit per liters) of hepatotoxic rats nourished on various diets. It might be observed that the mean value of (ALP)of control (+) group was greater in comparison with control (-) group, being 310.00 ±1.90 & 132.00 ±2.10 unit per liters, respectively, showed a significant variance with percent of reduction -57.42 % of control (-) group if comparing with control (+) group. All hepatic rats nourished on numerous experimental BL (5% and 10%) and BF (5% and 10%) diets discovered significant reductions in mean values changed from (-6.45 % to -25.56%) if comparing with control (+) group. All hepatic rats nourished on BL (5% and 10%) and BF (5% and 10%) diets discovered significant reductions in mean values in comparison with control (+) group. Group "4" (rats nourished on 10% BL) documented the best management of serum ALP enzyme. These outcomes are in agreement with Ma et al*,* (2021) found that buckthorn Fruits extract possess hepatoprotective activity. which Madawala et al*.,* (2018) concluded that the ethanolic extract of buckthorn leaves high antioxidant activity that can be because of presence of high amount of phytochemicals. Luksa et al*.,* (2019) demonstrated that the methanolic extract of buckthorn leaves can be attributed to its antioxidant and free radical scavenging activities, which are responsible for its powerful antioxidant and correlated hepatoprotective activity.

3.6 Effect of Buckthorn Leaves and Fruits on Total Albumin, Protein, Globulin and Serum /Glob Ratio of Hepatointoxicated Rats

Data of Table 5 demonstrated the mean value of serum T P (milligram per deciliters) of hepatotoxic rats nourished on several diets. It might be detected that the mean value of (T P) of control (+) group was lesser than control (-) group, being 7.00 ± 0.32 & 8.60 ± 0.09 mg/dl, correspondingly, representing a significant variance with percent of rise +22.86 % of control (-) group when comparing with control (+) group. All hepatotoxic rats nourished on different food demonstrated significant rises in mean values ranging from (+7.71 % to +18.57 %) in comparison with control (+) group. Insignificant variances were observed among groups "3" and "4". Moreover, rats in groups"5" & " 6" demonstrated insignificant variances among them. Numerically, the best management concerning the serum TP has been documented for group "5 "and "6 " (rats nourished on 5% and 10% BL) in comparison with control (+) group.

Data of Table 5 illustrated the mean value of serum albumin (ALB) milligram per deciliters of hepatotoxic rats nourished on several diets. It might be noted that the mean value of albumin of control (+) group was lesser compared to control (-) group, being 2.50 ± 0.50 & 5.60 ± 0.20 mg/dl, respectively, indicating a significant variance with percent of rise +124.00 % of control (-) group when comparing with control (+) group. All

Table 4. Effect of Buckthorn L eaves and Fruits on alanine aminotransferase, serum aspartate aminotransferase, and alkaline phosphatase unit per liters of hepatointoxicated rats

Parameters	Serum aspartate aminotransferase (unit per liters)		ALT(unit per liters)		Alkaline phosphatase (unit per liters)	
Groups	Mean± Standard Deviation	%Change of C(+)ve	Mean± Standard Deviation	%Change of C(+)ve	Mean± Standard Deviation	%Change of C(+)ve
GI: Control(-ve)	99.00^{g} ±1.60	-60.40	44.00^{f} ±1.80	-53.68	132.00^{f}±2.10	-57.42
G2: Control(+ve)	250.00^{a}±1.80	—	95.00^{a}±2.30	-———	310^{a}±1.90	—
G3: 5% (BL)	187.00^{b}±2.00	-25.20	81.50^{c}±0.25	-14.21	290^{b}±1.30	-6.45
G4: 10% (BL)	153.00^{f}±0.60	-38.80	76.00^{e}±0.59	-20.00	230.75^{e}±2.08	-25.56
G5: 5% (BF)	174.00^{c}±0.80	-30.40	82.80^{b}±0.39	-12.84	287^{c}±1.25	-7.42
G6: 10% (BF)	165.00^{d}±0.09	-34.00	79.00^{d}±1.09	-16.84	284^{d}±1.60	-8.39
LSD:	1.040		**1.033**		0.846	

Table 5. Effect of Buckthorn Leaves and Fruits on total protein, albumin, globulin and serum albumin / globulin ratio of hepatointoxicated rats

