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Research Article
Physiological and Biochemical Changes in Diabetic Rats Treated with Combined Extracts of *Artemisia herba-alba* and *Anabasis syriaca*

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Abstract

Background and Objective: Diabetes is a global health problem that affects various organs such as the liver, heart and kidney. Patients with diabetes mellitus (DM) who are unsatisfied with conventional therapy are more likely to utilize herbal medicine to improve the effectiveness of the conventional medication. Some herbal extracts such as *Artemisia herba alba* and *Anabasis syriaca* are more likely to prevent DM's consequences. Therefore, the present research was designed to examine the impact of a combined extract of *Artemisia herba alba* and *Anabasis syriaca* on blood glucose (BG) levels and lipid profile as well as kidney and liver functions in streptozotocin-induced diabetic rats. **Materials and Methods:** *Artemisia herba alba* and *Anabasis syriaca* leaves separately were collected and air-dried for 4 weeks at room temperature (23-27°C). A stock solution was prepared of 100 mg of dry ethanol extracts and dissolved in 10 mL ethanol. The 36 Wistar albino rats were randomly assigned into six groups (N = 6): Control group, Streptozotocin, (STZ-diabetic group), *Artemisia herba alba* with STZ (extract1 group), *Anabasis syriaca* with STZ (extract 2 groups), extract 1 and extract 2 (group) and metformin group. The experiment was applied for 28 days. **Results:** Significant blood glucose levels reduction was observed when administrated with combined extracts (161.03±19.6 mg dL^{-1}, $p<0.05$) compared with the STZ group with a mean value of 460.9±121.9 mg dL^{-1}. Significantly increased the level of HDL (67.06±38.8 mg dL^{-1}) compared with the diabetic group (34.33±1.07 mg dL^{-1}) when administrated E1 extract in diabetic rats combined extract decreased serum triglycerides level. Various plants extracts have not shown a significant effect on other study parameters cholesterol, LDL, AST and kidney function tests. **Conclusion:** The present study showed that the combined effect of *Artemisia herba alba* and *Anabasis syriaca* extracts has shown a potential antidiabetic and hypolipidemic impact in streptozotocin-induced diabetic rats.

Key words: Type 1 diabetes, *Artemisia herba alba*, *Anabasis syriaca*, glucose, LDL

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Diabetes Mellitus is a chronic condition that has become more common in recent years as a result of the two popular phenomena, ageing and changing lifestyles, which of them encouraged obesity[1]. The international diabetes federation (IDF) predicted that the number of individuals with diabetes aged 18-99 years around the world would increase up to 693 M by 2045, based on the available current global statistical studies[1,2]. According to the World Health Organization (WHO), this serious pathology has become a priority health problem in the twenty-first century[3]. Its rising prevalence is expected to have a greater social and economic impact due to disease-related complications[4]. Nonetheless, when risk factors are addressed and early diagnosis and treatment are provided, long-term problems can be avoided[5].

Traditional medicines (TMs) encompass a wide array of ancient and modern approaches in addition to disease prevention and treatment methods[6]. Spiritual healing, herbal medicines (HMs) and other techniques such as bone-setting are common examples of traditional medicines[3]. Traditional medicines have been adopted to treat age-related chronic disorders including diabetes mellitus (DM) and hypertension, for which there is no modern treatment or just palliative care are available[7]. Herbal medicines have been widely used, either alone or in combination with conventional treatments, in particular in low-resource settings. Due to its natural components and perceived lower side effects or discontent with traditional treatments, their usage in patients with chronic diseases like DM is very common[8,9]. Diabetes mellitus is one of the most serious global health crises of the twenty-first century. In 2015, 14.2 M people in Africa were expected to have diabetes, this number is expected to rise to 34.2 M by 2040[10]. According to the available literature, patients with DM who were unsatisfied with conventional therapy were more likely to utilize HM to improve the effectiveness of conventional medication[2]. Herbal medicines are typically complex combinations of multiple active ingredients that enhance the potential for interactions[11]. In China, for instance, patients with diabetes who use antidiabetic herbal medicines are expected to experience side effects such as hypoglycemia and lactic acidosis[12]. Such negative effects could affect any system and people of all ages and severity levels[11].

