Sudan Journal of Science and Technology
Journal homepage:
http://jst.sustech.edu/

Antidiabetic Activity of *Origanum Majorana* L in Glucose Fed Normal Rats and Alloxan-Induced Diabetic Rats

Iman A.A.Mohamoud[1], Idris.F.O[2], Shama.I.Y.Adam[3]

*Department of Biochemistry and Molecular Biology, Faculty of Science and Technology, AL-Neelain University, Sudan

ARTICLE INFO

ARTICLE HISTORY
Received: 31/7/2020
Accepted: 20/10/2020
Available online: December 2020

KEYWORDS:
Origanium majorana, Medicinal plants, Diabetes mellitus, alloxan, Hypoglycemic, Antidiabetic

ABSTRACT

Glycemic management medications have become increasingly complex and controversial. Plant-based traditional medicine has been proven worldwide as alternative treatment for diabetes.To evaluate the antidiabetic efficiency of *Origanum majorana* L extracts in normal and diabetic rats.Diabetes (Type 1 and type 2) were induced by administration of single intraperitoneal dose of 150 mg/kg of alloxan and ingestion of 20 mg/km of 50% w/v glucose once a day for 30 days respectively. The aqueous and methanolic extracts of *O. majorana* L was prepared and given to diabetic and hyperglycemic rats at 250 and 500 mg/kg/day orally for 30 days. Oral glucose tolerance test (GTT) was conducted in normal healthy rats using single dose of 350 mg/kg of each extract. At 30-day blood samples were collected for biochemical analysis. The result shows that alloxan induced diabetic groups treated with plant extracts had significantly lower fasting glucose level and glycosylated haemoglobin and improved lipid profile, insulin concentration was insignificantly changed. Blood glucose and cholesterol values were significantly decreased in glucose loaded rats treated with water extract at low dose. This study suggests that aqueous and methanolic extracts of *O. majorana* possess a potential antidiabetic activity for both type1 and type2 diabetes.

Introduction:

Diabetes mellitus is defined as a group of metabolic disorders characterized by chronic hyperglycemia as a consequence of defects in insulin secretion, insulin resistance/action or both entities in varying proportions. (Zimmet, *et al*., 2011). Diabetes mellitus is a

potentially morbid condition with high prevalence worldwide, with a major impact on the population of developing countries, thus the disease constitutes a major health concern. (Pareek, *et al*., 2009)

Diabetes is the causes of several complications include diabetic keto-acidosis and non-ketotic hyper-osmolar state (Kitabchi, *et al*., 2008). Microvascular complications (retinopathy, neuropathy and nephropathy) and macro-vascular complications (coronary artery disease, peripheral vascular disease and cerebrovascular disease). Nonvascular complications include gastroparesis, sexual dysfunction and skin changes (Fowler, 2008).

The advantages of traditional herbal medicines over conventional medicines are that they are readily available, have low cost and have very low side effects (Alarcon-Aguilara, *et al*.,1998).

The lack of scientific data proving the efficacy and safety of the medicinal plants is the major obstacle in the integration of herbal medicine into modern medical practices. Thus, Herbal derived remedies need a powerful and deep assessment using appropriate new biologic technologies for biological standardization, pharmacological qualities and safety evaluation and to determine the active component/s from these plant extracts. (Firenzuoli and Gori, 2007)

Origanum majorana is a perennial herb belongs to the family Lamiaceae, Origanum genus (Vagi, *et al*., 2002). And It is native to Cyprus, Anatolia (Turkey) and naturalized in parts of the Mediterranean region especially Egypt (Novak, *et al.*, 2002). *O. majorana* was initially used by Hippocrates as an antiseptic agent. It is a well-liked home remedy for chest infection, cough, sore throat, rheumatic pain, nervous disorders, cardiovascular diseases, epilepsy, insomnia, skin care, flatulence and stomach disorders (Faleiro, *et al.*, 2005; Yazdanparast and Shahriyary, 2008). It is known pharmacologically as a good; antioxidant (Erenler, *et al.*,2016), antimicrobial (Busatta, *et al*., 2008), anti-colon cancer (AlTamimi, 2015) and cytotoxic (Rao, *et al*., 2014).

