**Effect of Crataegus aronia on the Biochemical Parameters in Induced Diabetic Rats**

Omar Khaled Al-Mobideen1, Ali Abdallah Alquudah2, Ahmed Al-Mustafa3*, Fuad Alhawarat1, Hussam Mizher4

**ABSTRACT**

Crataegus aronia is widely known for its antioxidant, anti-inflammatory, and hypolipidemic properties, and it has traditionally been used to treat cardiovascular disorders. This study aimed to evaluate the impact of Crataegus aronia extract on the liver enzyme markers, blood glucose levels, lipid profiles, and kidney function biomarkers as well as hematological parameters in induced diabetic rats. Male Wistar rats were divided into seven groups: normal Control; Diabetic; and Diabetic animals treated with two doses of Crataegus aronia extract (5 and 10mg/kg) (DM+ extract), Control treated with the extract (5 and 10mg/kg) and induced diabetic treated with insulin. Streptozotocin (STZ)-induced diabetic rats (50mg/kg, ipland normal were orally administrated with Crataegus aronia extract once a day for 4 weeks. At the end of the experiment, the biochemical and hematological parameters were measured in all groups. Also, the phytochemicals and antioxidant activity of the Crataegus aronia extract were evaluated. According to findings, the total phenols, total flavonoid, and flavonol contents were 538.3 mg Gae acid equivalent / g extract, 149.3 mg Rutin equivalent / g extract, and 79.3 mg Rutin equivalent / g extract, respectively. The antioxidant activity according to 2,2-diphenyl-2-picrylhydrazyl (DPPH) IC50 assay, and ferric reducing antioxidant power (FRAP) assays were 28.02 µg/ml and in the range of 0.273 – 0.960 µmol Fe2+ / g dw, respectively. Crataegus aronia extract significantly (p <0.05) affects red blood cells, hemoglobin, hematocrit, white blood cells, lymphocytes, and platelets values. Also, Crataegus aronia had a significant (P < 0.05) effect on serum biochemical parameters, including glucose, total proteins, albumins, triglycerides, creatinine, bilirubin, and serum aspartate aminotransferase (AST). However, Crataegus aronia treatment had no significant effects (p < 0.05) on serum alanine aminotransferase, alkaline phosphatase, and cholesterol levels. Crataegus aronia exerts antioxidant activity and significantly improves the biochemical and hematological biomarkers in induced diabetic rats.

**Key words:** Crataegus aronia, diabetes mellitus, Insulin, antioxidant, biochemical parameters

**INTRODUCTION**

Many studies have been conducted to proof that plants are one of the most important sources of active substances. Plants have therapeutic potential to treat various diseases in humans1,2. The evaluation of pharmacological effects of plants can be used as a valuable tool for discovering new drugs and compounds of plant origin3,7. A world-wide revolution which is mainly focused on the belief that medicinal plants are safer and less damaging to the human body than synthetic drugs5. Based on scientific reports from World Health Organization about 80% of the world population depends on traditional medicine for primary health care and more than 30% of the plant species have been used medically7,10.

The interest of the biological as well as medical research has been focused on natural antioxidant molecules. Human body produces free radicals as byproducts during metabolism because of the oxidative phosphorylation effect. Free radicals such as reactive oxygen species (ROS) are species which contain one or more unpaired electrons, highly reactive chemical species formed in all tissues during normal aerobic cellular metabolism. ROS initiating a chain reaction with the potential to start proteins, DNA damage and cause peroxidation of membrane lipids5. ROS are the main reasons for ageing, tumors, arteriosclerosis, hypertension and diabetes. ROS are increasingly formed in diabetes mellitus (DM) by the auto oxidation of glucose and glycylated proteins. Even though insulin therapy and traditional folk medicine can control many aspects of diabetes complications, still DM is a complex metabolic disorder characterized by high blood glucose levels and is associated with a changed in lipid profiles as well as other metabolic biomarkers6,10.

Antioxidants are substances that are efficient to diminish the oxidation rate in proteins, DNA and membrane lipids. Antioxidants molecules can inhibit the process of oxidation include scavenging of the free radicals, chelating of free metals, and inhibition of enzymes responsible to produce the ROS. The antioxidant properties of medicinal plants can be attributed to the polyphenol, Flavonoids, essential oils contents which play an important role in improving DM disorders causes by mediated by oxidative stress11-13.

