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Evaluation of the Antidiabetic Effects of *Myrtus Communis L.* Fruit in A Rat Model of Diabetes: Anti-hyperglycemic Activity Through Pancreatic β-islet Cells Regeneration and Insulin Secretion Enhancement

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ABSTRACT

Background & Objective: Plant-based remedies have gained growing interest as effective options for managing diabetes and its associated complications. The purpose of this study was to assess the antiyperglycemic and protective properties of an aqueous extract from myrtle (*Myrtus communis* L.) fruit against the most prevalent diabetes-related complications in rats. This study provides a comprehensive assessment of the effects of myrtle fruit extract on diabetes-related complications, including liver and kidney dysfunction, as well as its potential role in pancreatic β-cell regeneration.

Materials & Methods: Streptozotocin (STZ)-induced diabetic rats were treated with varying doses of *M. communis* L. fruit extract (low, medium, and high) over a period of 3 weeks. Control rats received either no treatment or were administered a standard antidiabetic drug. Key parameters, including oral glucose tolerance test (OGTT), fasting blood glucose, two-hour postprandial glucose, insulin levels, lipid profile, and serum biomarkers of liver and kidney function, were measured. Histopathological analysis of the renal, liver, and pancreatic tissues were performed to assess tissue damage and regeneration.

Results: The antihyperglycemic, hepatoprotective, and renoprotective activities of myrtle extract were investigated. Treatment with *M. communis* L. notably improved both short-term and long-term high blood sugar levels, reduced two-hour post-meal glucose levels, enhanced oral glucose tolerance (OGTT), and increased insulin levels in diabetic rats. Additionally, the extract demonstrated antihyperlipidemic effects and improved both the atherogenic index (AI) and the coronary artery risk index (CRI) in diabetic rats. Also, liver serum biomarkers and kidney dysfunction were attenuated by the extract in diabetic rats. Furthermore, histopathological examination of the liver, kidney, and pancreas confirmed that the corresponding pathological changes were significantly attenuated by myrtle in diabetic rats.

Conclusion: The Current study demonstrates that *M. communis* L. fruit extract exhibits antihyperglycemic, antihyperlipidemic, hepatoprotective, and renoprotective properties in STZ-induced diabetic rats. These properties may be partly mediated by regenerative processes in the pancreas and increased insulin secretion. Nonetheless, more research is necessary to thoroughly recognize the underlying molecular mechanisms. Limitations of the research include the lack of long-term clinical validation and the need for mechanistic studies to define the role of β-cell regeneration better.

Keywords: *Myrtus communis*, pancreatic β-Cells, Type 2 Diabetes Mellitus, Hepatoprotective Agents, Antioxidants, Hypoglycemic Agents, Renal Insufficiency

1. Introduction

Diabetes is a type of chronic metabolic disorder that affects many people worldwide. It is associated with elevated blood glucose triggered by defects in insulin secretion, insulin function, or both; diminished metabolism of carbohydrates, proteins, and lipids, which can, in the long term, impair the function of various organs; and complications, for instance, retinopathy, neuropathy, nephropathy, and cardiovascular disorders (1, 2).

Diabetes is now recognized as the third leading cause of death in developing countries. These complications are far less common in patients whose blood glucose is well controlled. Given advances in medical science, there is currently no effective treatment for the definitive treatment of diabetes, and only insulin-based therapy and oral antidiabetic medications, including biguanides and sulfonylureas, are available. While effective in reducing blood sugar, these drugs come with side effects like hypoglycemia and weight gain. As a result, ongoing efforts are focused on developing high-efficacy medications with fewer adverse effects (3).

Herbal-based products have been popular worldwide for centuries. In the last decade, there has been a high tendency to use traditional herbs with antihyperglycemic effects in the treatment of diabetes (4). Ethnopharmacological reports have demonstrated that nearly 1200 plants have been utilized in traditional medicine for their probable antihyperglycemic activities. Studies have shown that some herbal remedies for diabetes can ameliorate the symptoms of this progressive disease and prevent its secondary complications. In addition to being effective in improving disease status, these herbs are associated with fewer side effects and are more cost-effective compared to synthetic oral antihyperglycemic drugs (4).

Myrtus communis Linn. Commonly called myrtle and belonging to the Myrtaceae family, it is a therapeutic plant native to the Mediterranean area and has been traditionally valued for its therapeutic properties since ancient times (5). The various extracts of this plant have a long history of therapeutic uses, containing antimicrobial, antioxidant, antinociceptive, and anti-inflammatory effects (5-11). For centuries, myrtle has been traditionally employed as a remedy for managing diabetes. Reports on the anti-diabetic properties of hydroalcoholic extracts of leaves have shown that they can have a powerful effect on lowering blood sugar (5, 8). A 2004 study reported that myrtle oil may also have hypoglycemic effects (12). Although limited research has explored the antidiabetic effects of *M. communis* L. fruit, recent studies have demonstrated its hypoglycemic and antioxidant properties in diabetic rats (13, 14). However, the full extent of its antidiabetic effects and underlying mechanisms remains unclear. The primary objective of the current study was to evaluate the antidiabetic properties of aqueous extracts of *M. communis* L. fruit (MC) from various perspectives in streptozotocin (STZ)-induced diabetic rats.

2. Materials and Methods

2.1 Chemicals

STZ was obtained from Sigma–Aldrich Co. (Taufkirchen, Germany). All other chemicals used in the research were of the highest commercially available quality.

2.2 Preparation of aqueous extract of *M. communis* L. fruit (MC)

In Iranian traditional medicine, myrtle fruit has been used in a macerated form to control blood glucose levels in diabetic patients; therefore, we employed a similar extraction technique to resemble traditional methods. Using this approach, we tried to obtain compounds identical to the old macerated form in our extraction. Maceration is a simple extraction technique widely used in medicinal plant research (15).

M. communis L. fruit was obtained in the summer of 2018 from Shahriar, Alborz Province, Iran. It was stored at the herbarium of the School of Pharmacy, Shahid Beheshti University of Medical Sciences (SBUMS), Tehran, Iran, with a Voucher No. 1110. The fruits were authenticated by Mr. Kamalinejad, a certified botanist at the Department of Botany, SBUMS. Fresh fruits, including their peels, were washed, and 100 g of fruit was extracted using the maceration method with 900 mL of distilled water for 30 minutes. The extract was then concentrated by drying in a water bath at 90°C. Afterward, it was filtered and stored at 20°C until it was use. The moisture content of the extract was measured by weighing 2 g of the final product after drying it in an oven at 60–65°C for 72 hours, which revealed a water content of 24%. (16, 17). The extract was freshly dissolved in distilled water immediately before use to achieve the required dose.

2.3 Animals

Male Sprague–Dawley rats weighing 200±20 g were utilized in this research. They were provided with a standard chow diet and water ad libitum, housed in stainless steel cages at a controlled ambient temperature of 22±2°C, with relative humidity maintained at 50±10%, and subjected to a 12-hour light/dark cycle. The research adhered to the principles of laboratory animal care (NIH publication No. 85-23, revised 1985). All procedures were conducted in accordance with ethical guidelines approved by the Animal Experimentation Committee of Zanjan University of Medical Sciences, Zanjan, Iran (Approval number: ZUMS.REC.1394.36).