Recently, due to economic factors, people scramble for available, easily accessible and less costly medication, even with the slightest knowledge of efficacy, and minimum idea of toxicity. Herbal remedies for most people, are natural and thus non-toxic. *O. majorana* L is one of the of traditional herbs which has been used for treatment of diabetes. This study aimed to evaluate the potential anti-diabetic effects of methanolic and aqueous extracts of *O. majorana* L in in vivo models of alloxan induced diabetic rats and normal rats.

Materials and method:

Study design:

An experimental study design was adopted.

Plants material and extract preparation:

The plant materials were purchased from a local market in Khartoum, Sudan (April, 2017), identified, and characterized by a taxonomist. The plant tissues were cleaned, shade-dried and grounded by electric grinder. The powder was subjected to extraction using various solvents of petroleum ether (40-60^{o}C), methanol and distilled water in order to obtain an organic extract while distilled water was used for aqueous extract which was carried out one after the other in a sequential manner based on their polarity.

Administration of plant extracts:

O. majorana was administrated orally at dose 250 and 500 mg/kg for 30 days, these doses were chosen for several reasons. For rats, the two doses represent nontoxic concentrations (Deshmane, *et al*., 2007) and of some plants exemplified by *Vatairea macrocarpa* (Oliveira, *et al*., 2008).

Animals:

This study was carried out on ninety Wistar albino rats of both sexes, with average body weight ranged from 150-200 g. The rats were obtained from the Medicinal and Aromatic Plants Research Institute, National Center for Research, Khartoum, they were clinically healthy and housed within the premises of the Elneelain University animal house under standard husbandry conditions, light/ dark cycle with feed and drinking water provided *ad libitum*. Three experiments were conducted.

Induction of Type1 Diabetes in Rats (T1DM):

Diabetes was induced by a single intraperitoneal dose of 150 mg/kg of body weight of alloxan dissolved in 0.1M fresh cold citrate buffer (pH 4.5) into overnight fasted rats. The animals were allowed to drink 5% glucose solution overnight to overcome the drug-induced hypoglycemia. After two days' interval of induction, the rats were tested and the rats having hyperglycemia (i.e. With fasting blood glucose above 150 mg/dl) were considered as diabetic rats for the experiment. (Lee, *et al*., 2008).

Experimental Protocol;

Forty-two rats were divided into 7 equal groups; Group 1 was maintained as normal control received normal saline 5ml/kg orally. All the animals of group 2 to 7 were alloxan induced diabetic rats. Group2 untreated diabetic animals. Group 3 was treated with subcutaneous insulin (3 IU/kg, daily) which served as standard treated group. Groups 4, 5, 6 and 7 animals were treated with 250 and 500 mg/kg/d *O. majorana* L aqueous and methanol extract, respectively. All the extracts were administered orally.

Induction of Type2 Diabetes in Rats (T2DM):

Hyperglycemia was induced with administration of supraphysiologic glucose concentration at a dose of 20m/kg of 50% w/v and given orally through cathedral tube once a day to each rat; the induction dose started seven days before the treatment with plant extracts and continued till the end of experiment. (Robertson, *et al*., 2003).

Experimental Protocol:

Thirty-six rats were divided into six groups of six animals each. Group 1 (the control) was orally received normal saline 5ml/kg. In group 2 hyperglycemia was induced by administrating a dose of 20m/kg of glucose solution, each day for 30 days. Groups 3,4,5 and 6 were treated in the same

manner as Group 2 except that they were also given (orally) 250 and 500 mg/kg of aqueous and methanolic extract of *O. majorana* L respectively.

At the end of the experimental period, rats were deprived of food overnight and sacrificed. Blood was collected and left for biochemical analysis.