As in many countries of the world, traditional medicine particularly herbal medicine is part of Jordanian culture14. Jordan is rich in a wide variety of medicinal plants which are not used only for treatment of mild diseases such as colds, headaches or the digestive system, but also in the treatment of long-term illnesses or incurable diseases, such as diabetes, high blood pressure or cancer14,16.

Crataegus is indigenous to the Mediterranean Basin. Crataegus is a low, dense, spiny tree with a beautiful inflorescence up to 6 m tall and with orange,
red or yellow fruits. Crataegus (Hawthorn) is very important in folk medicine (commonly called Zaarour in Arabic) and has exhibited various biological activities such as cardiovascular, immune systems disorders, anti-inflammatory, cytotoxic, antioxidant, anti-diabetic and anti-HIV activities. This study aims to determine the total phenol, flavonoids and flavonols contents of the methanolic for Crataegus aronia extracts, and to evaluate the antioxidant activity of Crataegus aronia extracts by using DPPH and FRAP methods. In addition, the study focuses on the effects of Crataegus aronia methanol extract on biochemical and hematological parameters in streptozotocin induced diabetic rats, as in vivo model.

MATERIALS AND METHODS

Chemicals and equipment

A list of chemicals and equipment used in this study is found in Appendix 1.

Plant Material and Extract Preparation

Crataegus aronia leaves were collected in May 2019 from Wadi Al-Thany, South of Al-Karak city, Jordan. The plant was identified by Prof. Saleh Al-Qura’n (Department of Biology Mutah Karak, Jordan). After being collected, the leaves were dried for 7-10 days in the shade at room temperature before being ground into powder and stored in plastic containers away from light, heat, and moisture until usage. The extract was prepared according to Odey et al. (2012) with some modifications. 50 g of plant powder was soaked in 500 ml of methanol in 1000 ml beaker, then kept in a shaker (150 rpm) for 3 days for continues agitation at 150 rpm. The solutions were then filtered and concentrated using a rotary evaporator at 45°C before being stored at -20°C.

Methanolic extract yield (gram/50 gram dry leaf extract) was calculated as follows:

\[
\text{Yield} = \frac{\text{Wt of dry extract}}{\text{Wt of dry sample}} \times 100\%
\]

Antioxidant activity

2, 2-diphenyl-1-picrylhydrazyl (DPPH) assay

The antioxidant activity of C. aronia leaves extract was determined using 2, 2-diphenyl-1-picrylhydrazyl (DPPH) assay and was performed according to a previous method with slight modifications. Different concentrations of the extract were added to DPPH methanolic solution (final absorption of 0.754 at 517 nm). The mixtures were incubated for 30 minutes at room temperature in the dark, and the absorbance at 517 nm was measured and converted to phenolic contents according to the calibration curve of Gallic acid.

\[
C = \frac{c \cdot V}{m}
\]

Where: C-total content of phenolic compounds, mg/g leaves extract, c-the concentration of Gallic acid established from the calibration curve, mg/ml. V-the volume of extract, m-the weight of pure leaves extract.

Total Flavonoid Content

Total flavonoid content of the extract was determined according to (Sharma and Agarwal, 2015) using the aluminum chloride colorimetric method with slight modification using rutin as standard and the results were expressed as mg of rutin equivalents per g dry weight of the plant (mg RE/g dw). Briefly, the extract solution, 0.5 ml of (10 mg/ml), 2 ml distilled water and 0.15 ml 5% NaNO\(_3\) solution were added. After 6 min, 0.15 ml 10% AlCl\(_3\) solution was added and kept for another 6 min. To this reaction mixture, 2 ml 4% NaOH solution and 0.2 ml water were added to make up the final volume 5 ml. The reaction mixture was mixed well and allowed to stand for 15 min after which absorbance was recorded at 510 nm. Total flavonoid content was expressed as mg rutin equivalent (RE)/g plant sample. Total content of flavonoids compounds in plant methanolic extracts in RE was calculated by the following formula:

\[
X = C \cdot V / m
\]

Where: X- Flavonol content, mg/g plant extract, C-the concentration of Rutin established from the calibration curve, mg/ml. V- the volume of extract, ml. m-the weight of plant methanolic extract.

