ISSN (Print 0974-2115) (Online 2349-8552)
www.jchps.com Journal of Chemical and Pharmaceutical Sciences

Hypolipidemic and Antioxidant Effect of Essential Oil of *Varthemia iphionoides* in Streptozotocin-induced Diabetic Rats

Ahmed Saber Abu-zaiton
Department of Biology, Al-albayt University, Jordan
***Corresponding author: E-Mail: abuzaiton@aabu.edu.jo, Mobile: 00962 776095004**

ABSTRACT

Hypolipidemic and antioxidant effect of *Varthemia iphionoides* essential oil at dose of 200 mg/kg of body weight was investigated for two weeks in streptozotocin-induced diabetic experimental rats.

21 albino rats weighing 190-200g were randomlly divided into three groups of seven rats: group A as acontrol, group B diabetic rats and group C diabetic treated with essential oil of *V.iphionoides*. Cholesterol, triglycerides, blood glucose levels and antioxidant enzymes superoxide dismutase (SOD) and malondialdehyde (MDA) levels were evaluated. The administration of essential oil extract of V. iphionoides significantly reduced blood glucose and total cholesterol level in diabetic rats compared to the control group, while there is no significant change in the triglycerides level. The activities of the enzyme superoxide dismutase (SOD) were increased and decrease the level of malondialdehyde (MDA)

It can be concluded that the essential oil of *V.iphionoides* has significant normalization of blood glucose range and exhibit good effect in lowering cholesterol levels. Taking together, decreasing in MDA and increasing in SOD levels clearly shows the antioxidant property of *Varthemia iphionoides*

KEY WORDS: Antioxidant enzymes, Streptozotocin, *Varthemia iphionoides*, Hypolipidemic effect.

1. INTRODUCTION

Diabetes Mellitus can be defined as chronic uncontrolled hyperglycemia. If untreated, the disease will result in multiple organ defects, which include brain, heart and renal system. The main causes of diabetes mellitus are either an inadequacy of insulin secretion or insulin sensitivity. Most cases of diabetes mellitus are classified to either type I, a complete defect of insulin secretion, or type II, both tissue insensitivity to insulin and defect in insulin secretion. (Sangameswaran and Lango, 2010).

In the meantime, diabetes mellitus management is directed toward the control of hyperglycemia, but with more studies showing the correlation between the disease and its vascular complications, the new treatment vision is directed towards the management of the disease complications (Aslan, 2007). It has been documented that the disease can increase the incidence of coronary artery disease by ten folds and increase in the mortality rate by three to four folds with 75% of the patients eventually dying from vascular disease (Basha, 2012).

The metabolic changes of the disease such as hyperlipidemia and hypertriglyceridemia influence vascular endothelial destruction through multiple molecules, multiple evidence attach the destructive effects caused by these metabolic changes to the increase in the oxidative stress(Calles-Escandon and Cipolla, 2001) .With all the efforts to find a better and a new generation of treatment, comes the role of antioxidant substances. The term Antioxidants describe any substance that, when present in low concentration, can delay or inhibit the oxidation of another oxidizable substrate (Halliwell and Gutteridge, 1995; Anusha and Anish, 2012).

Recent research is studying the use of non-vitamin antioxidants such as flavonoids in reducing the negative impact of oxidative stress that results from diabetes mellitus. Throughout history, Flavonoids and other plant-based treatments have been used in the management of different diseases. Large part of these plants pharmacological advantages could be attached to their antioxidant properties (Ramachandran, 2011).

A huge effort in the medical field has been placed to serve the ongoing challenge of management diabetes mellitus without any side effect. In the last few years, the interest in plants as a source of antidiabetic and antioxidants molecules that helps protecting against the negative effect caused by reactive oxygen species (Ranjbar, 2011).
However, little research has been done to study the effectiveness of *Varthemia iphionoides*, this study focusing on the effect of essential oil of *V. iphionoides* on hyperlipidemia and antioxidants enzymes level in streptozotocin-diabetic rats.

2. MATERIALS AND METHODS

Plant collection and Essential Oil extraction: The aerial parts of *Varthemia iphionoides* was collected from the Almafraq city at the north of Jordan and identified by a taxonomist, prof. Sawsan Aloran, Professor of Botany at Department of Biology, University of Jordan.