Oral Glucose Tolerance Test (OGTT):

The oral glucose tolerance test and sample collection were carried out according to a protocol described by (Andrikopoulos, *et al.*, 2008). The food-deprive rats for 12 h prior to the experiment were randomly divided into three groups each containing four rats. Group 2 and 3 was orally administered with 1ml dose of 350 mg/kg *O. majorana* aqueous

and methanolic extracts respectively, followed by oral administration of 2g/kg glucose solution, while the control group (Group I) received 1ml placebo dose, followed by oral administration of 2 g/kg oral glucose solution. Blood samples were subsequently collected from tail veins at 0, 30, 60, and 120 min following oral glucose administration and glucose levels were measure

Serobiochemical analysis:

Serum was analyzed for insulin concentration rates which can be accurately estimated from insulin hormone level, fasting blood sugar, serum cholesterol, serum triglycerides, serum HDL and serum LDL using (BS-380 Chemistry Analyzer, China,2013) and glycosylated hemoglobin (HbA1c) were also estimated using auto analyzer (Roche, Cobas C111 Chemistry Analyzer – Germany).

Statistical analysis:

Data were statistically analyzed by Statistical Package for Social Science (SPSS) version 21.0. The statistical significance of difference was tested at (P0.05) levels using one-way analysis of variance (ANOVA).

Results:

Body weight changes in (T1DM):

Table 1 showed that body weight gain was significantly decreased ($P< 0.05$) in alloxan injected rats Group 2 compared to normal control rats Group 1 throughout the experiment period, and it significantly increased in alloxan injected group which treated with insulin Group 3 and *O. majorana* extracts Group 4, 5, 6 and 7 as compared to diabetic control. Administration of aqueous extract of the plant at (250 and 500) mg/kg and 250mg/kg of methanolic extract Group 4, 5 and 6 showed significant increase weight gain when compare to their respective insulin control. After 4 weeks of treatment there were no significant variation in weight gain between diabetic group and all plant extracts groups.

Serobiochemical changes in (T1DM):

These data are summarized in Table 2 and 3. The administration of alloxan cause a significant elevation in fasting blood glucose (FBG) of diabetic rats when compared to normal rats. There was a reduction in the average mean of FBG in insulin treated group 3 and plant extracts treated groups (4, 5, 6 and 7) when compared to their respective non treated diabetic control group.

A significant decrease in serum insulin level was and observed in diabetic and treated rats compared with the normal control group ($P< 0.05$). However, treatment with *O. majorana* extracts showed no significant differences in mean insulin levels between the groups of rats treated with aqueous and methanolic extracts and insulin treated group. In compare with control group, the average mean of the diabetic rats showed significant increase in the level of glycosylated hemoglobin (HbA1c), while the treated group showed reduction in HbA1c level when compare to diabetic group at ($P< 0.05$), as table (2). The cholesterol (CL) level is significantly decreased in the group treated with 250mg aqueous and the group treated with 250mg methanolic extract when compared to diabetic control group ($P< 0.05$). As depicted in Table 3, there were significant increases in fasting cholesterol (CL), triglyceride (TG) and LDL-C (low density lipoprotein cholesterol) in diabetic rats Group 2 as compare with normal control Group 1, ($P< 0.05$), while HDL-C (high density lipoprotein cholesterol) concentration was insignificantly

deferent. All *O. majorana* treated groups showed significant decrease in LDL and triglyceride levels when compared to normal and insulin control groups, while there was insignificant different in HDL when compared to their respective non treated diabetic control group as in table 3.

Table (1) Body weight and body weight gain of experimental diabetic rats given different concentration of aqueous and methanolic extract of *O. majorana* orally for 4 weeks

Groups	1. Control	2.Alloxan Control	3.Insulin +Alloxan	4.Aqueous 250mg/kg + Alloxan	5.Aqueous 500 mg/kg +Alloxan	6.methanolic 250 mg/kg +Alloxan	7.methanolic 500 mg/kg +Alloxan
Body weight (g) at 0 day	160.8±4.9	159.6 ±7.1	154.6 ±8.7	158.6 ±9.4	165.6 ±7.6	165.8 ±2.4	161.6 ±3.0
Weight gain at week 2(g)	11.4±0.8	-4.6* ± 1.6	8.3 ± 2.4	15.9$^{*\#\$}$± 1.6	18.40$^{*\#\$}$ ± 1.3	17.4$^{*\#\$}$± 1.2	6.4$^{*\#\$}$± 0.8
Weight gain at week 4(g)	12.2±0.1	-8.0* ± 0.6	5.3$^{*\#}$ ± 1.2	4.5$^{*\#}$ ± 0.8	5.7$^{*\#}$ ± 0.4	6.5$^{*\#}$ ± 0.7	2.6$^{*\#}$ ± 1.0

Values are expressed as mean ± S.E; *Significant = (P< 0.05) as compared to normal control on corresponding day.
Significant in compare with diabetic control group
$ Significant in compare with insulin control group

Table (2) Serobiochemical changes of diabetic rats given different concentrations of aqueous and methanolic extracts of *O. majorana* orally for 4 weeks.