Artemisia, the white wormwood, is found over the world, mostly in Northern Africa and Western Asia[13]. Artemisia has been shown to produce a variety of phenolic metabolites that have attracted a lot of attention due to their antioxidant, antibacterial, antidiabetic, neuroprotective, anti-inflammatory and cytotoxic effects[14].

Anabasis species have been found in steppes and deserts worldwide, primarily in the Irano-Turanian and Saharo-Arabian regions[15]. There are four species in this group: *A. articulate*, *A. setifera*, *A. oropediorum* and *A. syriaca*[16]. *A. articulata* and *A. Setifera* are found throughout Egypt's deserts, demonstrating adaptation to a variety of habitats, including halic and xeric environments. In the meanwhile, the occurrence of *A. oropediorum* is quite rare. Accordingly, the present study aimed to examine the ethanol leave extracts of *Artemisia herba alba, Anabasis syriaca* and their combination on blood glucose (BG) levels and lipid profile as well as liver and kidney functions in streptozotocin-induced diabetic rats.

MATERIALS AND METHODS

Study area: Collection of leaves of the plant *Artemisia herba alba* and *Anabasis syriaca* from AL Mafraq/Jordan was done during the summer of 2020 and dried entirely. The Al-Al Bayt University herbarium received voucher specimens of the plants collected.

Plant extract preparation: *Artemisia herba alba* and *Anabasis syriaca* leaves were collected and air-dried for 4 weeks at room temperature (23-27°C). An electrical blender was used to pulverize dried plant materials. Approximately 600 g of each dried powdered plant material was extracted separately in 6 L of 70% ethanol (solvent to sample ratio of (10:1 v/w) solvent to dry weight ratio at 40°C water bath with shaking at 60 RPM for 48 hrs. After that, the extraction was filtered using Whitman No.1 filter sheets. The filtrates were concentrated (solvents evaporated) in a rotary evaporator at 40°C and then allowed to dry entirely. *Artemisia herba alba* extract was assigned as No.1 (E_1) while *Anabasis syriaca* extract as No. 2 (E_2).

Experimental study design

Animals: Thirty-six Wistar Albino rats weighing between 280 and 300 g. The rats were given water ad libitum and a standard diet. The animals were housed in metabolic cages in the laboratory unit of the animal house (Yarmouk University-Faculty of science). The rats were adapted to conditions (10-12 hrs light and dark cycles, 20-22°C) for ten days a week before the start of the experiment. All procedures were performed following international regulations for the care and use of laboratory animals.

The experiment continued for twenty-eight (28) consecutive days after induction of diabetes mellitus (DM) by streptozotocin (STZ). All extracts (E_1 and E_2) doses were orally administered via an intragastric tube at 1 mL/rat equivalent to a dose of 300 mg kg^{-1}. At the end of the treatment, rats were fasted overnight and sacrificed by cervical dislocation.

Thirty-six rats were assigned into six groups (6 animals per group) as the following:

- **Control:** Non-diabetic rats, received 1 mL of citrate buffer (twice a day)
- **STZ Group:** Streptozotocin-induced diabetic rats via intraperitoneal one dose (60 mg kg^{-1})
- **Met group:** Streptozotocin-induced diabetic rats via single intraperitoneal dose (60 mg kg^{-1})+standard drug metformin (400 mg/kg/day twice a day)
- **E_1 group:** Diabetic rats were orally received *Artemisia herba alba* extract (300 mg kg^{-1} twice a day)
- **E_2 group:** Diabetic rats were orally received *Anabasis syriaca* extract (300 mg kg^{-1} twice a day)
- **E_1+E_2 group:** Diabetic rats were orally received *Anabasis syriaca* (300 mg kg^{-1} twice a day)+*Artemisia herba alba* (300 mg kg^{-1} twice a day) extracts

Induction of diabetes mellitus: The STZ was dissolved in citrate buffer (0.01 M, pH 4) via i.p., injection of 60 mg kg^{-1} using insulin syringes. STZ induced DM in the rats (STZ-DM) was confirmed after 72 hrs of STZ injection. Gluco-Check device XL [TD-4277, Augsburg, Germany] was used for the measurement of blood droplet glucose twice with each test-strip lot from the animal's tail. Rats with serum glucose levels above 220 mg dL^{-1} were considered diabetic and used in experiments. Diabetic animals were defined as those with a blood sugar level of higher[17] than 200 mg dL^{-1} and used in experiments. Treatments with extracts were started on day 3 after STZ-injection.