2.4 Induction of experimental diabetes

Diabetes was induced in the rats via the intraperitoneal (i.p.) administration of 60 mg/kg freshly prepared STZ in 0.1 M citrate buffer (pH 4.5). Diabetes was confirmed 3 days after the injection of STZ by determining the tail vein blood glucose level with a standardized glucometer (ARKAY, INC., Japan). Animals with fasting blood

glucose (FBG) levels ≥ 300 mg/dL were considered diabetic (18).

2.5 Study design

The rats were randomly separated into eight groups, each consisting of six rats (n = 6). Group I- Normal control group (NC): Rats that received 0.5 mL of saline orally for the entire experimental period;

Group II- Normal control + MC (600 mg/kg) group (NC+MC-600);

Group III- Diabetic group (DM): Rats in this group were injected with 60 mg/kg STZ via a single i.p. injection and received 0.5 mL of saline orally throughout the entire experimental period;

Group IV- Diabetic + MC (200 mg/kg) group (DM+MS-200);

Group V- Diabetic + MC (400 mg/kg) group (DM+MS-400);

Group VI- Diabetic group + MC (600 mg/kg);

Group VII- Diabetic + Glibenclamide (10 mg/kg/day) (DM+Gli);

Group VIII- Diabetic + acarbose (20 mg/kg/day) group (DM+Ac-20).

MC (200, 400, or 600 mg/kg) was administered in a single daily mode via an intragastric tube for 21 days. The short- or long-term studies did not utilize the same animals. The doses of fruit extract used were determined based on an earlier study (14).

2.6 Determination of short-term and long-term fasting blood glucose (FBG) levels

Blood samples were collected from the tail vein of rats in the NC, DM, DM+MC-600, and DM+Gli groups at 0, 1, 3, 5, and 7 hours following a single dose of 600 mg/kg myrtle extract. FBG levels were estimated using a standardized glucometer (ARKAY, INC., Japan). Additionally, blood samples were taken from the tail vein of rats in all groups for further analysis (except the DM+Ac-20 group) at 0, 7, 14, and 21 days after the confirmation of diabetes by a standardized glucometer. All the rats were fasted for 12 hours on the day of blood sampling.

2.7 Determination of blood glucose levels two hours after a meal

Blood samples from the rats were collected through the tail vein 2 hours after gavage at 7, 14, and 21 days following confirmation of diabetes. Blood glucose levels were evaluated two hours after the meal via a standardized glucometer.

2.8 Oral glucose tolerance test (OGTT)

OGTTs are methods that can help to diagnose instances of diabetes (19). One prior tothe experiment's conclusion, OGTTs were performed in all groups. For this purpose, 2 g/kg glucose was administered orally to all overnight-fasted rats, and blood glucose levels were assessed at 0, 30, 60, 90, and 120 minutes after glucose administration through tail vein blood sampling using a standardized glucometer.

2.9 Biochemical parameter measurements

At the conclusion of the experiment, blood samples were drawn from the heart to assess various biochemical parameters. Levels of aspartate aminotransferase (AST), total triglycerides (TG), alkaline phosphatase (ALP), alanine transaminase (ALT), high-density lipoprotein cholesterol (HDL-c), total cholesterol (TC), creatinine, and urea were measured by commercially obtainable enzyme kits (Pars Azmoon, Tehran, Iran). Insulin levels were assessed using the Mercodia Rat Insulin ELISA Kit. Additionally, LDL-c, the atherogenic index (AI), and the coronary artery risk index (CRI) were calculated using the following formulas (20):

LDL-c (mg/dL) = [TC-HDL-(TG/5)]

CRI= TC (mg/dL)/HDL- c (mg/dL)

AI= (TC-HDL-c)/HDL-c

2.10 Evaluation of body weight variations

The initial and final weights of rats in each group were recorded and evaluated.

2.11 Histopathological analysis

Finally, after the experimentation, the rats were sacrificed, and the pancreas, kidney, and liver tissues were quickly removed and fixed in 10% neutral formalin. Afterward, the tissues were subjected to histopathological investigation via hematoxylin and eosin (H&E) staining. Photomicrographs of the samples subjected to histological examination were taken and analyzed. Two independent observers scored the histopathological changes on a scale of 1 to 4, corresponding to low, moderate, high, and severe pathological alterations, respectively.

2.12 Statistical analysis

Levene's test was performed to assess the homogeneity of variances. Data analysis was conducted by SPSS version 24 and is expressed as means ± SDs. Comparisons among groups were made using one-way ANOVA followed by Tukey's post hoc test. For comparisons between two groups, an independent t-test was applied. A p-value of <0.05 was considered statistically significant.

3. Result

3.1 Long-term effects of myrtle extract on FBG levels

The long-term effects of different concentrations of myrtle extract on FBG were investigated in the rats (Figure 1. A-B). No significant change was detected in FBG levels between the NC+MC600 group and the NC group. The results also showed that glucose levels were notably higher in diabetic rats than in normal rats on all investigated days ($P<0.001$). As shown in Figure 1. A, different concentrations of the extract decreased FBG in

diabetic rats (P<0.001). Moreover, FBG levels were markedly higher on the 21st day than on the initial day in diabetic rats (Figure 1. B). All the doses of the extract meaningfully reduced the FBG levels on the 21st day compared with those on the initial day (P<0.001). Additionally, statistical analysis of the data revealed that FBG decreased more effectively with increasing extract concentration. Moreover, no considerable difference was detected between the FBG levels of DM+MC600 rats and those of rats that received glibenclamide as the standard antihyperglycemic agent on day 21.

3.2 Effects of the *M. communis* L. fruit extract on blood glucose levels two hours after a meal

The results of blood glucose levels two hours after a meal are presented in Figure 1. C. Blood glucose levels were meaningfully lower in diabetic rats that received the extract at doses of 200, 400, and 600 mg/kg than in diabetic rats on all investigated days (P<0.001). Additionally, there was no difference in blood glucose level reduction between the group treated with 600 mg/kg extract and the acarbose-treated group (P>0.05).

3.3 Short-term effects of myrtle extract on FBG levels

The long-term effects of myrtle extract confirmed that the highest concentration of the extract (600 mg/kg) had the greatest antihyperglycemic effect. Therefore, the short-term effects of the highest concentration of the aqueous extract on the FBG level were measured at different time points after a single treatment with 600 mg/kg myrtle extract. The results indicated that glucose levels were significantly enhanced in diabetic rats compared to the control group at all measured time points (P<0.001) (Figure 1. D). Treatment with 600 mg/kg of the extract, as well as with glibenclamide, significantly reduced glucose amounts in diabetic rats (P<0.001). Furthermore, blood glucose levels were lower in the diabetic group treated with 600 mg/kg extract and glibenclamide at the 7th hour after treatment compared to the start of treatment (P<0.001) (Figure 1. E).

3.4 Effects of *M. communis* L. fruit extract on serum insulin

As shown in Figure 2. A, the fasting serum insulin levels in diabetic rats that received 200, 400, and 600 mg/kg myrtle extract were significantly greater than those in diabetic control rats (P<0.05, P<0.01, and P<0.05, respectively).