The essential oil were extracted by steam distillation of fresh areal part of *Varthemia iphionoides* Aerial parts were passed to steam distillation for 4.0 h using modified Clevenger-type apparatus and yielded essential oils range from 0.3 – 0.6 % (v/w) of *Varthemia iphionoids*. The collected essential oils were dried by anhydrous sodium sulfate after separation by separator funnel then keep in refrigerator for further process. The color may vary from a pale to deep yellow depending on the collection time.

Induction of experimental diabetes: Diabetic rats were made by intraperitoneal injection of prepared solution of streptozotocin at dose of 55 mg/kg body weight (Sigma–Aldrich Chemical, Steinheim, Germany). Glucose concentration was checked up many times to confirm hyperglycemia. After 1 week, sugar level more than 220 mg/dL were selected as diabetic rats then processed for the following experiment. Diabetic rats were emphasized by elevation of blood glucose, frequency urination and weight loss. To prevent the hypoglycemia in the diabetic rats, which formed after one day of streptozotocin induction, a solution of 5% glucose was administered to the diabetic rats (Hamed and Malek, 2007).

Experimental design: The rats were randomly distributed into 3 groups, consisting of seven rats each:

Group I: normal control rats.

Group II: diabetic control rats.

Group III: diabetic rats treated with essential oil at dose 200 mg/kg

At the end of experiment and treatment with essential oil of *V.iphionoides*, the rats were sacrificed and blood sample was collected in fresh vials containing heparin, then centrifuged at 3000 rpm for 20 minutes, then analyzed for glucose, cholesterol, triglycerides and antioxidant enzymes level.

Biochemical assay: Blood glucose level was estimated Spectrophotometric by glucose oxidase method using commercially available diagnostic kits (Trinder, 1969). During the experiment period, sugar level measured by electronic glucometer Accu Check (Bayers Diagnostic Pvt. Ltd., Germany).

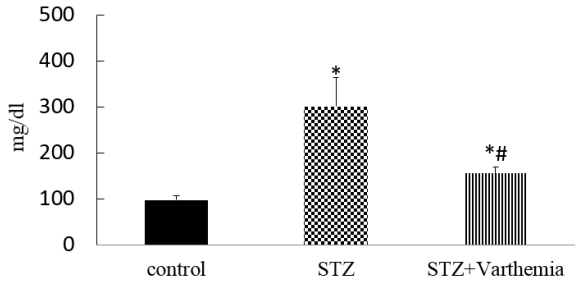
Serum cholesterol and triglyceride were measured spectrophotometrically using an enzymatic colorimetric BioMed assay kits and Ecoline diagnostic kit (Folch, 1959).

The serum levels of MDA and SOD were determined with a spectrophotometer according to the manufacturer's recommendations of comercial colorimetric assay kits. (Su, 2006).

Statistical analysis: All values of experimental results were given as Mean±SEM for 6 rats in each group. Statistical analysis was carried out using one-way ANOVA followed by Tukey's multiple-comparison test (TMRT). The minimum level of significance was considered at $p < 0.05$.

3. RESULTS

Serum glucose: The essential oil of *V.iphionoides* significantly decreased the blood glucose level in the STZ-diabetic rats compared to the control group. Administration of essential oil of *V.iphionoides* decreased the blood glucose level from 300.87±14 in diabetic group to 155.34±11, ($p < 0.05$) as represented in figuer.1.



Figuer 1. Effect of essential oil of *V.iphinoides* on blood glucose level in normal and STZ- diabetic rats

* compared to control ($P < 0.05$), # compared to diabetic control ($P < 0.05$)

Serum lipid: At the end of experiment the total cholesterol levels were increased significantly ($p<0.05$) in groups of streptozotocin-diabetic rats, when compared with normal rats. However, treatment of diabetic groups with essential oil of *V.iphionoides* significantly reduced serum cholesterol ($p<0.05$). There is no significant effect of *V.iphionoides* on triglyceride levels in the diabetic rats compared with normal control group. Table.1.

Table 1. Effect of essential oil of *V.iphionoides* on cholesterol and triglyceride levels in normal and STZ-diabetic rats

	Cholesterol	Triglycerides
Control	1.84±0.33	1.13±0.73
STZ	2.36±0.15*	0.88±0.02
STZ+Varthemia	1.99±0.27	1.12±0.15

**= compared to control (P < 0.05)*

Antioxidant enzymes levels: Regarding to hepatic biochemical values of SOD and MDA in experimental rats tissues. Streptozotocin-induced diabetes leads to increasing of MDA level and decreased SOD activity ($p<0.05$). However, administration of essential oil of *V.iphionoides* for 28 days marked lowered MDA content (figure.2) compared to diabetic groups. Meanwhile, there was no significant effect of *V.iphionoides* on the activity of SOD. Figure.3.