Blood collection and preparation: Three days after STZ injection, before the treatment day, 0.2 mL blood samples from each animal were collected into heparinized tubes by puncturing the retro-orbital plexus. At the end of the experiments (28 days): After scarification, blood samples (2-3 mL per animal) were drained into heparinized tubes before being transferred to plain centrifuge tubes. They were then centrifuged at 4000 g for 10 min within 1 hr of collection to separate the sera from the clot.

Biochemical analysis: Serum samples were assayed before the start and at the end of the experiment for fasting blood glucose (FBG), creatinine (Cr), urea (U), potassium (K^+), bilirubin (BR) using specific liquid-colour based kits. Lipid profile parameters, liver function alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured using reagent Kits (BioSystems, Spain).

Statistical analysis: The statistical analysis was performed using a Statistical Package for the Social Sciences (SPSS), version 19.0 for Windows (Chicago, IL, USA). Paired T-test was conducted to determine any significant differences in each trial group before and after injection of the supplements. Differences were considered significant at $p<0.05$.

RESULTS

Baseline mean differences in the biochemical parameters between control and STZ-induced diabetic rats (reference) (after 4 weeks): Table 1 shows the glucose level in the control group was 139.4±14.8 mg dL^{-1} and this level was significantly increased ($p = 0.039$) in the STZ group (460.9±121 mg dL^{-1}). Compared with the control group, the STZ group showed also a significantly higher mean potassium level ($p = 0.006$). In contrast, the STZ group observed a significant ($p = 0.011$) decrease in the mean HDL levels (34.33±1.07 mg dL^{-1}) when compared with the control group (42.93±3.16 mg dL^{-1}). The AST levels in the diabetic group significantly ($p = 0.068$) decreased compared with the control group.

Effects of the plant extract on FBG levels in STZ-induced diabetic rats: Administrated ethanolic extracts (*Artemisia herba alba* and *Anabasis syriaca*) showed significant blood glucose reducing effect (215.73±14.8 and 207.03±15.1 mg dL^{-1}, respectively) similar to the metformin effect (242.16±6.9 mg dL^{-1}) comparing with STZ group with mean value 460.9±121.9 mg dL^{-1} as shown in Table 2. A significant mean blood glucose levels difference was observed in the combined extracts (E_1+E_2) study group (161.03±19.6 mg dL^{-1}, $p<0.05$) compared with the diabetic group.

Effects of the plant extract on lipid profiles levels in STZ-induced diabetic rats: Table 3 shows the levels of cholesterol were insignificantly affected when administrated *Artemisia* extract in diabetic rats with a value of 55.6±32.2 mg dL^{-1} comparing with the STZ group

Table 1: Baseline mean differences in the biochemical parameters between control and STZ-induced diabetic rats (reference) (after 4 weeks)

	Groups			
	Control	STZ		
Parameters	Mean±SD	Mean±SD	Mean difference	*p-value
FBG (mg dL^{-1})	139.40±14.8	460.90±121.9	321.50	0.039
Chol (mg dL^{-1})	68.76 ±10.29	62.73±8.3	6.03	0.474
TG (mg dL^{-1})	88.00±24.13	67.76±2.9	20.24	0.283
HDL (mg dL^{-1})	42.93±3.16	34.33±1.07	8.60	0.011
LDL (mg dL^{-1})	20.00±8.25	15.40±3.90	4.60	0.432
Urea (mg dL^{-1})	8.47±2.92	7.69±262	0.78	0.749
Creatinine (mg dL^{-1})	0.61±0.27	0.64±0.26	0.03	0.909
Potassium (mg dL^{-1})	8.27±0.22	9.08±0.14	0.81	0.006
AST (mg dL^{-1})	575.30±4.2	346.80±159.7	228.50	0.068
ALT (mg dL^{-1})	104.80±13.1	133.50±14.3	28.70	0.063
Bilirubin (mg dL^{-1})	0.353±0.24	0.270±0.14	0.083	0.640