Total Flavonol Content

Total flavonol content was estimated using the AlCl\(_3\) colorimetric method as described by Sakat et al., 2010 with some modifications. 2 ml of plant extract (10 mg/ml) were mixed with 2 ml (20 mg/L) AlCl\(_3\) and 6 ml (50 mg/L) sodium acetate. The absorbance was measured at 440 nm after 2 h. The total flavonol concentration was given in mg Rutin equivalent (RE)/g plant extract. All measurements were made in triplicate. The content of Flavonols, in RE was calculated by the following formula:

\[
X = C \cdot V / m
\]

Where: X- Flavonol content, mg/g plant extract in RE. C-the concentration of Rutin solution, established from the calibration curve, mg/ml. V- the volume of extract, ml. m-the weight of pure plant methanolic extract.

Animals

Male albino Wister rats, weighing 180 - 225 g was used in this study. The chosen animals were housed in plastic well aerated cages at normal atmospheric temperature (25 ± 5°C) and normal 12 hour light/dark cycle. Moreover, they had free access to water and were supplied daily with a standard diet of known composition ad libitum.
Induction of Diabetes in Rats.
Albino Wister male rats were fasted overnight, and diabetes was induced by a single dose of streptozotocin (STZ) (65 mg/kg body weight) in a 0.1M citrate solution (pH 4.5) subcutaneously. Control rats were injected with normal saline only. Rats having serum glucose ≥ 300 mg/dl, after 3 days of the STZ injection, were considered diabetic and selected for further pharmacological studies. The rats were allowed to continue to feed on their respective diets until the end of the study. Treatment began on the fourth day after STZ injection and is considered the first day of treatment and continued for 4 weeks.

Determinations acute toxicity of LD50 for Crataegus aronia methanol extract
For this purpose, 10 diabetic rats were divided into 5 groups (2 rats in each group), then each group was injected subcutaneously with a single dose of extract. Group 1 was given 50 mg/kg of body weight, while groups 2, 3, 4 and 5 were given 100, 200, 500 and 1000 mg/kg respectively. After that, animals were monitored for 72 hours and so dead rats from each group were recorded.

Experimental design
The experimental animals were divided into seven groups, each group comprising five rats as detailed follows in Table 1. After 4 weeks of treatment, the rats were sedated, then blood samples were collected for further biochemical analysis.

Insulin treatment
Insulin was used in the present study, based on the desired pharmacological effect. First, insulin (Novo Nordisk A/S; Denmark; product number HS67C87) and second, insulin-releasing implants that release a basal dose of insulin (5 IU/implant). These implants were inserted subcutaneously on the rats under short-acting anesthetic conditions. The injection was performed subcutaneously by concentrated 200 µL insulin + 800 µL normal saline solution per rat.

Determination of blood glucose levels
Blood glucose concentration (mg/dl) was determined weekly using a blood glucose test meter (glucolab Auto-coding) manufactured by Infopia co., Korea. Animals were fasted overnight then blood samples were collected from the tip of tail.

Hematological assay
Hematological parameters, such as Hb, hematocrit (Hct), platelets, RBCs, WBCs, and lymphocytes were determined using an automated hematology analyzer (Orphee, mythic-18, Swiss). Also, biochemical parameters such as alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase activities, glucose, albumin, total protein, blood urea nitrogen, creatinine, total bilirubin, triglycerides, cholesterol were determined using an automated biochemical analyzer (Cormay accent-200, Poland) in the Integrated Laboratory, Private medical lab company, according to the manufacturer’s protocol.

RESULTS
Percentage yield determination
Extract yield of Crataegus aronia leaves prepared by soaking with continuous agitation methods using methanol is summarized in Table (3).

Quantitative analysis: Total phenols, flavonoids and phenolic compounds
As shown in Table (3) the total phenol, flavonoid and flavonol concentrations in Crataegus aronia are 538.5 mg GAE/g extract, 149.3 mg RE/g extract, and 79.3 mg RE/g extract, respectively.