3.5 Effects of the *M. communis* L. fruit extract on the OGTT

OGTTs are methods that can help to diagnose instances of diabetes. As presented in Figure 2. B, blood glucose levels were markedly greater in diabetic rats than in normal rats (P<0.001). Compared to untreated diabetic rats, those treated with the extract, acarbose, or glibenclamide exhibited significantly lower glucose levels at all measured time points following oral glucose administration (P<0.001).

3.6 Effects of *M. communis* L. fruit extract on the lipid profile, AI, and CRI

In the diabetic group, serum TG levels, TC, and LDL-C, along with the AI and CRI, were significantly increased, while HDL-C levels were notably reduced compared to the normal control group (P<0.001) (Table 1). Treatment with 200, 400, or 600 mg/kg of the extract or with glibenclamide significantly lowered TC and TG levels in diabetic rats compared to untreated diabetic controls (P<0.01, P<0.001, and P<0.001, respectively). Serum LDL-C levels were significantly reduced in diabetic rats treated with 400 or 600 mg/kg of the extract or with glibenclamide compared to untreated diabetic rats (P<0.05 and P<0.01). However, no significant changes were observed in HDL-C levels between the extract-treated groups and the diabetic control group.

Furthermore, administration of 200, 400, and 600 mg/kg of the extract significantly decreased the AI and CRI in diabetic rats compared to normal control rats (P<0.05, P<0.01, and P<0.01, respectively). However, no meaningful differences were found in the lipid profiles between the NC+MC-600 group and the normal control group.

3.7 Effects of myrtle extract on serum biomarkers of hepatotoxicity and renotoxicity

As shown in Figure 3, ALT, AST, and ALP levels, which are biomarkers of liver toxicity, along with creatinine and urea levels, which are biomarkers of kidney toxicity, were markedly greater in the diabetic group than in the normal group at the end of the experiment (P<0.001). ALT, ALP, AST, creatinine, urea, and levels were significantly lower in *M. communis L.*-treated rats than in diabetic control rats (P<0.001). However, treatment with the extract in normal rats did not result in any essential variations in these parameters compared to the normal group.

3.8 Effects of *M. communis* L. fruit extract on body weight

As shown in Figure 4. A, the body weights of diabetic rats were significantly lower than those of normal rats at the end of the study (P<0.001). Treatment with the fruit extract, glibenclamide, or acarbose significantly improved body weight compared to the diabetic normal group (P<0.01, P<0.001, and P<0.001, respectively) (Figure 4. A). However, no significant change in body weight was observed between the NC+MC-600 group and the normal control group. The changes in initial and final body weights across the different groups are illustrated in Figure 4. B. By day 21, body weight in the diabetic control group was significantly decreased compared to day one (P<0.01). Treatment with myrtle extract (600 mg/kg) led to a significant improvement in body weight compared to the initial measurement (P<0.05).

3.9 Effects of *M. communis* L. fruit extract on histopathological parameters of pancreatic tissue

The results of the histopathological evaluation of the pancreatic tissue are presented in Figure 5. A. Compared

with those in the normal group, pancreatic islet degradation, islet cell necrosis, and cellular inflammation were improved in the diabetic group (P<0.01). The results also demonstrated that administering 600 mg/kg of the fruit extract decreased islet degradation compared to the diabetic group (P<0.05). Additionally, treatment with 400 mg/kg of the extract meaningfully decreased inflammation in diabetic rats (P<0.05). However, the extract had no meaningful effect on the extent of pancreatic tissue necrosis.

3.10 Effects of *M. communis* L. fruit extract on histopathological parameters of liver tissue

The role of the extract on liver histopathological parameters is illustrated in Figure 5. B. Cell swelling, lipid degeneration, hepatocyte necrosis, and inflammation were significantly greater in the diabetic control group than in the normal group (P<0.001). The findings showed that treatment with 200, 400, and 600 mg/kg of the extract significantly reduced hepatic cell swelling (P<0.05, P<0.001, and P<0.001, respectively). Also, lipid degeneration, hepatocyte necrosis, and inflammation were meaningfully alleviated in the extract-treated groups compared to the diabetic control group (P<0.001).

3.11 Effects of *M. communis* L. fruit extract on histopathological parameters of kidney tissue

As shown in Figure 5. C, urinary tract degeneration, urinary tract necrosis, hyaline casts, glomerular degeneration, and cellular inflammation were significantly greater in the diabetic control group than in the normal group (P<0.05). The results also demonstrated that the administration of 200, 400, and 600 mg/kg extract reduced urinary tract degeneration (P<0.05, P<0.01, and P<0.001, respectively). Moreover, urinary tract necrosis and glomerular degeneration in the diabetic groups were significantly decreased in the myrtle extract-treated groups (P<0.001). However, no significant decrease in cellular inflammation or hyaline casts was observed in the extract-treated groups compared to the diabetic group.

Table 1. The effects of the *M. communis* L. fruit extract on lipid profile.

	NC	NC+MC600	DM	DM+MC200	DM+MC400	DM+MC600	DM+Gli
TG (mg/dl)	70.83±11.34	69.33±9.05	177±17.23$^{###}$	110.8±15.64**	95.8±12.56***	81.67±9.18***	105.2±18.63***
TC (mg/dl)	75.17±8.93	76.5±5.54	130.6±7.52$^{###}$	97.6±10.31**	90±10.7**	82.67±10.07**	85.4±7.27**
LDL-C (mg/dl)	9.83±8.86	15.30±7.71	69.40±7.20$^{###}$	40.24±9.58	34.24±13.7*	23.16±14.13**	24.4±15.10*
HDL-C (mg/dl)	51.17±6.18	47.33±8.19	25.8±8.58$^{##}$	35.2±4.82	36.6±5.08	42.83±10.19	41.2±5.45
AI	0.48±0.22	0.65±0.23	4.52±1.77$^{###}$	1.8±0.35*	1.52±0.57**	1.02±0.53**	1.12±0.44**
CRI	1.48±0.22	1.65±0.23	5.52±1.77$^{###}$	2.8±0.35*	2.52±0.57**	2.02±0.53**	2.12±0.44**

The data are presented as the means±SDs. ## P<0.01, ### P<0.001 compared with the normal control group; * P<0.05, ** P<0.01, *** P<0.001 compared with the diabetic group.

