PROTECTIVE EFFECT OF FLAME SEEDLESS RED GRAPE LEAVES AGAINST ALLOXAN- INDUCED DIABETES IN RATS

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ABSTRACT

This research aimed to determine the chemical composition and identify phenolic components of grape seedless leaves as well as the effect of their biological activity on type 2 diabetic albino rats that were stimulated by Alloxan solution. The rats were equally divided into six groups, seven rats for each group, orally administered daily for 5 weeks and designated as follows, fed with 25% grape leaves (normal control), fed with 50% grape leaves, (diabetic control), diabetic rats fed with 25% grape leaves and diabetic fed with 50% grape leaves. Serum glucose, liver and kidney functions and lipid profile were assessed. The results showed that Flame Seedless grape leaves were an abundant source of crude fiber, total chlorophyll, crude protein, total carbohydrates and total flavonoids as well as total phenols, which have a positive biological effect ($p < 0.05$) especially for diabetic rats orally fed with 50% grape leaves. Serum glucose levels were significantly different (179.2±0.42) compared to the diabetic control group (243.1±1.17). Lipid profile reached 171.5 ± 1.36 compared to the diabetic control group 187.2 ± 0.49. The cholesterol level recorded 123.6± 0.87 compared to the diabetic control group 134.7 ± 0.61. Liver and kidney functions were positively affected in rats that were fed on grape leaves than the control group.

Keywords: Antidiabetic Effect; Flame Seedless grape; Hyperlipidemia; Lipid profiles; kidney and liver functions.

INTRODUCTION

Although the pharmaceutical industry has helped protect humanity from disease pests, its harmful side effects have made it an addiction that disturbs many. Interest in traditional medicine and the use of natural medicine has grown in recent years. International sources show that type 2 diabetes is spreading significantly, which has prompted research into the disease and its potential cure in various parts of the world (Khan *et al.,* 2020). However, high costs and a lack of success with healthy pancreas transplants in diabetic patients' bodies have also been noted (Fadil and Yousef, 2021).

Diabetes mellitus (DM), referred to as just diabetes, is a collection of metabolic illnesses characterised by persistently elevated blood sugar levels. The symptoms of increased thirst, increased appetite, and frequent urination are brought on by this elevated blood sugar. Diabetes has several problems if left untreated. Diabetic ketoacidosis and nonketotic hyperosmolar coma are examples of its acute complications (Kumar *et al.,* 2020).

Globally, grape is one of the most important fruit crops (Gülcü *et al.,* 2020). Grape leaves are considered the most important biologically active component of grapevines, despite being neglected byproduct. (Maia *et al.,* 2019). Due to their disposal as waste, grape leaves pose a serious environmental threat in some nations. To tackle this problem, bioactive elements were separated and utilized from grape leaves (Lantzouraki *et al.,* 2020).

Even though grapevine leaves are full of bioactive substances that are good for human health, they are typically regarded as agro-industrial trash. This study gathers the most up-to-date and pertinent information on the phytochemical makeup and bioactive characteristics of red grape leaves. Both flavonoid and non-flavonoid phenolic compounds, including flavonols, hydroxycinnamic acid derivatives, carotenoid pigments, and chlorophylls, as well as fatty acids, which have been shown to have anti-inflammatory, anti-microbial, antidiabetic, cardio-, neuro-, and hepatoprotective qualities, are abundant in these by-products. (Carla Sousa *et al.,* 2024)

According to recent research, the bioactive substances found in red grape leaves are most prominent and well- studied called polyphenols. These compounds, which include phenolic acids, stilbenes, coumarins, lignans, and flavonoids, originate from the subsequent metabolism (Marabini *et al.,* 2020).

Interestingly, grape leaves contain polyphenols that can guard against oxidative damage. Polyphenols increase the activity of natural antioxidants; they also could delay or stop oxidative stress and reduce the generation of reactive oxygen compounds. The purification and isolation of many polyphenols from grape leaves present new and lucrative opportunities for the nutritional and medical sectors (Uddin *et al.,* 2020).