Antioxidant activity.
DPPH assay (Free radical scavenging activity)
DPPH and FRAP assays were used for the determination of antioxidant activity of the extract. Antioxidant capacities of the extract were expressed in terms of IC50 value of the extracts and low IC50 value corresponds to a high antioxidant capacity (Table 3; Figure 1 and 2). Figure (1) illustrated an increase of DPPH % inhibition due to the scavenging ability of methanolic leaves extract. The DPPH % inhibition (IC50) value of C. aronia leaves extract is 28.02 µg/ml.

Crataegus aronia LD50
Crataegus aronia is a well-tolerated plant. The results of this study are shown in Table (4), in this study the injection administration of the aqueous extract of Crataegus aronia at all given doses (50 to 1000 mg kg−1) did not produce any visible sign of acute toxicity or instant death in rats tested during the period of observation.

Blood glucose levels
The average blood glucose level for each group was estimated weekly for up to 4 weeks Table (5). The glucose level in the diabetic rats was significantly higher compared to the normal groups. Moreover, the

| Table 1: Experimental design |
|----------------------------|
| Group number | description | Extract | Injection type | Amount of the Extract/ kg |
| 1 | Normal rats (N) | - | - | - |
| 2 | Diabetic rats (DN) | - | - | - |
| 3 | Diabetic rats (D5) | Crataegus aronia | subcutaneous | 5 mg/kg |
| 4 | Diabetic rats (D10) | Crataegus aronia | subcutaneous | 10 mg/kg |
| 5 | Diabetic rats (DI) | Insulin | subcutaneous | 5 IU/implant |
| 6 | Normal rats | Crataegus aronia | subcutaneous | 5 mg/kg |
| 7 | Normal rats | Crataegus aronia | subcutaneous | 10 mg/kg |

| Table 2: Biochemical tests used in this study. |
|---------------------------------------------|
| Biochemical Markers |
|---------------------|
| Hepatotoxicity      | Total bilirubin; Alanine aminotransferase; Aspartate aminotransferase; Alkaline phosphatase |
| Nephrotoxicity      | Creatinine; Total protein; Albumin; Blood Urea |
| Glucose and lipid profile | Glucose; Triglycerides; Cholesterol |
Table 3: Yield, total phenols, flavonoids, Flavonol contents and DPPH IC_{50} values of the methanol extract of Crataegus aronia.

| Yield* (%) | Total phenols (mg GAE/g extract) | Total flavonoids (mg RE/g extract) | Total Flavonol (mg RE/g extract) | DPPH IC_{50} (µg/ml) |
|------------|----------------------------------|-----------------------------------|----------------------------------|----------------------|
| 25.68      | 538.5 ± 0.095                    | 149.3 ± 0.0847                    | 79.3 ± 0.061                    | 28.02 ± 2.53         |

*GAE: gallic acid equivalent; # RE: Rutin equivalent. (g extract / 100 g dry leaves)

Table 4: Crataegus aronia extract LD50

| Group number | Number of animals | Dose mg/kg* | No. of animals dead |
|--------------|-------------------|-------------|---------------------|
| 1            | 2                 | 50 mg kg^{-1} | ---                 |
| 2            | 2                 | 100 mg kg^{-1} | ---                 |
| 3            | 2                 | 200 mg kg^{-1} | ---                 |
| 4            | 2                 | 500 mg kg^{-1} | ---                 |
| 5            | 2                 | 1000 mg kg^{-1} | ---                 |

*Injection dose of Crataegus aronia extract.