SD: Standard deviation, *p = 0.05, STZ: STZ induced diabetic rats, E_1: STZ-induced diabetic rats treated with *Artemisia herba alba* extract (300 mg kg^{-1} twice a day), E_2: STZ-induced diabetic rats treated with *Anabasis syriaca* extract (300 mg kg^{-1} twice a day), E_1+E_2: Diabetic rats were treated with *Anabasis syriaca* (of 300 mg kg^{-1} twice a day)+*Artemisia herba alba* (300 mg kg^{-1} twice a day) extracts, Met: Diabetic rats+a standard drug metformin (400 mg/kg/day twice a day), ALT: Alanine aminotransferase, FBG: Fasting blood glucose, TG: Triglycerides, HDL: High-density lipoprotein LDL: Low-density lipoprotein, AST: Alanine aminotransferase aspartate transaminase

Table 2: Mean differences in FBG (mg dL^{-1}) between STZ-induced diabetic rats (reference) and different treated study groups (after 4 weeks)

Reference group	Mean±SD	Experimental group	Mean±SD	Mean difference	*p-value
STZ	460.9±121.9	E_1	215.73±14.8	245.2	0.026
		E_2	207.03±15.1	253.9	0.023
		E_1+E_2	161.03±19.6	299.9	0.048
		Met	242.16±6.9	218.8	0.036

SD: Standard deviation, *p = 0.05, STZ: Streptozotocin-induced diabetic rats, E_1: STZ-induced diabetic rats treated with *Artemisia herba alba* extract (300 mg kg^{-1} twice a day), E_2: Streptozotocin-induced diabetic rats treated with *Anabasis syriaca* extract (300 mg kg^{-1} twice a day), E_1+E_2: Diabetic rats were treated with *Anabasis syriaca* (300 mg kg^{-1} twice a day)+*Artemisia herba alba* (300 mg kg^{-1} twice a day) extracts, Met: Diabetic rats+a standard drug metformin (400 mg kg^{-1} day^{-1} twice a day)

Table 3: Mean differences in lipid profile parameters between STZ-induced diabetic rats (reference) and different treated study groups (after 4 weeks)

Parameters	Reference group	Mean±SD	Experimental group	Mean±SD	Mean difference	*p-value
Chol	STZ	62.73±8.3	E_1	55.6±32.2	7.13	0.457
			E_2	62.7±8.30	0.03	0.131
			E_1+E_2	59.0±7.40	3.73	0.593
			Met	30.8±26.7	31.93	0.145
TG		67.76±2.9	E_1	64.06±25.3	3.70	0.814
			E_2	70.56±8.30	2.80	0.611
			E_1+E_2	46.66±7.01	21.10	0.009
			Met	69.00±36.4	1.24	0.659
HDL		34.33±1.07	E_1	67.06±38.8	32.73	0.218
			E_2	40.63±1.72	6.30	0.006
			E_1+E_2	30.06±0.85	4.27	0.007
			Met	27.6±14.6	6.73	0.512
LDL		15.4±3.9	E_1	14.03±7.48	1.37	0.793
			E_2	19.70±6.01	4.30	0.201
			E_1+E_2	16.40±9.40	1.00	0.873
			Met	10.23±5.45	5.17	0.253

SD: Standard deviation, *p = 0.05, STZ: STZ induced diabetic rats, E_1: STZ -induced diabetic rats treated with *Artemisia herba alba* extract (300 mg kg^{-1} twice a day), E_2: STZ -induced diabetic rats treated with *Anabasis syriaca* extract (300 mg kg^{-1} twice a day), E_1+E_2: Diabetic rats were treated with *Anabasis syriaca* (300 mg kg^{-1} twice a day) + *Artemisia herba alba* (300 mg kg^{-1} twice a day) extracts, Met: Diabetic rats+a standard drug metformin (400 mg/kg/day twice a day)