Groups	1.Control	2.Alloxan Control	3.Insulin +Alloxan	4.Aqueous 250mg/kg + Alloxan	5.Aqueous 500mg/kg +Alloxan	6.methanol 250mg/kg +Alloxan	7.methanol 500mg/kg +Alloxan
Glucose (mg/dl)	93.6±8.1	159.3*±11.5	109.8*$^{\#}$ ±9.2	110.6$^{\#}$ ±5.1	108.2$^{\#}$±17.2	126.8*±16.3	123.6*±17.6
Insulin (U/L)	3.15±0.3	2.23*±0.6	2.68 ±0.2	2.14* ±0.1	2.37* ±0.2	2.24* ±0.1	2.41* ± 0.27
HbA1c (mg/dl)	4.2±.27	7.1*±3.0	3.9$^{\#}$ ±.47	4.7$^{\#}$ ±0.8	4.5$^{\#}$ ±.08	5.0$^{\#}$±2.7	4.5$^{\#}$ ±1.6

Values are expressed as mean ± S.E; *Significant = (P< 0.05) as compared to normal control.
Significant in compare with diabetic control group.
$ Significant in compare with insulin control group.

Table (3) Changes in lipid profile of alloxan induced diabetic rats given different concentrations of aqueous and methanolic extracts of *O. majorana* orally for 4 weeks.

Groups	1. Control	2.Alloxan Control	3.Insulin +Alloxan	4.Aqueous 250mg/kg + Alloxan	5.Aqueous 500 mg/kg +Alloxan	6.methanol 250 mg/kg +Alloxan	7.methanol 500 mg/kg +Alloxan
(CL) (mg/dl)	83.4±11.4	101.0*±12.0	89.2 ±16.12	74.5$^{\#\$}$ ±9.5	85.2 ±3.7	81.5$^{\#}$ ±5.0	89.0 ±7.1
(TG) (mg/dl)	81.4±4.3	86.0*±4.3	81.4 ±10.2	78.7$^{\#}$ ±8.3	88.7$^{\#*}$ ±4.0	78.5$^{\#}$ ±5.0	75.8$^{\#}$ ±6.0
LDL-C (mg/dl)	93.8±4.1	101.3*±3.0	93.0 ±3.2	41.5*$^{\#\$}$ ±2.6	44.5*$^{\#\$}$±5.0	40.2*$^{\#\$}$±2.0	36.2*$^{\#\$}$±6.5
HDL-C (mg/dl)	49.6±2.1	45.3±4.3	48.6 ±3.0	47.2 ±3.0	45.7 ±6.5	49.5 ±8.0	48.4 ±4.5

Values are expressed as mean ± S.E; *Significant = (P< 0.05) as compared to normal control.
Significant in compare with diabetic control group.
$ Significant in compare with insulin control group.

Body weight changes in (T2DM):

The effects of treatment with aqueous and methanol extracts of *O. majorana* Linn on body weight of the rats shown in Table 4. The hyperglycemic control rats group and the rats treated with 250mg of methanolic Origanium showed noticeable increase in body weight throughout the study.

Serobiochemical changes in (T2DM):

The changes in the serobiochemical parameters are shown in Table 5 and 6. There were significant hyperglycemia response in group of rats treated with supraphysiologic glucose throughout the experiment period as compare with control group. *O. majorana*in high and low doses of aqueous and methanolic extracts gave significant effect on glucose level when compared to untreated hyperglycemic control group ($P< 0.05$). High doses (500mg) of methanolic extracts of *O. majorana* significantly affected both insulin and HbA1c when compared to normal group. The aqueous extract of *O. majorana* in 250mg dose showed significant results on cholesterol, triglyceride and HDL-C levels in comparison with insulin control group. Triglycerides level of rats treated with 500mg aqueous *O. majorana* showed significant values when compared to normal control. Low doses of methanolic *O. majorana* gave significant effect on the HDL-C level of rats when compared to the insulin control rats ($P< 0.05$).