Table 5: Effect of Crataegus aronia leaves extract on blood glucose

| Group | Fasting blood glucose (mg/dl) | 1st week | 2nd week | 3rd week | 4th week |
|-------|------------------------------|---------|---------|---------|---------|
| N     | 98.0±15                      | 115.0±15| 121.0±15| 135.0±18|         |
| D     | 401.0±45                     | 616.0±57| 770.0±62| 878.0±81|         |
| D5    | 435.0±30                     | 459±51  | 430.0±43| 410.0±59|         |
| D10   | 446.0±42                     | 542.095 | 701.0±88| 845.0±58|         |
| D1    | 453.0±42                     | 320.0±14| 285.0±10| 236.0±12|         |
| N5    | 95.0±37                      | 130.0±45| 170.0±24| 192.0±15|         |
| N10   | 135.0±15                     | 168.0±49| 190.0±56| 221.0±51|         |

N, N5, N10: normal and normal treated by 5 and 10 mg/kg, respectively. D, D5, D10, D1: diabetic, diabetic treated by 5 and 10 mg/kg and insulin; respectively

Data means ± SD of rats/group. FBL: fasting blood sugar

**Figure 1:** DPPH % inhibition of C. aronia.

**Figure 2:** FRAP test absorption value of C. aronia.
glucose concentration was significantly decreased in the diabetic mice treated with *Crataegus aronia*.

The previous tables indicate that the probability value is statistically significant at p<0.05. Whereas results according to the ANOVA score showed a difference between the seven groups of blood sera variables. Comparing the observed probability values to the level of error margin of type I error (α=0.05), it could be noted that some probability values were >0.05, suggesting that no significant statistical means differences among the seven research groups over these blood sera variables. These variables include total bilirubin, (0.138), alanine aminotransferase (0.119), alkaline phosphatase (0.086), and cholesterol (0.146), respectively. On the other hand, the rest of the blood serum variables reflected a probability value that was <0.05 suggesting significant statistical differences among the seven research groups over these blood serum variables. Comparing the observed likelihood values with the level of margin of error (α=0.05), it can be seen that all the presented convertibility values were <0.05 indicating statistically significant differences in the averages between the seven research groups on blood content variables. To determine which groups may differ significantly from each other over the variables that suggested significant statistical differences; the Bonferroni post hoc test was used (Appendix 2).

Liver and kidney function biomarkers (ALT, AST, and ALP) were statistically analyzed and indicate that the probability value is statistically significant at 0.05 (Tables 7 and 8). Whereas results according to the ANOVA score showed a difference between the seven groups of blood sera variables. Comparing the observed probability values to the level of error margin of type I error (α=0.05), it could be noted that some probability values were >0.05, suggesting that no significant statistical means differences among the seven research groups over these blood serum variables. These variables include total bilirubin, (0.138), alanine aminotransferase (0.119), alkaline phosphatase (0.086), and cholesterol (0.146), respectively. On the other hand, the rest of the blood serum variables reflected a probability value that was <0.05 suggesting significant statistical differences among the seven research groups over these specified variables.

**DISCUSSION**

In this study, streptozotocin was used to induce diabetes in rats. It produced hyperglycemia, as well as elevated plasma TG. It is known

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**Table 6: Effect of Crataegus aronia leaves extract on the blood parameters in induced diabetic rats**

|                     | Control | Diabetic | Diabetic + 5 mg extract | Diabetic + 10 mg extract | Diabetic + Insulin | Control+ 5 mg extract | Control+ 10 mg extract |
|---------------------|---------|----------|-------------------------|--------------------------|-------------------|----------------------|------------------------|
| RBCs (10^6/µL)      | 6.352±1.036 | 5.590±0.701 | 6.815±0.573             | 5.715±1.775              | 8.325±1.387       | 5.768±0.616           | 6.464±0.523            |
| Hb (g/dL)           | 14.080±2.054 | 12.620±1.112 | 14.750±1.202            | 12.425±3.409             | 6.760±0.665       | 13.440±1.383          | 14.420±1.130           |
| WBCs (10^3/µL)      | 3.720±0.993  | 5.840±2.365  | 7.450±2.758             | 6.150±2.461              | 2.500±1.291       | 7.060±1.025           | 7.500±1.091            |
| Lympocytes (10^9/L) | 3.040±0.891  | 4.840±2.223   | 6.050±1.485             | 4.525±2.243              | 6.250±0.926       | 5.920±1.018           | 6.160±0.720            |
| Hematocrits (%)     | 39.700±4.445 | 35.760±3.186 | 43.050±0.919             | 33.900±10.576            | 15.075±2.030      | 36.360±3.917          | 40.300±3.081           |
| Platelets (10^9/L)  | 579.800±94.487 | 419.600±204.947 | 589.000±200.818          | 315.000±198.335          | 16.525±2.035      | 671.200±198.750       | 724.200±73.727          |

Data are means ± SD of (3-5) rats/group. *p < 0.05 vs. control.