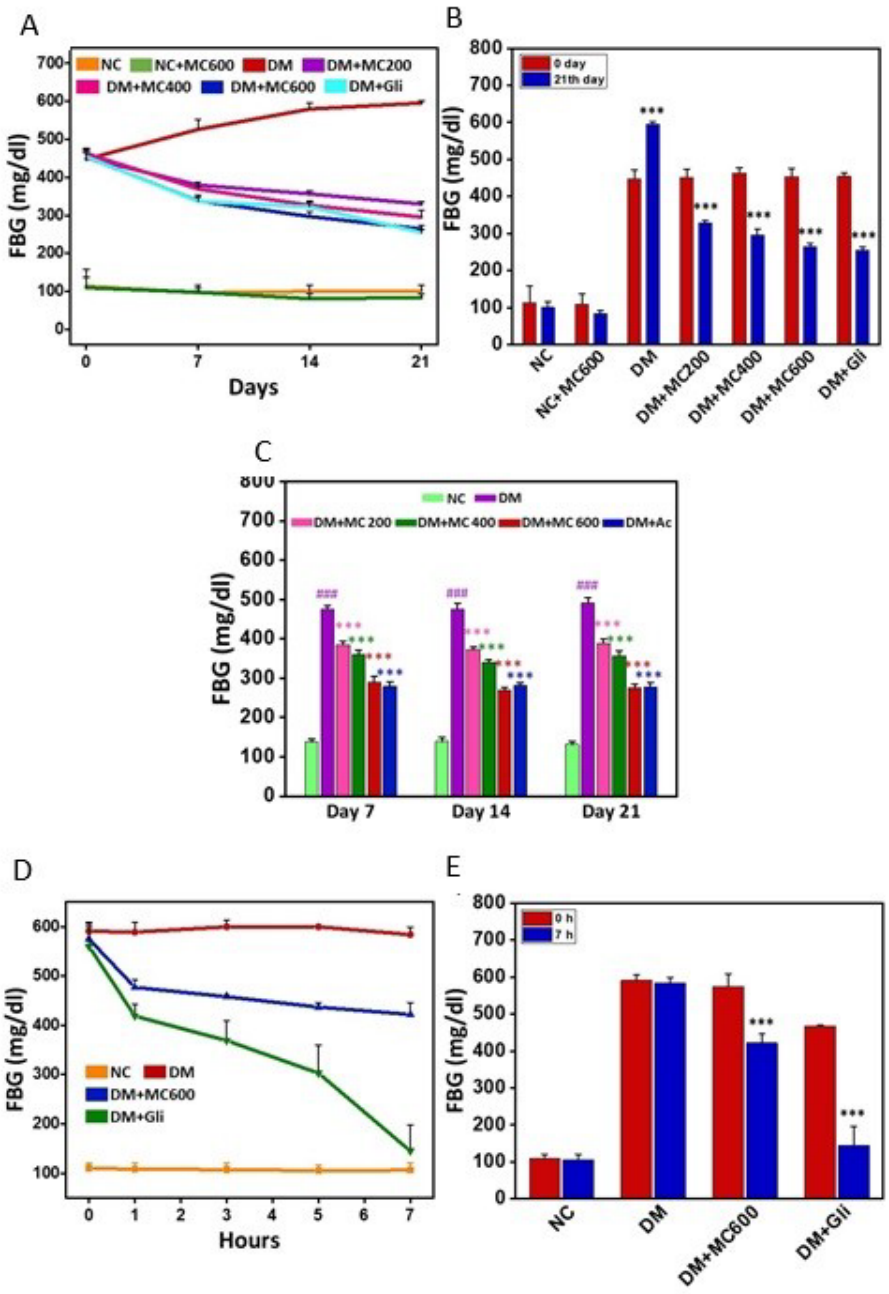


Figure 1. A) Long-term antihyperglycemic effects of the *M. communis* L. extract. The data are presented as the means±SDs. **B)** the *M. communis* L. extract antihyperglycemic effects at the beginning and end of the experiment. **C)** *M. communis* L. affects the extract on glucose levels two hours after a meal. **D)** Short-term, the *M. communis* L. extract has antihyperglycemic effects. The data are presented as the means±SD. **E)** Short-term myrtle extract antihyperglycemic effects at the start and end of the study. The data are presented as the means±SDs. ***P<0.001 compared with the initial day. NC: normal control; DM: diabetes mellitus; MC: *M. communis* L.; Gli: glibenclamide (**Prepared by Authors, 2025**).

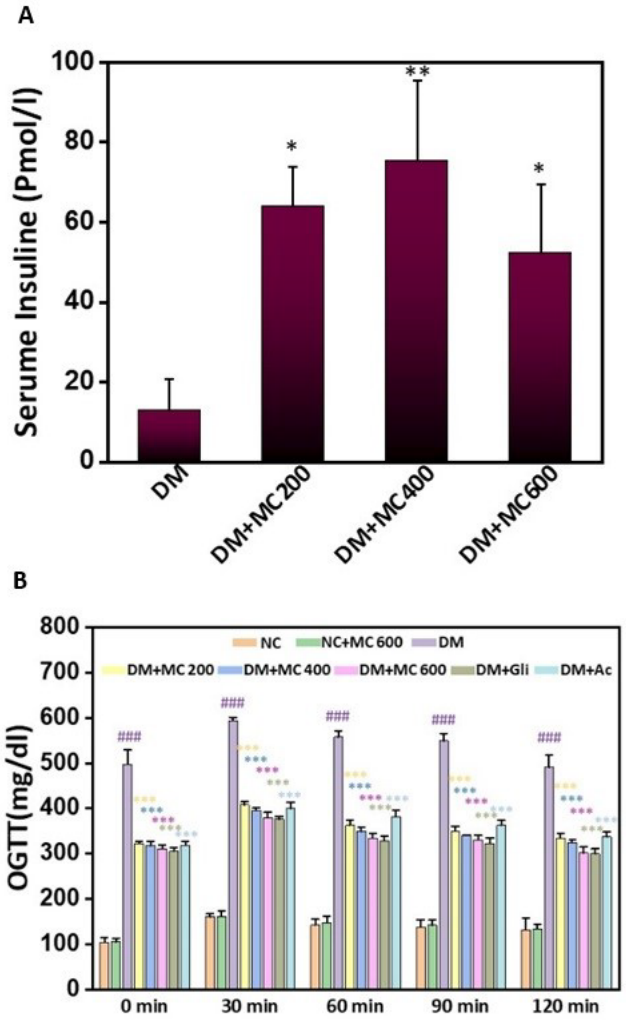


Figure 2. A) Effects of the *M. communis* L. extracts on the serum insulin level. **B)** Antihyperglycemic effects of the *M. communis* L. extract on the OGTT. The data are presented as the means±SDs. ### $P<0.001$ compared with the control group. *$P<0.05$, **$P<0.01$, ***$P<0.001$ compared with the diabetic group. NC: normal control; DM: diabetes mellitus; MC: *M. communis* L.; Gli: glibenclamide; Ac: acarbose (**Prepared by Authors, 2025**).