Table (4) Body weight and body weight gain of experimental hyperglycemic rats given different concentration of aqueous and methanolic extract of O. majorana orally for 4 weeks.

Groups	1.Control	2.glucose loaded control	3.Aqueous 250 mg/kg + glucose	4.Aqueous 500 mg/kg + glucose	5.methanolic 250 mg/kg + glucose	6.methanolic 500 mg/kg + glucose
Pretreatment Body weight (g)	123.6 ±4.2	124.2 ±10.2	123.2 ±12.1	125.2 ±10.2	128.8 ±4.2	125.4 ±8.9
Weight gain at week 2 (g)	14.2 ±0.2	25.8* ±3.5	14.2# ±3.1	14.2# ±1.1	25.2* ±4.4	13.6# ±1.4
Weight gain at week 4 (g)	12.1 ±1.3	21.2* ±0.7	9.2# ±3.3	15.0# ±1.3	17.0# ±1.2	14.6# ± 2.3

Values are expressed as mean ± S.E; *Significant = ($P< 0.05$) as compared to normal control on corresponding day.

Significant in compare with glucose loaded control group.

Table (5) Serobiochemical changes of experimental hyperglycemic rats given different concentrations of aqueous and methanolic extracts of *O. majorana* orally for 4 weeks.

Groups	1.Control	2.glucose loaded control	3.Aqueous 250 mg/kg + glucose	4.Aqueous 500 mg/kg + glucose	5.methanolic 250 mg/kg + glucose	6.methanolic 500 mg/kg + glucose
Glucose (mg/dl)	84.4 ± 9.1	123.2 ± 8.1	96.6# ± 9.4	85.4# ± 9.4	82.8# ± 8.1	86.6# ± 5.4
Insulin (U/L)	3.14 ± .03	3.13 ± .03	3.14 ± .03	3.12 ± .03	3.13 ± .02	3.09* ± .05
HbA1c (mg/dl)	3.42 ± .43	5.14 ± .86	4.31 ± .23	4.51 ± .83	3.91 ± .82	4.91* ± .70

Values are expressed as mean ± S.E; *Significant = ($P< 0.05$) as compared to normal control.

Significant in compare with glucose loaded control group

Table (6) changes in lipid profile of experimental hyperglycemic rats given different concentrations of aqueous and methanolic extracts of *O. majorana* orally for 4 weeks.

Groups	1.Control	2.glucose loaded control	3.Aqueous 250 mg/kg + glucose	4.Aqueous 500 mg/kg + glucose	5.methanolic 250mg/kg + glucose	6.methanolic 500mg/kg + glucose

ISSN (Print): 1605 427x e-ISSN (Online): 1858-6716

(CL) (mg/dl)	87.4±3.4	97.5*±0.3	86.8#±9.3	88.0±5.1	92.6±10.5	88.0±5.6
(TG) (mg/dl)	83.2±5.2	97.2*±8.6	84.6#±7.8	95.2±8.1*	92.6±4.6	92.8±11.5
LDL-C (mg/dl)	47.6±5.9	50.2±4.2	50.0±5.2	48.8±3.0	54.8±7.0	50.0±8.8
HDL-C (mg/dl)	47.2±3.0	38.2*±7.1	50.6#±6.1	43.0±6.4	46.8#±3.3	45.8±4.0

Values are expressed as mean ± S.E; *Significant = (P< 0.05) as compared to normal control.
Significant in compare with glucose loaded control group

Results of Oral Glucose Tolerance Test:

These data are presented in Table 7. The effects of aqueous and methanolic extracts of O. majorana at 350 mg/kg on fasting blood glucose concentration of normal rats were assessed at different time intervals (0, 30, 60, and 120 min). the aqueous extract showed significant reduction in blood glucose level (P< 0.05) at 30 and 60 min, while the methanolic extract showed reduction of glucose level at 60 and 120min.