**Table 7: Effect of Crataegus aronia leaves extract on the Liver biomarkers enzymes in induced diabetic rats**

|                     | Control | Diabetic | Diabetic + 5 mg extract | Diabetic + 10 mg extract | Diabetic + Insulin | Control+ 5 mg extract | Control+ 10 mg extract |
|---------------------|---------|----------|-------------------------|--------------------------|-------------------|----------------------|------------------------|
| Alanine aminotransferase (U/L) | 146.460±63.786 | 122.120±75.406 | 181.600±41.581          | 104.000±21.737       | 371.250±65.589     | 121.360±97.022       | 86.400±39.129          |
| Aspartate aminotransferase (U/L) | 212.120±45.380 | 228.800±89.893 | 513.733±72.707          | 391.800±178.359      | 348.200±188.704    | 208.000±93.365       | 129.180±26.799         |
| Alkaline Phosphatase (U/L)     | 132.200±11.606 | 324.200±131.732 | 324.333±115.678         | 290.500±114.884      | 451.000±50.516     | 171.000±130.704      | 91.800±31.673          |

Data are means ± SD of (3-5) rats/group. *p < 0.05 vs. control.

**Table 8 Effect of Crataegus aronia leaves extract on the blood biochemical marker in induced diabetic rats**

|                     | Control | Diabetic | Diabetic + 5 mg extract | Diabetic + 10 mg extract | Diabetic + Insulin | Control+ 5 mg extract | Control+ 10 mg extract |
|---------------------|---------|----------|-------------------------|--------------------------|-------------------|----------------------|------------------------|
| glucose (mg/dL)     | 156.200±38.402 | 962.600±23.093 | 421.333±187.897         | 897.750±141.474       | 394.500±117.323    | 202.400±29.407       | 221.800±81.211         |
| Creatinine (mg/dL)  | 0.384±0.044 | 0.332±0.068 | 0.197±0.147              | 0.308±0.039             | 0.318±0.051       | 0.348±0.043          | 0.338±0.058            |
| Total bilirubin (mg/dL) | 0.326±0.072     | 0.524±0.343 | 0.820±0.538              | 0.413±0.114             | 0.393±0.178       | 0.424±0.233          | 0.290±0.084            |
| Blood Urea Nitrogen (mg/dL) | 23.680±5.077     | 35.960±3.071 | 50.667±11.809            | 40.725±9.163           | 22.725±3.021      | 22.080±1.242         | 20.060±12.217           |
| Albumin (g/dL)      | 3.442±0.164 | 1.116±1.528 | 2.807±0.502              | 2.125±1.428             | 3.373±0.092       | 3.612±0.126          | 3.614±0.325            |
| Triglycerides (mg/dL) | 31.066±4.476      | 104.632±25.261 | 66.327±31.215            | 82.563±33.732          | 54.020±29.879     | 36.786±5.368         | 39.110±6.932           |
| Cholesterol (mg/dL) | 65.000±0.707     | 68.400±5.273 | 70.000±30.050            | 71.000±10.100           | 68.250±6.602     | 82.200±8.228         | 82.600±12.422          |
| Total protein (g/dL) | 6.152±0.118 | 5.056±0.447 | 6.253±0.216              | 5.493±0.418             | 6.295±0.261       | 6.418±0.238          | 6.716±0.537            |

Data are means ± SD of (3-5) rats/group. *p < 0.05 vs. control.
that alkylation agents such as streptozotocin are toxic to cells by causing damage to the DNA, the release of nitric oxide, increased pancreatic proteins, glycation, and increased production of ROS. These will induce pancreatic β-cell damage. C. aronia reduced the hyperglycemia of streptozotocin-induced diabetic rats but had a slight effect on the plasma glucose level of normal rats. This effect of C. aronia is consistent with many studies indicating a glucose-lowering effect of plant phytochemicals such as polyphenols and flavonoids. Aronia melanocarpa leaves extracts Stimulate glucose uptake in PC12 pheochromocytoma cells and I. 929 fibroblasts (PC 12 and I. 929 cells) 33, 34.