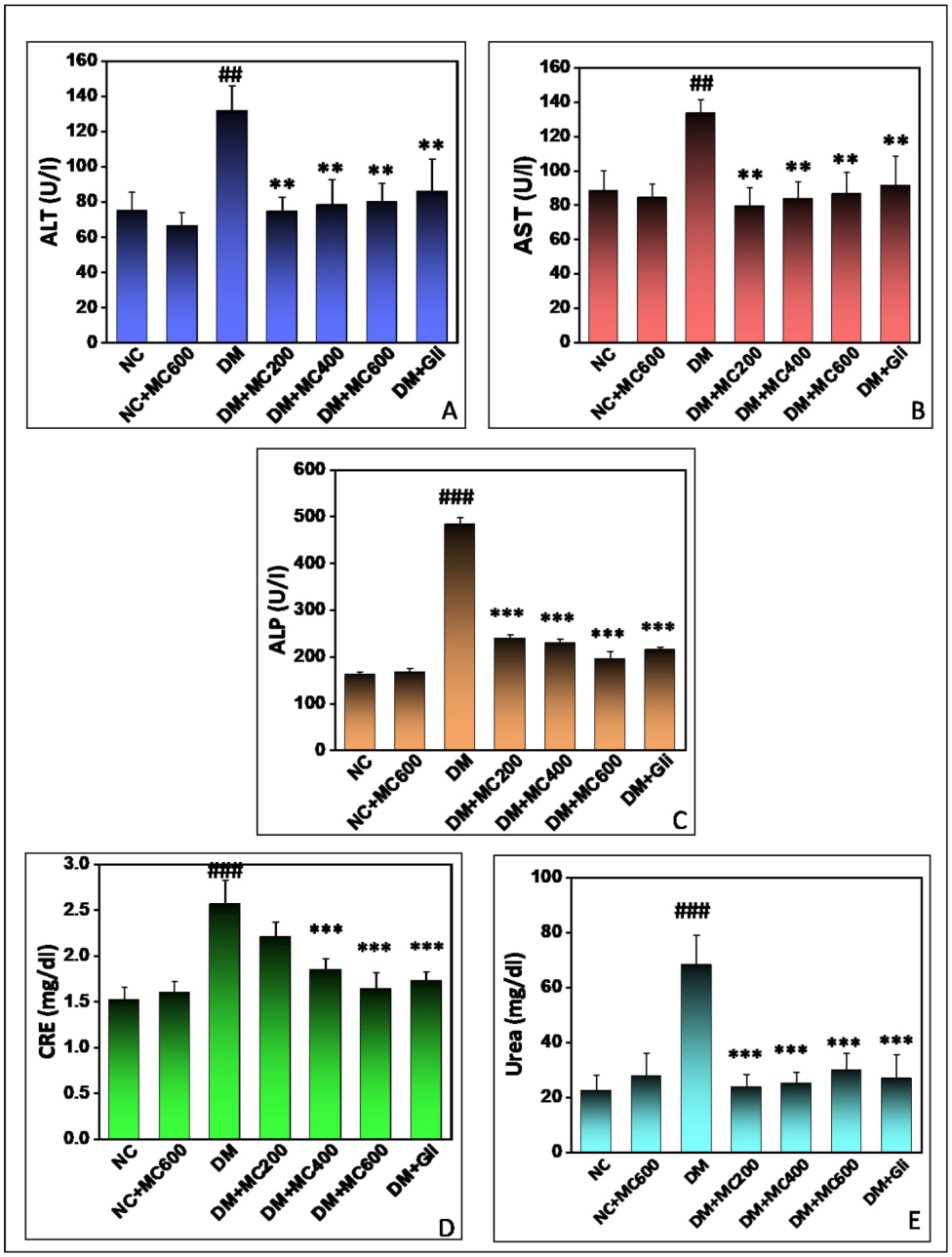


Figure 3. Effects of *M. communis L.* fruit extract on hepatotoxicity and renotoxicity biomarkers. The data are presented as the means±SDs. ###P<0.001 compared with the normal group, ** P<0.01, ***P<0.001 compared with the diabetic group. NC: normal control; DM: diabetes mellitus; MC: *M. communis* L.; Gli: glibenclamide (**Prepared by Authors, 2025**).

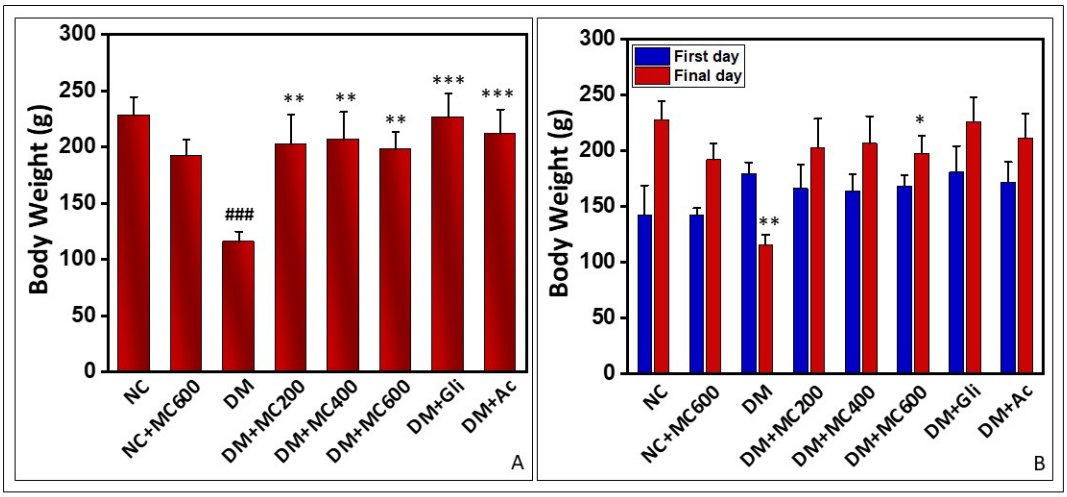
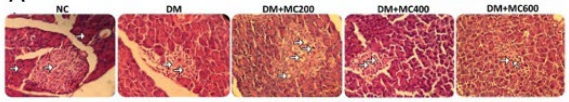


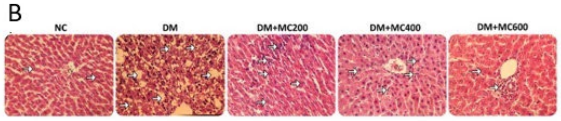
Figure 4. Effects of myrtle extract on body weight. **A)** Comparison between the end and start of the experiment. The data are shown as the means±SDs. **P*<0.05, ***P*<0.01 compared with the initial day. **B)** Comparison between groups at the end of the experiment. ### *P*<0.001 compared with the normal group. ***P*<0.01, ****P*<0.001 compared with the diabetic group. NC: normal control; DM: diabetes mellitus; MC: *M. communis* L.; Gli: glibenclamide; Ac: acarbose (**Prepared by Authors, 2025**).