62.73±8.3 mg dL^{-1} ($p>0.05$). The combination of two extracts has shown a potential synergistic effect on triglycerides (46.66±7.01 mg dL^{-1}) where their mean levels significantly reduced groups ($p<0.05$) compared with the diabetic group (67.76±2.9 mg dL^{-1}). Administration of *Artemisia herb alba* extract in diabetic rats revealed a significantly increased level of HDL (67.06±38.8 mg dL^{-1}) compared with the diabetic group (34.33±1.07 mg dL^{-1}) p = 0.218. No significant differences in the mean levels of LDL when they were compared with the reference group (STZ).

Table 4: Mean differences in kidney function testes (U, Cr and potassium) between STZ-induced diabetic rats (reference) and different treated study groups (after 4 weeks)

Parameter	Reference group	Mean ± SD	Experimental Group	Mean ± SD	Mean Difference	*p-value
Urea	STZ	7.69±262	E_1	7.05±1.86	0.64	0.748
			E_2	7.92±2.75	0.23	0.924
			E_1+E_2	6.77±1.91	0.92	0.362
			Met	7.89±2.87	0.2	0.933
Creatinine		0.64±0.26	E_1	0.63±0.19	0.01	0.960
			E_2	0.63±0.18	0.01	0.569
			E_1+E_2	0.62±0.21	0.02	0.610
			Met	0.65±0.10	0.01	0.967
Potassium		9.08±0.14	E_1	7.38±0.20	1.7	< 0.001
			E_2	7.91±0.10	1.17	< 0.001
			E_1+E_2	7.90±0.11	1.18	< 0.001
			Met	7.66±0.14	1.42	< 0.001

SD: Standard deviation, *p = 0.05, STZ: STZ induced diabetic rats, E_1: STZ-induced diabetic rats treated with *Artemisia herba alba* extract (300 mg kg^{-1} twice a day), E_2: STZ -induced diabetic rats treated with *Anabasis syriaca* extract (300 mg kg^{-1} twice a day), E_1+E_2: Diabetic rats were treated with *Anabasis syriaca* (of 300 mg kg^{-1} twice a day)+*Artemisia herba alba* (300 mg kg^{-1} twice a day) extracts, Met: Diabetic rats+a standard drug metformin (400 mg/kg/day twice a day)

Table 5: Mean differences in liver function tests (AST, ALT, and TBIL) between STZ-induced diabetic rats (reference) and different treated study groups

Parameter	Reference group	Mean±SD	Experimental group	Mean±SD	Mean Difference	*p-value
AST	STZ	346.8±159.7	E_1	334.3±33.5	12.5	0.901
			E_2	401.1±18.13	54.3	0.590
			E_1+E_2	312.2±28.7	34.6	0.731
			Met	268.8±244.4	78	0.668
ALT		133.5±14.3	E_1	101.7±6.11	31.8	0.024
			E_2	113.2±5.05	20.3	0.081
			E_1+E_2	81.26±0.96	52.3	0.003
			Met	89.13±10.1	44.37	0.012
TBIL		0.270±0.14	E_1	0.243±0.91	0.027	0.554
			E_2	0.201±0.13	0.069	0.652
			E_1+E_2	0.233±0.10	0.037	0.552
			Met	0.196±0.05	0.074	0.111

SD: Standard deviation, *p = 0.05, STZ: STZ induced diabetic rats, E_1: STZ -induced diabetic rats treated with *Artemisia herba alba* extract (300 mg kg^{-1} twice a day), E_2: STZ -induced diabetic rats treated with *Anabasis syriaca* extract (300 mg kg^{-1} twice a day), E_1+E_2: Diabetic rats were treated with *Anabasis syriaca* (of 300 mg kg^{-1} twice a day)+*Artemisia herba alba* (300 mg kg^{-1} twice a day) extracts, Met: Diabetic rats+a standard drug metformin (400 mg/kg/day twice a day)