Parameters	Total protein milligram per deciliters		Albumin milligram per deciliters		Globulin milligram per deciliters	
Groups	Mean± Standard Deviation	%Change of C(+)ve	Mean± Standard Deviation	%Change of C(+)ve	Mean± Standard Deviation	%Change of C(+)ve
GI: Control(-ve)	8.60^{d}±0.09	+22.86	5.60^{e}±0.20	+124.00	3.00^{d}±0.003	-33.33
G2: Control(+ve)	7.00^{a}±0.32	—	2.50^{a}±0.50	—	4.50^{a}±0.50	—
G3: 5% (BL)	7.54^{b}±0.02	+7.71	4.06 ^{c} ±0.02	+62.40	3.48^{c}±0.002	-22.67
G4: 10% (BL)	7.95^{b}±0.25	+13.57	4.79^{d}±0.012	+91.60	3.16^{d}±0.011	-29.78
G5: 5% (BF)	8.06^{c}±0.001	+15.14	3.93^{b}±0.025	+57.20	4.13^{b}±0.01	-8.22
G6: 10% (BF)	8.28 ^{c} ±0.03	+18.29	4.78 ^{d} ±0.01	+91.20	3.50^{c}±0.001	-22.22
LSD:	0.148		0.249		**0.240**	

hepatotoxic rats fed on different food demonstrated significant variances with percent of increases ranging from (+57.20 % to +91.60%) if comparing with control (+) group. Insignificant differences have been demonstrated among groups " 4" and 6". them. Numerically, the best management considering the serum albumin has been documented for group"4" (rats nourished on 10% BL) in comparison with control (+) group.

Data of Table 5 illustrated the mean value of serum globulin (milligram per deciliters) of hepatotoxic rats nourished on several diets. It might be detected that the mean value of globulin of control (-) group was lower than control (+) group, being 3.00 ± 0.003& 4.50 ± 0.50 milligram per deciliters, respectively representing a significant variance with percent of reduction -33.33 % of control (-) group if comparing with control (+) group. All hepatotoxic rats nourished on experimental food demonstrated significant reductions in mean values changed with percent from (-8.22 % to -22.67%) as compared to control (+) group. Insignificant variances have been observed among groups "3"and "6" indicated insignificant variances among them. Numerically, the best management concerning serum globulin (milligram per deciliters) has been documented for groups "5" (rats fed on 5% FL)) in comparison with control (+) group.

Wang et al*.,* (2016) examined the antioxidant effects of elnabek Fruits effectively protect the liver of male rats subjected to aflatoxins that triggered nephrotoxicity and hepato and oxidative stress. buckthorn leaves reduced significantly liver enzymes. This msy be attributed to the presence of antioxidants that comprise phenolic compounds that may act by scavenging free radicals. Liu et al., (2015).

3.7 Effect of Buckthorn Leaves and Fruits on Serum Urea Nitrogen, Uric Acid and Creatinine Milligram Per Deciliters of Hepatointoxicated Rats

Data of Table 6 illustrated the mean value of serum urea (milligram per deciliters) of hepatotoxic rats nourished on several diets. It might be observed that the mean value of blood urea nitrogen (BUN) of control (+) group was greater than control (-) group, being 58.00 ± 2.00 & 28.40 ± 0.40 (milligram per deciliters), respectively, representing a significant variance with percent of reduction -51.03 % of control (-) group if comparing with control (+) group. All hepatotoxic rats nourished on various experimental diets discovered reductions with percent of change from (-28.45% to -32.76%) if comparing with control (+) group. The best management has been documented for group"4" (rats fed on 10% BL) if comparing with control (+) group of serum urea.

Data of Table 6 indicated the mean value of serum creatinine (mg/dl) of hepatotoxic rats nourished on several diets. It might be detected that the mean value of creatinine of control (+) group was greater than control (-) group, being 1.12 ± 0.09 & 0.54 ± 0.04 (mg/dl), correspondingly, demonstrating a significant variance with percent of reduction - 51.79% of control (-) group if comparing with control (+) group. All hepatic rats nourished on different experimental food discovered significant reductions that ranging from (-16.07 % to -33.93%) in comparison with control (+) group. The best management has been documented for group "6" (rats nourished on 10% BF) in comparison with control (+) group.