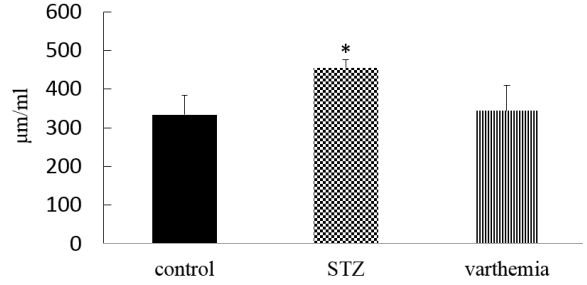


Figure.2. Serum MDA level in control and STZ-diabetic rats treated with essential oil of *V.iphionoides*

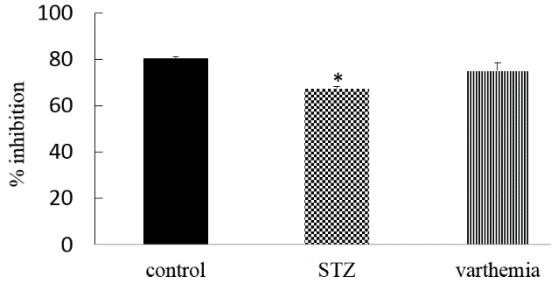


Figure3. Serum SOD level in control and STZ-diabetic rats treated with essential oil of *V.iphionoides*

DISCUSSION

Streptozotocin is anti- microbial agent that causes cytotoxicity to β-Langerhans cells of pancreas, and it is a suitable model for diabetes in experimental animals by producing nitric oxide and free radicals causing β-pancreatic cells damage resulting in elevated blood sugar levels, lipid peroxidation, and decreased plasma insulin concentration (Goud, 2015; Chinedum, 2013).

Blood glucose level of streptozotocin-induced diabetic rats administrated with essential oil of *V.iphionoides* showed significant decrease compared to the streptozotocin-diabetic control rats. Our results support the previous studies reported on (Afifi, 1997). The Mechanism behind the hypoglycemic effect of essential oil extract of *V.iphionoides* thought to be due to increase in the effect of insulin on carbohydrate metabolism, in streptozotocin-diabetic rats, specifically by increasing the sensitivity of adipose tissue to insulin, suggested that it activates the tyrosine phosphorylation that leads insulin to bind to the cell receptors and prevents enzymes that block this process which result in greater effect of insulin (Hegab, 2018).

In the current study, high plasma level of cholesterol was noticed in the STZ-diabetic rats and hypercholesterolemia has been documented in STZ-diabetic animals by Ramachandran (2011). The cause of hyperlipidemia in streptozotocin-diabetic rats is the increasing of mobilization of free fatty acids from the adipose tissue as a result of the decrease in insulin uptake and metabolism (Sriplang, 2007). Significant decrease of cholesterol level following administration of essential oil of *V.iphionoides* in diabetic rats compared with normal control group rats suggests that the *V.iphionoides* extract effect is due to activation of insulin secretion. The hypolipidemic effects of V.iphionoides administration seen in streptozotocin-diabetic rats also, may be suggested by reduced food consumption and inhibit digestion and absorption of the nutrients in the gastrointestinal tract (Elberry, 2018). Our results revealed that there is no significant effect of *V.iphionoides* extracts on triglycerides level.

Lipid peroxidation caused by reactive oxygen species which is generated by hyperglycemia results in reactive molecules. A 28 day-treatment with *V.iphinoides* extract was noticed to reduce plasma malondialdehyde (MDA) levels, indicating a protective effect of *V.iphinoides*. This effect thought to be caused by the presence of phytochemicals such as lavonoids. Other studies showed the presence of high levels of phytochemicals in natural plants extracts that have a potential in reducing oxidative stress. (Kandasamy, 2006).

4. CONCLUSION

The essential oil of *V.iphinoides* showed significant antihyperlipidemic activity and antioxidant effect in streptozotocin diabetic rats. Taking together, the present study hypotheses that the *V.iphinoides* possesses antidiabetic potential .Further investigations are required to know the exact mechanism.

5. KNOWLEDGMENTS

This work is performed during sabbatical leave 2017-2018 provided by Al-albayt University to Dr.Ahmed abu-zaiton, which was spent at University of Jordan. Amman, Jordan.