Effects of plant extracts on kidney function tests in STZ-induced diabetic rats: Table 4 revealed that, treatment of the diabetic rat group with *Anabasis syriaca* extract insignificant changes in serum creatinine levels 0.63±0.18 mg dL^{-1} compared to the diabetic control group 0.64±0.26 mg dL^{-1}, also little changes of urea level when the administration of the combined extract (Artemisia *herba alba* and *Anabasis syriaca*) in diabetic rats with mean value 6.77±1.91 mg dL^{-1} comparing with streptozotocin-induced diabetic rats 7.69±262 mg dL^{-1}. Administration of various plant extracts in diabetic rats decreases blood potassium levels with a mean value of 7.38±0.20 mg dL^{-1} compared with streptozotocin-induced diabetic rats at 9.08±0.14 mg dL^{-1}.

Effect of plant extracts on liver function tests in STZ-induced diabetic rats: Treatment with E_1 significantly decreased the level of ALT (101.7±6.11 mg mL^{-1}, p = 0.024). A similar result was observed in the combined extract which decrease the level of ALT with a mean value of 81.26±0.96 mg mL^{-1} compared with the diabetic group 133.5±14.3 mg mL^{-1} (p = 0.003). Treatment with metformin also significantly decreased the level of ALT (p = 0.012). No significant changes in the level of AST or Bilirubin in all treated study groups (p>0.05 in all groups) when compared with the reference group (STZ) as shown in Table 5.

DISCUSSION

The present study results showed that the diabetic model using STZ was successfully able to induce diabetes compared with the control group (p = 0.039). The STZ has been used in many studies to induce diabetes by cytotoxic effects in pancreatic cells[18-23]. These results showed that the ethanolic extracts of *Artemisia herba alba, Anabasis syriaca* and their combination significantly lowered blood glucose in STZ diabetic rats. The treatment with

Artemisia herba alba extract (Extract 1) significantly lowered the level of glucose (215.73±14.80 mg dL^{-1}, p = 0.026). Similar findings were reported by Abdallah *et al.*[14], who was reported *Artemisia herba alba* administration at different a concentration results in normalization of blood glucose and homocysteine levels as well as increased plasma insulin levels as compared with streptozotocin-induced diabetic rats.

The use of *Anabasis syriaca* (extract 2) significantly lowered the levels of glucose (207.033±15.05 mg dL^{-1}, p = 0.023). Unfortunately, the antihyperglycemic effect of *Anabasis syriaca* is not clinically proven while, there are a few previous types of research exploring the effect of another relevant species on diabetic animal models, *Anabasis articulata*[24].

Hamza *et al.*[23] reported that the extract of *Anabasis articulata* can decrease blood sugar levels in diabetic patients and diabetic mice. In this context, the results of the present study were similar to some recent studies that showed the anti-hyperglycemic effect of *Anabasis articulata* species. The extract of *Anabasis articulata* at a dose of 400 mg kg^{-1} significantly decreases plasma glucose in alloxan-induced diabetic animal[24]. At the end of the experiment, Kambouche *et al.*[24] found that Saponin was the active ingredient of the *Anabasis articulata* extract and with a close effect on glibenclamide. In the current research, when compared to the effect of the anti-hyperglycemic drug Metformin at a dose of 400 mg kg^{-1}, the hypoglycemic effect of *Anabasis articulate* extract in streptozotocin-induced diabetic rats was consistent with that reported by Kambouche *et al.*[24].

The comparative or combined hypoglycemic effect of metformin is widely used in laboratory animal model[25]. The hypoglycemic effect revealed in the present study might be consoled to an insulin-like effect of saponins[23] or Inhibitory effects of phenolic compounds on α-amylase and α-glucosidase[26].

The use of both extract1 and extract 2 significantly lowered the level of glucose (161.03±19.60 mg dL^{-1}, p = 0.048). The idea of using multitherapeutic options against diabetes has been indicated by several studies, including insulin, Metformin and possibly others[27,28]. The use of Metformin significantly lowered glucose level (242.17±6.90 mg dL^{-1}, p = 0.036). Metformin can alter the composition of the gut microbiota[28] and stimulate mucosal AMP-activated protein-kinase (AMPK), which helps preserve the intestinal barrier's integrity. Metformin appears to lower lipopolysaccharide (LPS) concentrations in blood circulation and the hepatic according to these mechanisms, in combination with the stimulation of AMPK in liver cells[29].