Results of Table 5 revealed the mean value of serum uric acid (UA) (milligram per deciliters) of hepatotoxic rats nourished on several diets. It might be detected that the mean value of uric a` of control (+) group was greater compared to control (-) group, being 6.90 ±0.40 & 1.20 ±0.50 (milligram per deciliters), respectively, representing a significant variance with percent of reduction -82.61% of control (-) group in comparison with control (±)group. All hepatotoxic rats nourished on various experimental diets discovered significant reductions with percent of change from (-34.35 %to -51.59 %) in comparison with control (+) group. Groups three and five demonstrated insignificant variances among them. The best management has been discovered for group"4" (rats fed on ten percent BL) if comparing with control (+) group.

Table 6 outcomes in agreement with that stated by Su et al*.,* (2017) stated that buckthorn Fruits decoctions are used as laxatives for urinary tract infections. While Socaci et al,. (2023) suggested that acetone extract of buckthorn leaves has a kidney-protective impact against H2O2 induced oxidative stress and bad impacts on kidney and possess in vitro antioxidant activities.

Table 6. Impact of Buckthorn leaves and Fruits on serum urea nitrogen,creatinine and uric a` milligram per deciliters of hepatointoxicated rats

Parameters	Urea milligram per deciliters		Creatinine milligram per deciliters		Uric acid milligram per deciliters	
Groups	Mean± Standard Deviation	%Change of C(+)ve	Mean± Standard Deviation	%Change of C(+)ve	Mean± Standard Deviation	%Change of C(±)ve
GI: Control(-ve)	28.40 ^{f} ±0.40	-51.03	0.54 ^{f} ±0.04	-51.79	1.20^{f}±0.50	**-82.61**
G2: Control(+ve)	58.00^{a}±2.00		1.12^{a}±0.09	—	6.90^{a}±0.40	—
G3: 5% (BL)	40.60^{c} ±0.06	-30.00	0.94^{b}±0.018	-16.07	4.53^{b}±0.013	-34.35
G4: 10% (BL)	39.00^{e} ±0.20	-32.76	0.79^{d}±0.002	-29.46	3.34^{de}±0.004	-51.59
G5: 5% (BF)	41.50^{b}±0.45	-28.45	0.89^{c}±0.005	-20.54	4.44 ^{c} ±0.03	-35.65
G6: 10% (BF)	40.00^{cd}±0.05	-31.03	0.74^{de}±0.004	-33.93	3.67 ^{d} ±0.02	**-46.81**
LSD:	**1.022**		**0.045**		**0.329**	

3.8 Effect of Buckthorn Leaves and Fruits on Triglycerides(TG) Milligram per Deciliters, Serum Total Cholesterol (TC), Low Density Lipoprotein (LDL) Milligram Per Deciliters, High Density Lipoprotein (HDL) Milligram Per Deciliters, Very Low Density Lipoprotein (VLDL) Milligram Per Deciliters and Atherogenic Index (AI) of Hepatointoxicated Rats

Data of Table 7 illustrated the mean value of serum cholesterol (milligram per deciliters) of hepatotoxic rats nourished on variant diets. It might be detected that the mean value of (TC) of control (+) group was greater in comparison with control (-) group, being 185.00 ± 2.00 & 99.00 ± 2.00 milligram per deciliters, respectively, demonstrating a significant variance with percent of reduction - 46.49 % of control (-) group if comparing with to control (+) group .All hepatotoxic rats nourished on variant experimental food discovered significant reductions with percent of change from (-22.16 % to-29.84 %) in comparison with control (+) group. Groups 3 and 5 revealed insignificant variances among them. The best serum (TC) has been demonstrated for group"4" (rats nourished on 10% BL) if comparing with control (+) group.

Table 7 showed the mean value of serum triglycerides (milligram per deciliters) of hepatotoxic rats nourished on different diets. It might be noted that the mean value of (TG) of control (+) group was greater in comparison with control (-) group, being 170.00 ±1.80 & 55.00 ± 2.00 milligram per deciliters, respectively representing a significant variance with percent of reduction - 67.65% of control (-) group in comparison with control (+) group. All hepatotoxic rats nourished on different experimental diets revealed significant reductions with percent of change from (-14.12% to -22.35%) if comparing with control (+) group. The best serum (TG) was recorded for group"6" (rats fed on 10% BF) when compared to control (+) group.