Table (7) Glucose Tolerance Test of rats orally, given a single dose of 350 mg/kg of aqueous or methanolic extracts of *O. majorana*

Groups	Fasting BG mg\kg	Half hour BG mg\kg	One Hour BG mg\kg	Two hours BG mg\kg
Control	99.0± 5.5	147.6±13.5	137.3±10.4	101.3±14.3
Origanium Aqueous 350mg/kg	92.6± 7.5	125.67*±18.7	109.6*±8.0	92.6±10.6
Origanium Methanolic 350mg/kg	94.6 ± 6.5	147.5±12.8	115.6*±11.3	85.3*±12.2

Values are expressed as mean ± S.E; *Significant = (P< 0.05) as compared to normal control on corresponding time.

Discussion:

It was clear from the current study that administration of *Origanium majorana*, a traditional medicinal plant can reduce elevated blood glucose level in rats and it is not toxic as evidenced by the absence of mortality, of clinical changes and of growth impairment.

In the present study, impairment of growth and elevated concentration of glucose, cholesterol, triglyceride and LDL and decreased insulin level in the serum of the untreated alloxan induced diabetic rats indicate pancreas damage and increase lipolysis. Treatment of diabetic rats with *O. majorana* at a doses of 250 and500mg/kg probably have glycemic control as evidenced by significant gain of body weight in the treated rats compared to untreated diabetic control.

The reduction in the average mean of FBG and HbA1c in the groups of rats treated with 250 and 500 mg/kg of water and alcohol extracts indicated antidiabetic activity. The results obtained from these groups suggest that both extracts of *O. majorana* are effective in maintaining glycemic status of diabetic rats, with aqueous being the more effective than methanolic extract at a dose level of 250mg/kg. LDL, cholesterol and triglyceride lowering potential of both extracts of *O. majorana* indicates the efficacy of the plant to inhibit mobilization of fat and muscle protein dramatically occur in defective insulin conditions. The mechanism whereby the plant had effects cannot be accurately state but this antidiabetic role of *O. majorana* probably result from insulin-like action such as improving the uptake of cellular glucose or enhancing glycogenosis. It is necessary, however, to exclude the efficacy of the plant to normalize the pancreatic injury induced by alloxan as the levels of insulin concentration of rats treated with aqueous and methanolic extracts were not statistically changed. These results are further supported with the finding of (Babu, *et al*., 2003) how had reported that in streptozotocin diabetic rats 200 mg/kg of alcohol extract of *Cassia Kleinii* leaf showed significant antidiabetic activity as improved body weight, serum glucose, lipid profile and liver glycogen levels. However, in both diabetic and normoglycemic rats the extract did not significantly influence the level of serum insulin.

Type 2 Diabetes Mellitus (T2DM) is one of the most common, costly, and preventable chronic health problems, according to (Inzucchi,2012) Glycemic management in type 2 diabetes mellitus has become increasingly complex and, to some extent, controversial, with a widening array of pharmacological agents now available, mounting concerns about their potential adverse effects and new uncertainties regarding the benefits of intensive glycemic control on macrovascular complications.

In this study, supraphysiologic dose of glucose solution at a concentration 20m/kg of 50% w/v was given orally once a day to each rat through the experimental period to induced a model of chronic hyperglycemia resemble to untreated T2DM condition. A significant reduction of glucose concentration at dose dependent manner was the main biochemical parameter observed in normal Wistar rats treated with aqueous extracts of *O. majorana*. There were no significant differences in HbA1c and lipid profile except on group treated with 250 aqueous extract.it seems, therefore, that the susceptibility of *O. majorana* to recovering T2DM is dependent, at least, on the type and concentration of the plant extracts. These data were in agreement with the result of (Pareek, *et al*., 2009) who report that the sub-chronic treatment with *Tridaxprocumbens* L extract for a period of 30 days produced a significant decrease in fasting blood glucose level and improved glucose tolerance of alloxan diabetic rats as well as in glucose-loaded normal rats. The optimum activity showed at 250 mg/kg and further increase in extract dose did not result in a further significant decline in blood glucose levels, thus it appears that unlike insulin and other common hypoglycemic agents overdose of the drug may not result in hypoglycemia.