Therefore, this study aims to evaluate the biological activity of grape leaves on diabetic rats to assess the possibility of recommending their use as food additives for diabetic patients as therapeutic feeding.

MATERIALS AND METHODS

Plant material

This investigation was conducted during 2022-2023 seasons on Flame Seedless grape leaves, which originated from a vineyard located in El-Beheira Governorate, Egypt.

Animals

A total number of 42 male albino rats weighing approximately 150 -190 g used in the current study were obtained from Animal house, Agriculture Research Center, Cairo, Egypt. The rats were housed in plastic cages, maintained on standard pellet diet and water ad libitum. After randomization into various groups and before initiation of experiment, the rats were acclimatized for a period of seven days to laboratory conditions [temperature (25± 2°C) and 12 h light/dark cycle]. The rats were kept under normal laboratory conditions and fed on a formulated basal diet consisting of corn starch 70%, casein 10%, corn oil 10%, salts mixture 4%, vitamin mixture 1% and cellulose 5% (Reeves et al., 1993) for one week as an adaptation period before starting the experiment. All protocols and procedures adopted for the present investigation were in accordance with the approval of the Faculty of Agriculture, Ain Shams University Ethics Committee approved this animal study, which was conducted in conformity with international guidelines for the care and welfare of laboratory animals [Approval No. 9-2024-06]

Chemicals and reagent methodology kits

Alloxan was attained from the house of animals, A.R.C., Cairo, Egypt. Glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride, total protein, urea, and creatinine kits were obtained from the Egyptian Company for Biotechnology, Obour City, Cairo, Egypt.

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Estimation of phytochemical composition of grape leaves

Several chemical compositions were determined in grape leaves: moisture, ash, crude fiber and crude protein (A.O.A.C., 2005), total chlorophyll (Wood *et al.,* 1992), total carbohydrates (Dubois *et al.,* 1956), total flavonoids (Marinova *et al.,* 2005) and total phenols (Shahidi and Naczk 1995).

Grape leaves phenolic Compounds Separation

The separation of phenolic compounds was performed via an Agilent 1260 series HPLC (Goupy *et al.,* 1999 and Gökbulut., 2015).

HPLC conditions

HPLC analysis was carried out using an Agilent 1260 series. The separation was carried out using Eclipse C18 column (4.6 mm x 250 mm i.d., 5 μm). The mobile phase consisted of water (A) and 0.05% trifluoroacetic acid in acetonitrile (B) at a flow rate of 0.9 ml/min. The mobile phase was programmed consecutively in a linear gradient as follows: 0 min (82% A); 0–5 min (80% A); 5-8 min (60% A); 8-12 min (60% A); 12-15 min (82% A); 15-16 min (82% A) and 16-20 (82%A). The multi-wavelength detector was monitored at 280 nm. The injection volume was 5 μl for each sample solution. The column temperature was maintained at 40 °C. (Moldoveanu *et al.,* 2016).

Induction of Diabetes Mellitus

Experimental diabetes was motivated by a freshly prepared liquid of alloxan (45 mg/kg bw) in 0.1 M cold citrate buffer, pH 4.5, where the solution of alloxan was inoculated via the abdomen. Blood was taken from fasting alloxan-treated animals 72 hours after alloxan administration. Diabetic rats were those with blood glucose levels greater than 240 mg/dL, taken as a model for type 2 diabetes, and used for further experiments (Layam and Reddy, 2006).

Experimental design

The following six treatments were used in this experiment, with seven experimental rats for each treatment:

(1) Non-diabetic rats unmodified diet (basal diet) (Non-diabetic control)

(2) Non-diabetic rats modified diet (25% grape leaves)

(3) Non-diabetic rats modified diet (50% grape leaves)

(4) Diabetic rats unmodified diet, (Diabetic control)

(5) Diabetic rats modified diet (25% grape leaves)

(6) Diabetic rats modified diet (50% grape leaves).

Preparing a blood sample:

The therapies were administered to the rats for a duration of five weeks. After the experiment ended, serum was separated and kept at -20 °C for biochemical examination after blood was obtained from the retro-orbital plexus.