Data of Table 7 indicated the mean value of serum (HDLc) (milligram per deciliters) of hepatotoxic rats nourished on different diets. It might be noted that the mean value of (HDLc) of control (+) group was lower in comparison with control (-) group, being 25.00 ± 1.28 & 68.00 ± 2.00 (milligram per deciliters), respectively, demonstrating a significant variance with percent of rise +172.00 of control (-) group if comparing with control (+) group. All hepatotoxic rats nourished on different experimental diets revealed significant increases with percent of change ranging from (+80.00 % to +136.00%) if comparing with control (+) group. The best serum (HDLc) has been observed for group"6" (rats nourished on 10% BF) if comparing with control (+) group.

Data in Table 8 demonstrate the mean value of serum low density lipoprotein (milligram per deciliters) of hepatotoxic rats nourished on different diets. It might be detected that the mean value of (LDLc) of control (+) group was greater in comparison with control (-) group, being 126.00 ±1.90 &20.00 ± 2.70 (milligram per deciliters), respectively, demonstrating a significant variance with percent of reduction - 84.13 % of control (-) group if comparing with control (+) group. All hepatotoxic rats nourished on different experimental diets revealed significant reductions with percent of change ranging from (- 52.54% to -63.49%) as compared to control (+) group. Group"4 " (rats nourished on ten percent BF) if comparing with control (+) group. Recorded the best serum (LDLc) if comparing with control (+) group.

Table 8 indicated the mean value of serum (VLDLc) (milligram per deciliters) of hepatotoxic rats nourished on different diets. It might be detected that the mean value of (VLDLc) of control (+) group was more in comparison with control (-) group, being 34.00 ±1.50 & 11.00 ± 2.00 (milligram per deciliters), respectively, demonstrating a significant variance with percent of reduction - 67.65% of control (-) group if comparing with control (+) group. All hepatotoxic rats nourished on different experimental diets demonstrated significant reductions with percent of change ranging from(-14.12% to -22.35%) if comparing with control (+) group., the best treatment has been documented for Group"4 " (rats nourished on ten percent BF)concerning serum (VLDLc).

Data of Table 8 discovered that the mean value of serum (AI) of hepatic rats nourished on different diets. It might be observed that the mean value of (AI) of control (+) group was greater than control (-) group, being 6.40 ±1.05 & 0.46 ± 0.20, respectively, demonstrating a significant variance with percent of reduction - 92.81% of control (-) group if comparing with control (+) group. All hepatotoxic rats nourished

Table 7. Effect of Buckthorn leaves and Fruits on serum total cholesterol, high density lipoprotein milligram per deciliters and triglycerides milligram per deciliters of hepatointoxicated rats

Parameters Groups	TC milligram per deciliters		TG milligram per deciliters		HDL milligram per deciliters	
	Mean± Standard Deviation	%Change of C(+)ve	Mean± Standard Deviation	%Change of C(+)ve	Mean± Standard Deviation	%Change of C(±)ve
GI: Control(-ve)	99.00 ^{f} ±2 .00	-46.49	55.00 ^{k} ±2.00	-67.65	68.00^{f}±2.00	+172.00
G2: Control(+ve)	185.00^{a}±2.00	—	170.00^{a}±1.80	—	25.00^{a}±1.28	—
G3: 5% (BL)	143.00^{b}±0.10	-22.70	146.00^{b}±1.30	-14.12	54.00^{c}±1.04	+116.00
G4: 10% (BL)	129.80^{d}±1.00	-29.84	139.00^{d}±1.40	-18. 24	56.00^{d}±1.00	+124.00
G5: 5% (BF)	144.00^{b}±0.30	-22.16	142.00^{c}±0.68	-16.47	45.00^{b}±1.12	+80.00
G6: 10% (BF)	136.00^{c}±0.65	-26.49	132.0 ^{e}± 1.20	-22.35	59.00^{e}±0.25	+136.00
LSD:	**1.154**		**0.878**		**0.763**	

Table 8. Impact of Buckthorn leaves and Fruits on serum low density lipoprotein milligram per deciliters, very low density lipoprotein milligram per deciliters and atherogenic index (AI) of hepatointoxicated rats