A



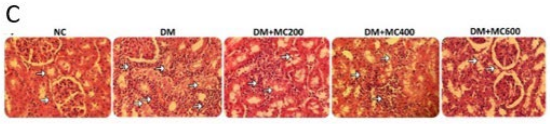
	NC	DM	DM+MC200	DM+MC400	DM+MC600
Islets degradation	0	2.83±0.41##	2.6±0.55	2.4±0.55	1.33±0.82*
Islet cell necrosis	0	1.83±0.41##	1.6±0.55	1±0	1.17±0.41
Cellular inflammation	0	1±0#	0.6±0.55	0*	0.33±0.52

B



	NC	DM	DM+MC200	DM+MC400	DM+MC600
Cell swelling	0	3.17±0.41###	2±0*	1.33±0.52**	1.17±0.41***
Lipid degeneration	0	3±0###	0***	0.33±0.52***	0***
Hepatocyte necrosis	0	1±0###	0***	0.33±0.52***	0***
Inflammation	0	2.8±0.45###	1.4±0.55**	1±0***	1±0***

C



	NC	DM	DM+MC200	DM+MC400	DM+MC600
Urinary tract degeneration	0	3±0###	1.8±0.45*	1.4±0.55**	0.83±0.41***
Urinary tract necrosis	0	0.83±0.41##	0**	0**	0**
Hyaline cast	0	1±0#	0.8±0.45	0.4±0.55	0.16±0.41
Glomerular degeneration	0	1±0###	0.4±0.55***	0.4±0.55***	0.33±0.52***
Cellular inflammation	0	1±0#	0	0.2±0.45	0

Figure 5. A) Effects of *M. communis L.* fruit extract on the pancreas histopathology of STZ-induced diabetic rats. Pancreatic histopathology. The normal pancreas histology of beta cells and islets was normal in the NC group. The DM group contained damaged islets. The treated groups show the recovery of islets. **B)** Effects of *M. communis L.* fruit extract on the liver histopathology of STZ-induced diabetic rats. **A)** Liver histopathology. The NC group presented normal liver histology with normal hepatocytes. Liver sections from the DM group showed periportal inflammation, cell swelling, and lipid degeneration. The treated groups presented normal hepatocyte morphology with mild periportal inflammation. **C)** Effect of *M. communis L.* fruit extract on the kidney histopathology of STZ-induced diabetic rats. Renal histopathology. The NC group presented normal kidney tissue morphology with a normal glomerulus. The DM group presented with tubular injury and periglomerular inflammation. The treated groups presented normal renal tissue morphology. The data are presented as the means±SDs. # *P*<0.05, ## *P* <0.01 compared with the normal control group. * *P* <0.05 compared with the diabetic group. NC: normal control; DM: diabetes mellitus; MC: *M. communis* L. (**Prepared by Authors, 2025**).

4. Discussions

Diabetes mellitus is a metabolic disorder characterized by insulin resistance and impaired function of pancreatic beta cells, which are unable to secrete adequate insulin in response to hyperglycemia or raised blood glucose levels. Hyperglycemia results from inadequate insulin secretion, function, or both and is accompanied by altered lipid metabolism (21). Since ancient times, medicinal plants have served as vital sources of therapeutic agents, and a significant number of modern medicines continue to be derived from herbal origins due to their effective therapeutic and preventive effects as well as their low toxicity (4).

This study explored the potential antidiabetic effects of aqueous extracts of *M. communis* L. fruit in a diabetic rat model from a mechanistic perspective. To identify the specific mechanisms underlying the fruit extract's antidiabetic effects, controls such as glibenclamide (which stimulates pancreatic beta cells to secrete insulin) and acarbose (which inhibits alpha-glucosidase) were used either individually or in combination. The results showed that myrtle fruit exhibited antihyperglycemic effects, demonstrated by a meaningful decrease in both short-term and long-term FBG levels, along with increased serum insulin levels in the extract-treated diabetic rats. Additionally, the fruit showed protective effects on the lipid profile, hepatotoxicity, nephropathy, and pancreatic histopathology-key complications associated with diabetes.

This study verified that the fruit extract lowered both short-term and long-term fasting blood glucose (FBG) levels in diabetic rats, with the magnitude of reduction comparable to that achieved by glibenclamide, a standard antihyperglycemic medication. Furthermore, the results confirmed that myrtle, along with acarbose, a standard alpha-glucosidase inhibitor, and reduced two-hour postprandial blood glucose levels in diabetic rats. Also, a lack of integrity in pancreatic beta cells and pancreatic cell inflammation in histopathological studies of the pancreas, in addition to a decline in serum insulin levels, were detected in diabetic rats. However, improvements in serum insulin levels are possibly due to pancreatic islet remodeling, including reduced islet degradation and cellular inflammation. In other words, myrtle can increase the level of insulin secretion by modifying the performance of the pancreas. So, it can be concluded that the antihyperglycemic properties of myrtle fruit are mediated through alpha-glucosidase inhibition and stimulation of pancreatic beta cells to secrete insulin (22). In accordance with our findings, the outcomes of a study by Tas et al (13) revealed that long-term treatment with a hydroalcoholic extract of *M. communis* L. fruit reduced FBG in diabetic rats. A study by Talebianpoor et al. also revealed a reduction in serum glucose in diabetic rats after long-term treatment with a hydroalcoholic extract of *M. communis* L. fruit. More, previous studies confirmed the antihyperglycemic effects of the hydroalcoholic extracts of *M. communis* L. leaves and myrtle oil in diabetes (8, 12).

M. communis L. extracts are valuable for human health because of their pharmacological activities. In terms of phytochemical composition, fruits are primarily composed of total polyphenols, flavonoids, anthocyanins, tannins, and organic acids, such as citric and malic acids, which may be the reasons for their antioxidant, hypolipidemic, antimicrobial, antireflux, anti-inflammatory, antiulcer, antidiarrheal, and antidiabetic activities (23, 24). Previous studies confirmed that the potency of polyphenols has an important role in diabetes management. They can modify carbohydrate metabolism, decrease blood glucose levels, and promote insulin resistance. Additionally, flavonoids exhibit potent antioxidant activity, which can be beneficial in managing this chronic disease. Antioxidants have many beneficial effects on reducing and preventing diabetes complications and can also improve glucose metabolism and glucose uptake in patients with diabetes mellitus (25). Thus, the antihyperglycemic activity of myrtle fruit, at least in part, may be mediated through its antioxidant activity.

Diabetes is accompanied by weight loss, and STZ is likely a contributing factor to the induction of diabetes in STZ-treated rats, which reduces body weight by increasing muscle wasting and reducing tissue protein levels. In the present study, myrtle treatment compensated for the weight loss in diabetic rats. This result may result from the inhibition of glycogenolysis and gluconeogenesis (26). Consistent with our results, the report by Tas et al (13) also demonstrated that the extract of *M. communis* L. fruit can counteract diabetes-related weight loss.

In this study, the usage of myrtle fruit extract improved the lipid profile in diabetic rats. Raised TG, TC, and LDL-C levels in individuals with diabetes mellitus are recognized as major risk factors for atherosclerotic heart and coronary artery disease, which are among the main complications linked to diabetes (27). Our findings confirmed that the fruit extract reduced levels of AI and CRI, both of which are reliable indicators of atherosclerosis risk and coronary heart disease in diabetic patients. Earlier reports have also demonstrated the antihyperlipidemic effects of myrtle fruit extract and essential oils from *M. communis* L. in diabetic rats (28). Moreover, another study confirmed the hypolipidemic and antithrombotic effevts of the aqueous extracts of *M. communis* L. fruit in cholesterol-fed rabbits (29). The improvement of the lipid profile by myrtle fruit could be attributed to its flavonoid content, anthocyanins, and polyphenols. Flavonoids possess hypolipidemic and hypocholesterolemic properties and can have a role in the treatment of hyperlipidemia, atherosclerosis, and cardiovascular diseases (30). Additionally, polyphenols may play an essential role in lipid metabolism, thereby improving dyslipidemia (20). In addition, several studies have shown that anthocyanin-containing extracts can lower serum cholesterol and triglyceride levels and raise HDL levels (31).