7. REFERENCES

Afifi F, Munib S,Madi J, Al-Eisawi A, Effect of *Varthemia iphionoides* on blood glucose level of normal rats and rats with streptozocin-induced diabetes mellitus, Current Therapeutic Research, 58, 1997, 888-892.

Anusha B, Anish K. Antihyperglycemic, antioxidant and hypolipidemic effect of Punica granatum L flower extract in streptozotocin induced diabetic rats, Asian Pacific Journal of Tropical Biomedicine, 2012, 1764- 1769.

Aslan M, Orhan DD, Orhan N, Sezik E, Yesilada E, *In vivo* antidiabetic and antioxidant potential of Helichrysum plicatum ssp, plicatum capitulums in streptozotocin-induced-diabetic rats, Journal of Ethnopharmacology, 109, 2007, 54-59.

Basha S, Samuel C, Triggle R and Ding H, Endothelial Dysfunction in Diabetes Mellitus, Possible Involvement of Endoplasmic Reticulum Stress, Journal of Diabetes Research, 2012.

Calles-Escandon and Cipolla M, Diabetes and endothelial dysfunction: a clinical perspective, Endocr. Rev, 22, 2001, 36-52.

Chinedum O, Eleazu K, Chinedum E, Sonia C, Udeme N, Review of the mechanism of cell death resulting from streptozotocin challenge in experimental animals, its practical use and potential risk to humans. J Diabetes Metab Disord, 12, 2013, 60.

Elberry AA, Harraz FM, Ghareib SA, Gabr SA, Nagy AA, Abdel-Sattar E, Methanolic extract of M arrubium vulgare ameliorates hyperglycemia and dyslipidemia in streptozotoci-induced diabetic rats, Int J Diabetes mellitus, 3, 2011.

Folch J, Lees M, Stanley GHS, A simple method for the isolation and purification of total lipids from animal tissues, J Biol Chem, 226, 1957, 497-509.

Goud B.J, Dwarakanath V, Chikka B, swamy Streptozotocin – a diabetogenic agent in animal models, Ijppr Human, 3, 2015, 253-269.

Halliwell B and Gutteridge J, The definition and measurement of antioxidants in biological systems, Free Radic. Biol. Med., 18, 1995, 125-126.

Hamed H.A. Malek A, Effect of telmisartan in experimentally induced diabetetes mellitus in rats, Int J Health Sci, 1, 2007, 2

Hegab I, Ameliorative effect of apelin on streptozotocin-induced diabetes and its associated cardiac hypertrophy, Alexandria Journal of Medicine, 54, 2018, 119-127.

Kandasamy M, Veerendra Y, Deepak Kumar D, a Pinaki S, Bhim C, Antidiabetic, Antioxidant and Antihyperlipidemic Status of Heliotropium zeylanicum extract on Streptozotocin-Induced Diabetes in Rats. Biol. Pharm. Bull, 29 (11), 2006, 2202-2205.

Ramachandran V, Mandal D, Payyavala U, angai P, Muthureddy N, Shanish A and Kannan Elango, Hypoglycemic, antioxidant and hypolipidemic activity of Asparagus racemosus on streptozotocin-induced diabetic in rats, Advances in Applied Science Research, 2 (3), 2011, 179-185.

Ranjbar SH, Larijani B, Abdollahi M. Recent update on animal and human evidences of promising anti-diabetic medicinal plants: A mini-review of targeting new drugs. Asian J Animal and Veterinary Advances, 6, 2011, 1270-1275.

Sangameswaran B, and Lango K, Evaluation Anti-hyperglycemic and antihyperlipidic activities of Andrographis Lineata Nees on Streptozotocin induced diabetic Rats, Jordan J. Biological Sci, 3, 2010, 83-36.

Sriplang K, disakwattana S, Rungsipipat A, Yibchok-anun S, Effect of Orthosiphon stamineus aqueous extract on plasma glucose concentration and lipid profile in normal and streptozotocin-induced diabetic rats, J Ethnopharmacol, 109, 2007, 510-514.

Su I, Hui C, Li M Hung, and Jan-Kan C, Resveratrol, a red wine antioxidant, possesses an insulin-like effect in streptozotocin-induced diabetic rats, Am J Physiol Endocrinol Metab, 290, 2006, 1339-1346.

Trinder A, Determination of Glucose in Blood Using Glucose Ox.pdf., 1969, 90.