Blood biochemical assay:

Biochemical assays were determined in serum by using reagent kits; glucose (Tietz, 1995). Total cholesterol (Roeschlau *et al.,* 1974), triglycerides (McGowan *et al.,* 1983), high-density lipoprotein cholesterol (NCEPR, 1995) and low-density lipoprotein cholesterol (Makni *et al.,* 2008), aminotransferase (AST and ALT) enzymes activity (Young, 1990), total proteins and albumin (Alb) (Tietz, 1995), urea (Tietz, 1995) and creatinine (Spencer and Price, 1980)

Statistical analysis

Data was presented as mean ± SD to compare between replicates for each treatment. The means of treatments were tabulated by using one-way analysis of variance (ANOVA); Duncan's multiple range tests, significance at $p < 0.05$ was used to compare among means of treatments according to Snedecor and Cochran, (1980).

RESULTS

Chemical composition of Flame Seedless grape leaves.

As shown in Table 1, results revealed that chemical composition of Flame Seedless grape leaves contained the highest percentage of total carbohydrates followed by crude fiber followed by crude protein, while both the moisture and ash recorded the lowest one. One the other hand, total chlorophyll recorded 37.29 mg/100g, total flavonoids recorded 2.69 mg/100g and total phenols recorded 7.23 mg/100g.

Table 1. Chemical composition of Flame Seedless grape leaves.

CHARACTER	VALUE
Moisture (%)	8.67
Ash (%)	5.69
Crude fiber (%)	31.23
Total Chlorophyll (mg/100g F.W.)	37.29
Crude protein (%)	11.49
Total carbohydrates (%)	42.83
Total flavonoids (mg/100g D.W.)	2.69
Total phenols (mg/100g D.W.)	7.23

Quantitative analysis of polyphenolic compounds identified by HPLC

Results in Table 2 and Figure 1 showed that sixteen phenolic compounds were identified in Flame Seedless grape leaves as compared with reference substance HPLC chromatograms according to retention time. The obtained data showed that coumaric acid (970.03 µg/g) was the major component of the total phenolic compounds, followed by vanillin, gallic acid, naringenin, catechin, ferulic acid, rutin, chlorogenic acid, cinnamic acid, pyrocatechol, apigenin, methyl gallate, kaempferol, quercetin and daidzein, while, caffeic acid recorded the least one (2.21 µg/g).

Table 2. Quantitative analysis of phenolic compounds identified by HPLC in Flame Seedless grape leaves

NO.	COMPOUND	RT (MIN)	CONCENTRATION (µG/G/ DRY LEAVES)
Phenolic acids constituents			
1	Gallic acid	3.350	206.03
2	Pyrocatechol	6.699	18.89
3	Chlorogenic acid	4.145	27.34
4	Caffeic acid	6.082	2.21
5	*p*- Coumaric acids	9.178	970.03
6	Ferulic acid	10.367	63.11
7	Methyl gallate (ester)	5.535	14.27
8	Cinnamic acid	13.817	26.13
Flavonoids			
1	Daidzein	12.647	3.22
2	Quercetin	12.903	9.45
3	Kaempferol	15.319	10.65
4	Apigenin	14.856	16.68
5	Catechin	4.684	149.95
6	Vanillin	9.491	248.24
7	Rutin	8.192	59.09
8	Naringenin	10.612	183.92