This study showed that *M. communis* L. fruit extract therapy decreased serum levels of ALT, AST, and ALP, biomarkers of hepatotoxicity. In addition, myrtle fruit improved hepatic histopathology and significantly decreased reduced the rates of hepatic cell swelling, lipid degeneration, hepatocyte necrosis, and inflammation in the extract-treated rats. Kumar and colleagues considered the protective effects of an aqueous extract from *M. communis* L. leaves against liver damage caused by paracetamol overdose in albino rats. These authors suggested that the effect may be due to the leaves' antioxidative and free radical-scavenging properties (32). More recently, another study reported the hepatoprotective effect of the essential oil from *M. communis* L. flowers against CCL_4-induced acute hepatotoxicity in rats, and current research also suggests that this effect may be due to a reduction in oxidative stress by preventing free radicals (33). Importantly, the liver is a significant organ vulnerable to oxidative stress, with parenchymal cells as the primary targets of oxidative damage (34). Therefore, it seems that myrtle fruit has a hepatoprotective effect because of its antioxidant activity.

Finally, our findings demonstrated that myrtle fruit diminished renal serum biomarkers, including urea and creatinine, which are essential indices for evaluating the glomerular filtration rate (23). Furthermore, histopathological changes in the kidney, including urinary tract degeneration, urinary tract necrosis, hyaline casts, glomerular degeneration, and cellular inflammation, were attenuated by myrtle fruit in diabetic rats. The renoprotective activity of *M. communis* L. fruit is likely due to its inhibitory effects on oxidative stress.

One limitation of this research is that it was performed exclusively on STZ-induced diabetic rats. Additional research is essential to validate the effectiveness and safety of myrtle fruit extract in human clinical trials or in other animal models representing various forms of diabetes.

5. Conclusion

Our study revealed that aqueous fruit extract of *M. communis* L. has antihyperglycemic activity and can increase serum insulin levels. It can also attenuate the lipid profile, hepatotoxicity, and renotoxicity. Therefore, this valuable fruit can be suggested as an appropriate treatment option for managing diabetes and its prevalent complications. The antidiabetic function of myrtle fruit could be partly mediated by alpha-glucosidase inhibition and regeneration of pancreatic beta cells.

6. Declarations

6.1 Acknowledgments

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6.2 Ethical Considerations

All procedures were conducted in accordance with ethical guidelines approved by the Animal Experimentation Committee of Zanjan University of Medical Sciences, Zanjan, Iran (Approval number: ZUMS.REC.1394.36).

6.3 Authors' Contributions

SA contributed to the design and execution of experimental studies, data acquisition, and manuscript writing. FAR and MM participated in conducting the experimental studies and data collection. MK and MRE conceived the main idea, developed the theoretical framework, and contributed to the experimental work. SA and SM supervised the study planning, processed and analyzed the experimental data, drafted the manuscript, and designed the figures. MN was responsible for the overall conceptualization, study design, project supervision, and interpretation of data. All authors reviewed and approved the final manuscript.

6.4 Conflict of Interest

The authors declare no conflict of interest.

6.5 Fund or Financial Support

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6.6 Using Artificial Intelligence Tools (AI Tools)

The authors were not utilized AI Tools.

References

1. Khodaie S-A, Razavi R, Nikkhah H, Namiranian N, Kamalinejad M. Topical Remedy for Diabetic Neuropathy in Persian Medicine and Modern Phytotherapy: A Narrative Review. J Adv Med Biomed Res. 2025;33(158):172-8. [DOI:10.30699/jambr.33.158.172]

2. Heidari H, Kamalinejad M, Noubarani M, Rahmati M, Jafarian I, Adiban H, et al. Protective mechanisms of Cucumis sativus in diabetes-related modelsof oxidative stress and carbonyl stress. Bioimpacts. 2016;6(1):33-9. [DOI:10.15171/bi.2016.05] [PMID] [PMCID]

3. Chong K, Chang JK, Chuang LM. Recent advances in the treatment of type 2 diabetes mellitus using new drug therapies. Kaohsiung J Med Sci. 2024;40(3):212-20. [DOI:10.1002/kjm2.12800] [PMID] [PMCID]
4. Shayesteh R, Kamalinejad M, Adiban H, Kardan A, Keyhanfar F, Eskandari MR. Cytoprotective Effects of Pumpkin (Cucurbita Moschata) Fruit Extract against Oxidative Stress and Carbonyl Stress. Drug Res (Stuttg). 2017;67(10):576-82. [PMID] [DOI:10.1055/s-0043-110484]
5. Panjeshahin MR, Azadbakht M, Akbari N. Antidiabetic activity of different extracts of Myrtus communis in streptozotocin induced diabetic rats. Rom J Diabetes Nutr Metab Dis. 2016;23(2):183-90. [DOI:10.1515/rjdnmd-2016-0022]
6. Kesari AN, Kesari S, Singh SK, Gupta RK, Watal G. Studies on the glycemic and lipidemic effect of Murraya koenigii in experimental animals. J Ethnopharmacol. 2007;112(2):305-11. [DOI:10.1016/j.jep.2007.03.023] [PMID]
7. Aleksic V, Knezevic P. Antimicrobial and antioxidative activity of extracts and essential oils of Myrtus communis L. Microbiol Res. 2014;169(4):240-54. [DOI:10.1016/j.micres.2013.10.003] [PMID]
8. Elfellah MS, Akhter MH, Khan MT. Anti-hyperglycaemic effect of an extract of Myrtus communis in streptozotocin-induced diabetes in mice. J Ethnopharmacol. 1984;11(3):275-81. [DOI:10.1016/0378-8741(84)90073-4][PMID]
9. Djenane D, Yangüela J, Amrouche T, Boubrit S, Boussad N, Roncalés P. Chemical composition and antimicrobial effects of essential oils of Eucalyptus globulus, Myrtus communis and Satureja hortensis against Escherichia coli O157:H7 and Staphylococcus aureus in minced beef. Food Sci Technol Int. 2011;17(6):505-15. [DOI:10.1177/1082013211398803] [PMID]
10. Hosseinzadeh H, Khoshdel M, Ghorbani M. Antinociceptive, anti-inflammatory effects and acute toxicity of aqueous and ethanolic extracts of Myrtus communis L. Aerial parts in mice. J Acupunct Meridian Stud. 2011;4(4):242-7. [DOI:10.1016/j.jams.2011.09.015] [PMID]
11. Alipour G, Dashti S, Hosseinzadeh H. Review of pharmacological effects of Myrtus communis L. and its active constituents. Phytother Res. 2014;28(8):1125-36. [DOI:10.1002/ptr.5122] [PMID]
12. Sepici A, Gürbüz I, Cevik C, Yesilada E. Hypoglycaemic effects of myrtle oil in normal and alloxan-diabetic rabbits. J Ethnopharmacol. 2004;93(2-3):311-8. [DOI:10.1016/j.jep.2004.03.049] [PMID]
13. Tas S, Tas B, Bassalat N, Jaradat N. In-vivo, hypoglycemic, hypolipidemic and oxidative stress inhibitory activities of Myrtus communis L. fruits hydroalcoholic extract in normoglycemic and streptozotocin-induced diabetic rats. Biomed Res. 2018;29(13):2727-34. [DOI:10.4066/biomedicalresearch.29-18-708]
14. Talebianpoor MS, Talebianpoor MS, Mansourian M, Vafaiee-Nejad T. Antidiabetic activity of hydroalcoholic extract of Myrtus communis (Myrtle) fruits in streptozotocin-induced and dexamethasone-induced diabetic rats. Pharmacogn Res. 2019;11(2):115-20. [DOI:10.4103/pr.pr_160_18]
15. Colvin DM. A review on comparison of the extraction methods used in licorice root: Their principle, strength and limitation. Med Aromat Plants. 2018;7(6):323. [DOI:10.4172/2167-0412.1000323]
16. Amereh Z, Hatami N, Shirazi FH, Gholami S, Hosseini SH, Noubarani M, et al. Cancer chemoprevention by oleaster (Elaeagnus angustifoli L.) fruit extract in a model of hepatocellular carcinoma induced by diethylnitrosamine in rats. EXCLI J. 2017; 16:1046-56.
17. Gholami S, Hosseini MJ, Jafari L, Omidvar F, Kamalinejad M, Mashayekhi V, et al. Mitochondria as a Target for the Cardioprotective Effects of Cydonia oblonga Mill. and Ficus carica L. in Doxorubicin-Induced Cardiotoxicity. Drug Res (Stuttg). 2017;67(6):358-65. [DOI:10.1055/s-0043-101824] [PMID]
18. Mousavi M, Abedimanesh N, Mohammadnejad K, Sharini E, Nikkhah M, Eskandari MR, et al. Betanin alleviates oxidative stress through the Nrf2 signaling pathway in the liver of STZ-induced diabetic rats. Mol Biol Rep. 2022; 49(10):9345-54. [PMID] [DOI:10.1007/s11033-022-07781-8]
19. Kurylo K, Budniak L, Volska A, Zablotskyy B, Klishch I. Influence of Phytocompositions on Dynamics of Changes in Basal Glycemia and Glycemia In Oral Glucose Tolerance Test In Rats With Streptozotocin-Nicotinamide-Induced Diabetes Mellitus Type 2. Georgian Med News. 2020(300):112-6.
20. Yu Z, Xu H, Yu X, Sui D, Lin G. Hypolipidemic effects of total flavonoide extracted from the leaves of Actinidiakolomikta in rats fed a high-fat diet. Iran J Basic Med Sci. 2017;20(10):1141-8.