The results of cholesterol levels did not show any significant variations in all groups (p>0.05 for all groups). This implied that type 1 diabetes is induced by injury to the pancreas and not due to cholesterol involvement. Furthermore, other studies reported similar findings and such findings could be linked to high cholesterol and sterol absorption in general and low cholesterol production in comparison to type 2 diabetes[30]. Triglycerides tend to insignificantly decrease in all groups (p>0.05), except in the combined group, in which a significant reduction of triglycerides level was obtained (46.66±7.011 mg dL^{-1}, p = 00.009) this can be due to glucose control[31].

The levels of HDL significantly decreased in diabetic group (p = 0.011). Treatment options using *Artemisia herba alba* extract significantly increased the level of HDL (p = 0.006). It was found that the use of both extracts 1 and 2 significantly decreased the level of HDL (30.0667±0.85, p = 0.07). These findings may suggest that multitherapeutic effects using herbs could have side effects[32].

No significant variations were observed for LDL in all study groups. This may reflect the consumption of cholesterol involved in LDL[30]. In a most recent study, a significant decrease in the level of triglycerides and low-density lipoprotein, a significant increase in blood glucose with mixed data concerned with high-density lipoprotein, was observed in non-diabetic rats treated with *Anabasis syriaca*[15]. Inconsistent results were observed in the present study and Kloub[32] study due to the different animal models, experimental design, as well as different doses of plant extract that used in the two studies. However, it has been shown that *Anabasis syriaca*, the extract contains potential antioxidants[33,34].

The results showed that neither urea nor creatinine was significantly affected by the induced diabetes or the other treatments (p>0.05 in all groups). These findings were in agreement with different studies, such as the study of Amartey *et al.*[35], which found little changes in urea and creatinine levels in diabetic groups compared with the control group. Potassium levels were statistically varied in all study groups. Diabetic induction significantly increased the level of potassium (p = 0.006). Changes in potassium levels were associated with diabetic control. As far as diabetes is controlled, potassium levels are more likely to be within the normal range[36].

The levels of AST were not statistically varied in all groups ($p>0.05$ in all groups). This can be explained by considering that type 1 diabetes in this study does not involve severe liver injury. Usually, liver injury is more involved in type 2 diabetes[37]. The levels of ALT increased insignificantly in the diabetic group ($p = 0.063$). Treatment with extract1 and combined extract significantly decreased the level of ALT ($p = 0.024$ and $p = 0.003$, respectively). Metformin also significantly decreased the level of ALT ($p = 0.012$). It seems that liver injury in diabetic type 1 is more likely to exhibit improvement by various treatment options in this study. Furthermore, this may reflect good glycemic control[38]. The levels of Bilirubin were not significantly statistically varied in all study groups ($p>0.05$ in all groups). These findings were understood through good control of glycemic status[39].

CONCLUSION

The present study showed that type 1 diabetes-induced in rats using STZ was successful. The use of multiple therapeutic options was proved successful in reducing glucose, triglycerides and ALT levels as well as increasing HDL concentrations in blood circulation. Various plants extracts have not shown a significant effect on other study parameters cholesterol, LDL and kidney function tests. The extracts appeared to be safe because no side effects were reported and all tests were unaffected during and after treatment with extracts. Nonetheless, future research is required to determine the nature of the active substance(s) of extracts that are involved in lowering increased blood sugar levels and assessing the therapeutic significance of this finding.

SIGNIFICANCE STATEMENT

Herbal medicines (HMs) have been widely used, either alone or in combination with conventional treatments. The HMs are of great importance, especially in low-resource settings. They generally have lower side effects or are discontent with traditional treatments. However, the increased use of HMs is associated with mixed impacts (positive and negative). Some diabetic patients who were taking herbal antihyperglycemic medicines have reported side effects such as hypoglycemia and lactic acidosis. This study provides the vision to understand the impact of some herbal extracts, including *Artemisia herba alba, Anabasis syriaca* on glucose levels, lipid profile and liver and kidney function tests of diabetic rats.

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