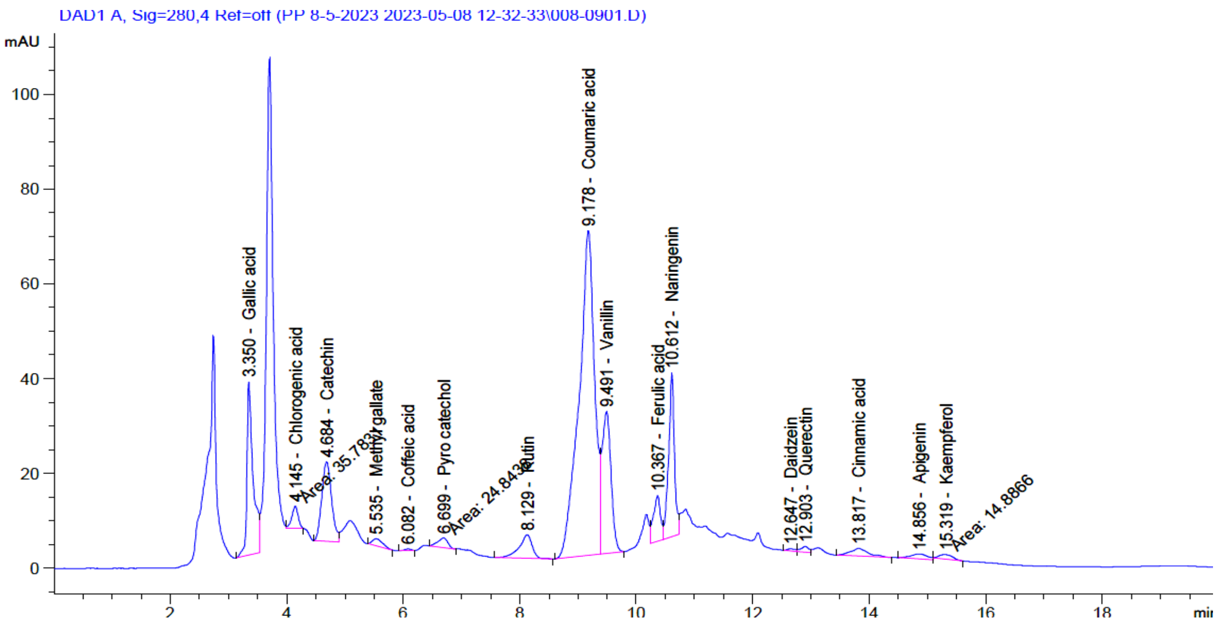

Figure 1. HPLC chromatogram of Flame Seedless grape leaves.

Serum glucose:

The rats that were orally administered grape leaves had significantly lower blood glucose levels than the control group, according to the findings in Table 3. The blood glucose level in the group of diabetic rats fed a modified diet containing 50% grape leaves considerably fell to 179.2 mg/dL as compared to the group of diabetic control, which recorded 243.1 mg/dL.

Table 3. Effect of grape leaves on the levels of serum glucose and lipid profile

GROUPS	*GLUCOSE (MG/DL)*	**LIPID PROFILE**			
		TC (mg/dL)	**TG (mg/dL)**	**HDL (mg/dL)**	**LDL (mg/dl)**
Normal control	115.6^{d} ± 1.23	162.1^{d} ± 0.61	112.9^{c} ±1.07	63.4^{c} ± 0.74	98.7^{d} ± 1.17
25% grape leaves	106.7^{de} ± 0.74	157.4^{e} ± 0.53	107.5^{cd} ±1.26	67.1^{b} ± 0.43	90.3^{e}± 0.69
50% grape leaves	99.4^{e} ± 0.35	149.7^{f} ± 1.19	101.3^{d} ± 0.83	72.6^{a} ± 1.07	77.1^{f} ± 0.31
Diabetic control	243.1^{a}± 1.17	187.2^{a} ± 0.49	134.7^{a} ± 0.61	55.7^{e} ± 0.09	131.5^{a} ± 1.16
Diabetic+25% grape leaves	216.7^{b}± 1.03	175.9^{b} ± 0.74	131.9^{a} ± 1.29	59.5^{d} ± 0.38	116.4^{b} ± 0.91
Diabetic+50% grape leaves	179.2^{c}± 0.42	171.5^{c} ± 1.36	123.6^{b}± 0.87	61.8^{c} ± 1.13	109.7^{c} ± 0.35

*** The mean ±SD displayed for each treatment. Significant differences among treatments ($p < 0.05$) were shown by different letters (a, b, c, etc.)**

Lipid profile

Data presented in Table (3) mentioned that as compared to control, the rats that were fed grape leaves had a positive influence on total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol and low-density lipoprotein cholesterol levels (LDL-Ch and LDL-Ch). Regarding the diabetic rats fed a modified diet containing 50% grape leaves, serum TC, TG and LDL-Ch levels significantly decreased to 171.5, 123.6 and 109.7 mg/dL, respectively with pronouncedly elevated in the level of in HDL-Ch to 61.8 mg/dL than those in the diabetic control group, which recorded 187.2, 134.7, 131.5 and 55.7 mg/dL, respectively.