21. Consultation WHO. Definition, diagnosis and classification of diabetes mellitus and its complications. 1999.

22. Patel DK, Prasad SK, Kumar R, Hemalatha S. An overview on antidiabetic medicinal plants having insulin mimetic property. Asian Pac J Trop Biomed. 2012;2(4):320-30. [PMID] [DOI:10.1016/S2221-1691(12)60032-X]

23. Bouaoudia-Madi N, Boulekbache-Makhlouf L, Kadri N, Dahmoune F, Remini H, Dairi S, et al. Phytochemical analysis of Myrtus communis plant: Conventional versus microwave assisted-extraction procedures. J Complement Integr Med. 2017;14(4):20160098. [DOI:10.1515/jcim-2016-0098] [PMID]

24. Giampieri F, Cianciosi D, Forbes-Hernández TY. Myrtle (Myrtus communis L.) berries, seeds, leaves, and essential oils: New undiscovered sources of natural compounds with promising health benefits. Food Frontiers. 2020;1(3):276-95. [DOI:10.1002/fft2.37]

25. Sarian MN, Ahmed QU, Mat So'ad SZ, Alhassan AM, Murugesu S, Perumal V, et al. Antioxidant and Antidiabetic Effects of Flavonoids: A Structure-Activity Relationship Based Study. Biomed Res Int. 2017;2017: 8386065. [DOI:10.1155/2017/8386065] [PMID] [PMCID]

26. Sepici-Dincel A, Açikgöz S, Cevik C, Sengelen M, Yeşilada E. Effects of in vivo antioxidant enzyme activities of myrtle oil in normoglycaemic and alloxan diabetic rabbits. J Ethnopharmacol. 2007;110(3):498-503. [DOI:10.1016/j.jep.2006.10.015] [PMID]

27. Mirmohammadlu M, Hosseini SH, Kamalinejad M, Esmaeili Gavgani M, Noubarani M, Eskandari MR. Hypolipidemic, Hepatoprotective and Renoprotective Effects of Cydonia Oblonga Mill. Fruit in Streptozotocin-Induced Diabetic Rats. Iran J Pharm Res. 2015; 14(4):1207-14.

28. Karimlar S, Naderi A, Mohammadi F, Moslehishad M, Delrish E, Aghajanpour L, et al. Hypoglycemic and Hypolipidemic Effects of Myrtus communis, Trachyspermum copticum and Ferula gummosa Essential Oils on Streptozotocin Induced Diabetic Rats. Nutr Food Sci Res. 2019;6(1):1-8. [DOI:10.29252/nfsr.6.1.1]

29. Khan RA, Feroz Z, Jamil M, Ahmed M. Hypolipidemic and antithrombotic evaluation of Myrtus communis L. in cholesterol-fed rabbits. Afr J Pharm Pharmacol. 2014;8(8): 235-9. [DOI:10.5897/AJPP2013.3488]

30. Salvamani S, Gunasekaran B, Shaharuddin NA, Ahmad SA, Shukor MY. Antiartherosclerotic effects of plant flavonoids. Biomed Res Int. 2014;2014:480258. [PMID] [PMCID] [DOI:10.1155/2014/480258]

31. Murase T, Nagasawa A, Suzuki J, Hase T, Tokimitsu I. Beneficial effects of tea catechins on diet-induced obesity: stimulation of lipid catabolism in the liver. Int J Obes Relat Metab Disord. 2002;26(11):1459-64. [DOI:10.1038/sj.ijo.0802141] [PMID]

32. Kumar MR, Phaneendra P, Bodhanapu S, Rahiman OMF, Niyas KM, Tamizmani T. Antioxidant and hepatoprotective activity of the aqueous extract of Myrtus communis (Myrtle) Linn. leaves. Pharmacologyonline. 2011;1(1): 1083-90.

33. Hsouna AB, Dhibi S, Dhifi W, Mnif W, Hfaiedh N. Chemical composition and hepatoprotective effect of essential oil from Myrtus communis L. flowers against CCL 4-induced acute hepatotoxicity in rats. RSC Adv. 2019;9(7):3777-87. [PMID] [PMCID] [DOI:10.1039/C8RA08204A]

34. Namdar F, Bahrami F, Bahari Z, Ghanbari B, Elahi SA, Mohammadi MT. Evaluation of the Effects of Fullerene C60 Nanoparticles on Oxidative Stress Parameters at Liver and Brain of Normal Rats. J Adv Med Biomed Res. 2019; 27(124):8-15. [DOI:10.30699/jambs.27.124.8]

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