Cignarella et al. (1996) showed that blueberry leaves are traditionally used as a folk medicine treatment for diabetes and reduced plasma glucose levels 34. Vaccinium myrtillus L. leaf caused a significant reduction in blood glucose levels compared with control diabetic rats. Bilberry supplementation resulted in a significant reduction of glucose compared with the diabetic control 35, 36. Also, anthocyanin from grapes, red wine polyphenolic, grape seed-derived proanthocyanidins, myricetin, and rutin reduced glucose levels in streptozotocin-induced diabetic rats 37, 38.

The phytochemical analysis of C. aronia leaves extracts showed that they contained a high concentration of polyphenols 538.5 mg GAE, followed by flavonoids 149.3 mg RE, and flavonols 79.3 mg RE. C. aronia is very rich in phenolic antioxidants. C. aronia extract has an antioxidant capacity of DPPH (IC50) value of 28.02 μg/ml for the radical scavenging activity compared to gallic acid. According to the FRAP assay, C. aronia is a reducing powers capacity and it was increased in concentration and so in DPPH-dependent matter. Therefore, Probably, by acting as an antioxidant C. aronia might protect pancreatic β-cells from streptozotocin-induced increased production of ROS.

In this study, C. aronia significantly reduced the TG levels in treated diabetic rats when compared with untreated diabetic rats. This lipid-lowering effect might be due to the improvement of the diabetic condition in C. aronia -treated rats. A similar TG-lowering effect in streptozotocin-diabetic rats have been demonstrated for anthocyanins from blueberry leaves 39. In this study, streptozotocin did not induce significant changes in the levels of TC.

Crataegus Aronia reduced serum levels of oxidized LDL and protects and reverses vascular inflammation in a high-fat diet rat as described previously 40. Many studies have examined the probable mechanisms of the hypolipidemic effect of C. aronia and showed that C. aronia could inhibit the activity of intestinal acyl-CoA cholesterol acyltransferase 20, suppressing lipogenesis in the rat’s liver 41 and reducing TGs synthesis by C. aronia flavonoids 42. Previous work described the administration of C. aronia associated with a significant increase in the antioxidant potential of the aortic cells through the decrease of MDA levels and increases of GSH levels and SOD activity 43.

Crategus extract can effectively inhibit oxidative processes in the laboratory and the extract of this plant is a highly effective radical scavenger and agree with the previously described. Treatment of diabetic rats with two different concentrations of C. aronia extract caused a concentration-dependent drop in plasma blood sugar levels and this will improve the antioxidant protective mechanism against the oxidative stress that worsens in diabetes 44, 45.

Diabetic rats given the supplementation of Crategus for four weeks significantly restored the WBC count and lymphocytes and hemoglobin and platelets near the control level. This was noted by One Way ANOVA score concerning the differences between the seven groups of blood content variables. Probability values check was (0.002) for WBC; (0.025) for LYM; (0.013) for RBC; (0.000) for Hb; (0.000). (0.000) for PLT. By comparing the observed likelihood values with the level of margin of error of type I error (α = 0.05).

According to results of total protein, albumin, and liver enzyme values in this study clearly show the positive effects of C. aronia on the improvement of liver function through increasing antioxidant capacity of C. aronia, which is, agrees with previous research 26, 47. According to previous work, Esfrat (2003) shows that treatment of Streptozotocin-induced albino rats with water extract of A. augusta plus C. indica at a dose of 300 mg/kg body wt brought down fasting blood glucose to a normal value, while in the untreated group it is increased. Also A. augusta plus C. indica affect the fasting blood sugar, glucose tolerance, and lipid profile 41.

It has been noted that A. Indica leaf extract significantly decreased total cholesterol, LDL-and VLDL-cholesterol, triglycerides, and total serum lipids in streptozotocin-induced diabetic rats, but HDL-cholesterol levels remained unchanged when compared to streptozotocin-induced diabetic control animals 42. The combined extracts of Moringa oleifera and Vernonia amygdalina decreased significantly (P<0.05) in the alamine aminotransferase, aspartate aminotransferase, alkaline phosphatase and total protein of induced diabetic albino Wistar rats 43.