Liver functions

Results in Table 4 declared that rats that were orally fed 50% grape leaves had a significant decrease on the aspartate transaminase and alanine transaminase enzymatic activity as well as total protein and albumin levels as compared to control groups. As compared to the diabetic control group, the levels of AST and ALT enzymes activity as well as total protein and albumin in diabetic rats group fed a modified diet containing 50 % grape leaves significantly reduced in serum.

Table 4. Effect of seedless grape leaves on liver functions in rat groups

GROUPS	AST (U/L)	ALT (U/L)	TP (G/DL)	ALB (G/DL)
Normal control	$58.2^{d} \pm 0.09$	$81.6^{d} \pm 1.27$	$7.56^{cd} \pm 1.39$	$3.77^{d} \pm 0.12$
25% grape leaves	$54.6^{de} \pm 1.34$	$79.1^{de} \pm 0.81$	$7.53^{de} \pm 1.23$	$3.74^{d} \pm 0.47$
50% grape leaves	$52.9^{e} \pm 1.25$	$76.3^{e} \pm 1.43$	$7.49^{e} \pm 0.91$	$3.69^{e} \pm 1.38$
Diabetic control	$74.3^{a} \pm 0.72$	$99.6^{a} \pm 0.85$	$7.76^{a} \pm 0.37$	$3.98^{a} \pm 0.29$
Diabetic + 25% grape leaves	$68.5^{b} \pm 1.59$	$93.2^{b} \pm 1.16$	$7.64^{b} \pm 0.52$	$3.91^{b} \pm 0.94$
Diabetic + 50% grape leaves	$63.7^{c} \pm 1.24$	$87.4^{c} \pm 0.78$	$7.58^{c} \pm 0.16$	$3.84^{c} \pm 1.35$

*** The mean ±SD displayed for each treatment. Significant differences among treatments ($p < 0.05$) were shown by different letters (a, b, c, etc.)**

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Kidney functions

As shown in Table 5 data unveiled the groups of rats that were fed grape leaves orally had a positive influence on the serum urea and creatinine levels as compared to control. In the diabetic rats fed a modified diet containing 50% grape leaves, serum urea and creatinine levels significantly decreased to 55.3 and 0.66 mg/dL, respectively, then those in the diabetic control, which recorded 73.8 and 0.714 mg/dL, respectively**.**

Table 5. Effect of grape leaves on kidney function of rat groups

TREATMENT	SERUM UREA (MG/DL)	SERUM CREATININE (MG/DL)
Normal control	$49.1^{c} \pm 0.86$	$0.64^{c} \pm 1.24$
25% grape leaves	$41.3^{d} \pm 1.37$	$0.63^{c} \pm 0.67$
50% grape leaves	$38.7^{d} \pm 0.51$	$0.61^{d} \pm 0.98$
Diabetic control	$73.8^{a} \pm 1.43$	$0.71^{a} \pm 0.87$
Diabetic + 25% grape leaves	$61.9^{b} \pm 1.29$	$0.67^{b} \pm 0.55$
Diabetic + 50% grape leaves	$55.3^{c} \pm 0.81$	$0.66^{b} \pm 1.07$

*** The mean ±SD displayed for each treatment. Significant differences among treatments (*p* < 0.05) were shown by different letters (a, b, c, etc.)**