Parameters Groups	LDL milligram per deciliters		VLDL milligram per deciliters		AI	
	Mean± Standard Deviation	%Change of C(+)ve	Mean± Standard Deviation	%Change of C(+)ve	Mean± Standard Deviation	%Change of C(±)ve
GI: Control(-ve)	20 .00^{e} ±2.70	-84.13	11.00^{g}±2.00	**-67.65**	0.46 ^{g} ±0.20	-92.81
G2: Control(+ve)	126.00^{a}±1.90	—	34.00^{a}±1.50	—	6.40^{a}±1.05	—
G3: 5% (BL)	59.80 ^{c} ±2.00	-52.54	29.20^{b}±0.21	-14.12	1.65^{cd}±0.031	-74.22
G4: 10% (BL)	46.00 ^{1} ±0.50	-63.49	27.80^{d}±0.28	-18.24	1.32^{de}±0.003	-79.38
G5: 5% (BF)	70.60 ^{b} ±0.10	-43.97	28.40^{c}±0.09	-16.47	2.20^{bc}±0.012	-65.63
G6: 10% (BF)	50.60 ^{d} ±0.60	-59.84	26.40^{e}±0.12	-22.35	1.31^{de}±0.001	-79.53
LSD:	**1.475**		**1.069**		**0.499**	

Table 9. Effect of Buckthorn leaves and Fruits on serum glucose of hepatointoxicated rats

Parameters	Serum glucose milligram per deciliters	
Groups	**Mean± Standard Deviation**	**Change %**
GI: Control(-ve)	79.00 ^{h}±1.00	-50.63
G2: Control(+ve)	160.00 ^{a}±2.00	—
G3: 5% (BL)	132.00 ^{b}±2.00	-17.50
G4: 10% (BL)	118.00 ^{c} ±1.30	-26.25
G5: 5% (BF)	105.00 ^{d}±0.90	-34.38
G6: 10% (BF)	103.00 ^{e}±1.40	-35.63
LSD:	**0.781**	

on various experimental diets demonstrated significant reductions with percent of change ranging from (-65.63 % to --79.53%) if comparing with control (+) group. Groups 4 & 6 showed insignificant variances among them.

Garcia et al*.,* (2019) recommended that In vitro antioxidant potential was demonstrated by methanolic extracts of buckthorn fruits, which showed hypolipidemic activities and enhanced cytotoxicity as a result of their increased phenolic content and antioxidant potential. while Hao et al*.,* (2019) demonstrated that managing rats with hepatotoxicity with a standard diet that contains the 3 levels (five percent, four percent , and six percent) of buckthorn, clove, and anise reduced triglycerides, cholesterol, LDL-c, and VLDL-c, whereas HDL-c i McKay & Blumberg, (2010) demonstrated that buckthorn leaves possess cholesterol-lowering properties. Marsinach et al*.,* (2019) reported that the infusion of a blend of buckthorn and other aromatic plants was efficient in enhancing lipid metabolism, thereby enhancing the lipid profile.

3.9 Effect of Buckthorn Leaves and Fruits on Serum Glucose of Hepatointoxicated Rats

Table 9 revealed the mean value of serum glucose in hepatotoxic rats. The results recorded that the mean value of control (+) group was greater than control (-) group, being 160.00 ±2.00 and 79.00 ±1.00 milligram per deciliters correspondingly, showing significant variance with percent of reduction of control (-) group was -50.63 % if comparing with control (+) group. All hepatotoxic rats nourished on various experimental diets illustrated significant reductions with percent of change ranging from (-17.50 % to -35.63%) if comparing with control (+) group. The best treatment has been documented for group ”6(rats nourished on 10% BF) concerning serum glucose.

These outcomes (Table 9) are in agreement with buckthorn Fruits extract can have anti-diabetic characteristic Ranard et al*.,* (2019). Additionally, Pop et al*.,* (2012) stated the rise in the size of islets of Langerhan cell with the buckthorn administration. Tu et al., (2015)reported that buckthorn leves and fruits have antidiabetic activities.

4. CONCLUSION

Buckthorn is a plant utilized for centuries in traditional medicine. Research findings indicate its beneficial impact on liver and enhancement of liver tissue condition. it is crucial to acknowledge that research on buckthorn is under progress, requiring further investigations to validate its potential therapeutic applications and identify the appropriate dosages & length of administration. Furthermore, it is crucial to evaluate the buckthorn safety, especially when administered with other drugs or supplements. Consequently, more research is essential to clarify the possible advantages and risks of buckthorn as a medicinal drug.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

ETHICAL APPROVAL

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

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://prh.mbimph.com/review-history/4516