**CONCLUSIONS**

This study indicates the positive effect of C. aronia in reducing glucose levels and hyperlipidemia, improving the antioxidant in control and diabetic rats, and the following conclusions were reached. *Crataegus aronia* reduced hyperglycemia in diabetic rats and significantly decreased TG levels in diabetic mice. In addition, Diabetic rats given the supplementation of *Crataegus* significantly restored the WBC count and lymphocytes and hemoglobin, and platelets near the control level. The improvement of liver function through the increased antioxidant capacity of *C. aronia* also noted was.

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Omar Khaled Al-Mobideen was born and raised in Al-Karak city, Jordan. He is a master student in Mu’ta University. Throughout his education, he always on the honor roll and received numerous awards for academic achievement. After graduating from high school with high honors, he went on to pursue his biology degree at Mu’ta University. His interest in biochemistry research and currently works as a lecturer in Prince Al-Hussein bin Abdullah II Academy of Civil Protection, Al-Balqa Applied University, Jordan.

M.S., Biology, Mu’tah University, Jordan.
B.A., Biology, Mu’tah University, Jordan.

Ahmed Hussein Al-Mustafa was born in Ajloun (Jordan) in 1965. He received his Ph.D. in Biochemistry in 2001 from Heinrich-Heine-University/ Duesseldorf, Germany. He is an associate professor and his main research interests in Biochemistry and microbiology. He has established an advanced research laboratory, emphasizing on Biochemistry studies. Over 20 papers in SCI ranked journals and conference, he has experience in different fields of academic and administration. After serving in Chairman of Biology department, Mut’ah University, Jordan.

1983: General Secondary Certificate (Scientific Stream) –Jordan.
1987: B.Sc Nutrition, Faculty of Public Health and Medical Sciences, Yarmouk University, Irbid, Jordan.
1993: M.Sc. Biochemistry, Faculty of Science, Yarmouk University, Irbid, Jordan.
2001: Ph.D. Biochemistry, Biochemistry and Molecular biology dept., Faculty of Medicine, Heinrich-Heine-University/ Duesseldorf, Germany.

Prof. Dr. Ali Alqudah is an Assistant Professor at the department of applied biology of the Tafila Technical University. He received his Ph.D. in Biotechnology in 2017 from the International Islamic University Malaysia. He is the author or coauthor of more than 20 papers in international refereed journal and his research interests cover several aspects of Biotechnology, Microbiology and Biochemistry. He currently serves as Head of Department and teaches several topics including genetic, ecology and forensic science.

2017. Ph.D., Biotechnology, International Islamic University Malaysia.
2010. M.S., Biology, Mu’tah University, Jordan.
2008. B.A., Biology, Mu’tah University, Jordan.

Dr. fuad Mansour abed Alhawarat is currently Assistant Professor at Department of paramedics, Prince Al-Hussein bin Abdullah II Academy of Civil Protection, Al- Balqa’ Applied University, Jordan. He obtained his PhD in biology from the University of Jordan, Jordan in 2019. He did his First Degree in biology in 2003 from Yarmouk University, Jordan. He also obtained his Master of Biotechnology at the Al- Balqa’ Applied University in 2012. His areas of interests are Microbiology, Cancer Stem Cells Molecular biology.

2017. Ph.D., Biology, International Islamic University Malaysia.
2010. M.S., Biology, Mu’tah University, Jordan.
2008. B.A., Biology, Mu’tah University, Jordan.

Hussam is an assistant professor of pharmacology at faculty of pharmacy, International Islamic University Malaysia located in Kuantan, Malaysia. He obtained his basic bachelor degree in Pharmacy from Al-Zaytoonah University of Jordan (2011), followed with Master in Pharmacology (2015) and PhD in pharmacy practice (2019) from International Islamic University Malaysia. His research involves in-vivo and ex-vivo using different animal models. During his PhD, he worked on a project in Pharmacy Practice, specifically in the field of pharmacotherapy and clinical drug safety which involve evaluating the available scientific evidence for the use of opioids in pain management for non-cancer pain patients.

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