DISCUSSION

This study's primary goal was to determine which phytochemicals were found in grape leaves. protein, carbohydrate, polyphenol, and flavonoid content. Numerous research has suggested that the anti-hyperglycemic and anti-hyperlipidemia effects are caused by phytochemicals. The acquired outcomes correspond with the findings published by Farhadi *et al*. (2016) who reported that grape leaf contained 0.9–2.6 µg/g gallic acid, 36–89 µg/g catechin, 22–94 µg/g epicatechin, 3.3–5.7 µg/g caffeic acid, 30–212 µg/g rutin, 1.2–3.9 µg/g resveratrol, and 126–198 µg/g quercetin In this respect, Pintać *et al*. (2019) who determined that leaves of grape varieties contained 11.5–72.9 mg/kg protocatechuic acid, 9.22–66.1 mg/kg p-hydroxybenzoic acid, 19.2–38.4 mg/kg gallic acid, 10.6–21.7 mg/kg syringic acid, 21.0–88.7 mg/kg p-coumaric acid, 16.1–108.0 mg/kg caffeic acid, 7.63–38.3 mg/kg ferulic acid, 2.33–657 mg/kg chlorogenic acid, 118–147 mg/kg quercetin, 1.73–1.99 mg/kg. In addition, Moldovan *et al*. (2020) who identified ten polyphenolic compounds in V. vinifera leaves extracts including 5.50 µg gallic acid/g, 1.71 µg protocatechuic acid/g, 0.01 µg caftaric acid/g, 23.31 µg catechin/g, 7.10 µg epicatechin/g, 147.09 µg hyperoside/g, 903.49 µg isoquercitrin/g, 385.63 µg rutin/g, 188.74 µg quercitrin/g and 10.54 µg quercetin/g. Recently, Abdel-Khalek and Mattar (2022), who analyzed the phenolic composition of Egyptian grape leaves, and they found that 1.32 mg/gDW Epicatechin, 2.89 mg/gDW Gallic acids, 6.6 mg/gDW Catechin, 1.78 mg/gDW Ferulic acids, 1.66 mg/gDW Chlorogenic acids, 3.11 mg/gDW Caffeic acids, 0.5 mg/gDW Coumaric acids and 5.45 mg/gDW Vanillic acids.

The experiment showed that group of diabetic rats given a modified meal that contained 50% grape leaves, the blood glucose level dramatically dropped. The results obtained are in accordance with those mentioned by Orhan *et al.* (2007), Beheshtipour *et al.* (2018) and Negm *et al*. (2020), who found that comparing with the positive control, serum glucose in rat groups treated with diets containing 5% grape leaves significantly decreased.

Finding out how grape leaves affected the anti-hyperglycemic impact of alloxan-induced diabetic rats was the study's second goal. Reactive Oxygen Species (ROS) caused by alloxan caused diabetes by rapidly destroying beta cells in the pancreas, which resulted in hyperglycemia. Stanely *et al*. (2000) Consequently, hyperglycemia causes glucose auto-oxidation, which raises the production of free radicals. (Bajaj and Khan, 2012).

Determining the anti-hyperlipidemia impact of grape leaf in rats with diabetes induced by alloxan was the third goal. The study demonstrated how feeding grape leaves to diabetic rats affected their levels of low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), triglycerides (TG), and total cholesterol (TC). Rats fed grape leaves in the control group showed improvements in their levels of low-density lipoprotein (LDL-Ch), very low-density lipoprotein (LDL-Ch), triglycerides (TG), and total cholesterol (TC). Serum levels of low-density lipoprotein (LDL-Ch) and total cholesterol (TC) dramatically dropped in diabetic rats given a modified diet that contained 50% grape leaves. The outcomes correspond with the findings published by Suresh *et al.* (2019) and Negm *et al.* (2020) they found that rats orally received grape leaf extract significantly improved serum lipid profile.

The study also demonstrated that, in comparison to the control group, the mice who were given grape leaves orally showed improvements in their serum levels of urea and creatinine. The acquired outcomes correspond with the findings published by Orhan *et al.*

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(2007) who mentioned that ethanol extracts of *Vitis vinifera L*. at 250 mg/kg dose were found effective to protect kidney from oxidative damage in rats. In addition, Lafta (2016) reported that 100 mg/mL of grape leaves extract was treating Rabbits for 2 months significantly decreased both blood urea and creatinine. Recently, Negm *et al*. (2020) studied the impact of grape leaves on serum urea and serum creatinine in rats suffering from acute liver disease. As compared to the positive control, serum urea and creatinine in rats treated with diets containing 50% grape leaves significantly decreased.

It was also observed that rats orally fed with 50% grape leaves had a significant decrease in the enzymatic activity of aspartate transaminase and alanine transaminase as well as total protein and albumin levels compared to the control groups. Compared to the diabetic control group, the activity levels of AST and ALT enzymes as well as total protein and albumin in the diabetic rats fed a modified diet containing 50% grape leaves were significantly decreased in the serum. The obtained results are in line with those mentioned by Orhan *et al*. (2007) who mentioned that ethanol extracts of *Vitis vinifera* L. at 250 mg/kg dose was found effective to protect liver from the oxidative damage in rats. In addition, Heibatollah *et al*. (2009) mentioned that the alcoholic extract of grape at 800mg/kg showed a pronounced liver protective influence by decreasing the serum of AST and ALT enzymes. In addition, Lafta (2016) reported that 100 mg/mL of grape leaves extract was treating rabbits for 2 months significantly decreased the activities of AST and ALT enzymes. Moreover, Negm *et al*. (2020) studied the impact of grape leaves on AST and ALT enzymes activity in rats suffering from acute liver disease. As compared to the positive control group, AST and ALT activities in rats treated with diets containing 50% grape leaves were significantly decreased. Recently, Saadaoui *et al*. (2023) showed that mice were pretreated orally with *Vitis vinifera* leaves extracts at 30 mg/kg for 7 days reduced activities of AST and ALT enzymes, which may indicate that grape leaf extracts have a positive effect in reducing liver enzymes.

CONCLUSION

This study demonstrates the potential of grape leaves as antidiabetic, and hypolipidemic, the chemical profile showed that grape leaves are considered a rich source of crude fiber, total chlorophyll, crude protein, total carbohydrates and total flavonoids as well as total phenols. These compounds have a positive biological effect on the serum glucose levels, lipid profile and the liver and kidney functions for diabetes. With further research, naturally sourced phenolic compounds can provide safe and economic replacement to treat diabetes and oxidative stress-linked diseases.

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التأثير الوقائي لمستخلص أوراق العنب الأحمر الخالي من البذور ضد مرض السكرى الناتج عن مادة الألوكسان في الفئران

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المستخلص

هدف هذا البحث إلى تحديد التركيب الكيميائي والتعرف على المكونات الفينولية لأوراق العنب وتأثير نشاطها البيولوجي في الجرذان المصابة بالسكري والتي تم تحفيزها بمحلول الألوكسان. تم تقسيم الفئران بالتساوي إلى ست مجموعات، كل مجموعة تحتوي على سبعة فئران تم تغذيتهم على أوراق العنب الجافة المخلوطة بالعليقة يوميًا لمدة 5 أسابيع وتم تصنيفها على النحو التالي: المجموعة الضابطة الطبيعية، وأخرى غذيت بأوراق العنب 25%، وثالثة غذيت بورق العنب 50%، والمجموعة الضابطة على مرض السكري، والمجموعة المصابة بالسكري التي تم تغذيتها على 25% أوراق العنب، ومجموعة السيطرة على مرض السكري. التي تم تغذيتها على 50% أوراق العنب. تم تقييم نسبة الجلوكوز في الدم ووظائف الكبد والكلى ومستوى الدهون. أظهرت النتائج أن ورق العنب الأحمر خالي البذور يعتبر مصدراً وفيراً للألياف الخام والكلوروفيل الكلي والبروتين الخام والكربوهيدرات الكلية والفلافونويدات الكلية وكذلك الفينولات الكلية والتي لها تأثير بيولوجي إيجابي خاصة للفئران المصابة بالسكري التي تتغذى عن طريق الفم على 50% أوراق العنب. كما تأثرت وظائف الكبد والكلى بشكل إيجابي في الفئران التي تم تغذيتها على ورق العنب مقارنة بمجموعة الضابطة.

الكلمات المفتاحية: التأثير المضاد لمرض السكري، العنب الخالي من البذور، صورة الدهون في الدم، مستويات الدهون، مؤشرات وظائف الكبد.