In many individuals, hyperlipidemia has no symptoms and the disorder is not discovered until laboratory tests reveal elevated cholesterol and triglyceride levels, elevated LDL-C levels, and decreased HDL-C levels, so it is good health sign to find a home applied food flavouring with efficient hypolipideamic efficacy, however, it is clear from the results of

the present investigation that the administration of diabetic rats with *O. majorana* extracts revealed hypolipideamic activity. likewise, the glucose loaded rats (T2DM) treated with 250 mg/kg of *O. majorana* water extract also caused significant decrease in cholesterol and triglyceride concentration and the treatment with 500 mg/kg of methanolic extract reduced the LDL-C level. This hypo-lipideamic effects suggest the efficacy of the plant to decrease the risk of vascular disease in diabetic rats. These result are further supported with the finding of Tripathy,*et al*., (2018) who had found that the ethanolic leaf extract of *O. majorana* possesses significant antidiabetic and anti-hyperlipidemia activities in Streptozotocin induced diabetic rat. Pimple and Kadam (2012) had, also, reported the order oflowering the diabetes induced lipid level was in thefollowing order *O. majorana* water extract>methanolic extract >*O. majorana*volatile oil. This pronouncedeffect may be due to Vitamin C and the phenols like tanninspresent in *O. majorana* water extract.

The scientific literatures have shown that following the consumption of carbohydrates, glucose is absorbed into the bloodstream elevating blood glucose levels. This rise in blood glucose levels stimulates the secretion of insulin. Insulin binds to specific cellular receptors and facilitates entry of glucose into the cell, Insulin-stimulated glucose uptake by skeletal muscle and adipose tissue is a key process responsible for the normalization of postprandial blood glucose level. (Mealey and Oates, 2006; Paul, *et al*., 2007). One of the therapeutic approaches in Type 2 diabetes is to lower the corresponding postprandial blood glucose values. (Dinesh kumar, 2010). In the present study, oral glucose tolerance test was performed in normoglycemic rats to explain the hypoglycemic effect of *O. majorana* extracts observed on elevated blood glucose of diabetic rats in the study groups. After half h of glucose administration, the significant decrease in blood glucose was recorded with the group of rats treated with 350 mg/kg aqueous extract when compared to control point to lack of glucose absorption. The ability of both extracts to reduce blood glucose after one and two hours of glucose consumption indicate the efficiency of *O. majorana* to normalize postprandial blood glucose level in rats. Andrade-Cetto, *et al.*, (2008) have performed antidiabetic study on four medicinal plants and reviewed that *Cecropia obtusifolia, Acosmiumpanamense* and *Malmea depressa* produced both a reduction in plasma glucose in the animal model and an inhibition of glucosidase in vitro in a degree similar to or greater than agarose. This result indicates that, in the n-STZ model loaded with maltose, a reduction in the plasma glucose curve 30 min after an oral load of maltose, is mainly due to the inhibition of intestinal glucosidase(s), and it can be assumed that glucose absorption at the gut level is inhibited.

Conclusion:

O. majorana mediated good glycemic management and restoration of metabolic disorders caused by glucose toxicity in Wistar rats.

Administration of O. majorana can modulate glucose homeostasis and potentially improve lipid parameter.

The study highlighted the inability of the plant to normalize defective insulin values of pancreatic injured rats.

Acknowledgement:

Deepest thanks are prerogative to the Advanced Diagnostic Laboratory, Khartoum, Sudan, for helps and facilities.

References:

1. Al Tamimi, N. F. (2015). Anti-Colon Cancer Activity of *Origanum Majorana*. Theses. Paper 212. https://scholarworks.uaeu.ac.ae/all_theses/212.

2. Alarcon-Aguilara, F.J., Roman-Ramos, R., Perez-Gutierrez, S., Aguilar-Contreras, A., Contreras-Weber, C.C. and Flores-Saenz, J.L., (1998). Study of the anti-hyperglycemic effect of plants used as antidiabetics. *Journal of ethnopharmacology*, 61(2), 101-110.

3. Andrade-Cetto A, Becerra-Jimenez J, Cardenas-Vazquez R (2008). Alfa-glucosidase-inhibiting activity of some Mexican plants used in the treatment of type 2 diabetes. *Journal of ethnopharmacology*, 116(1)27–32.

4. Andrikopoulos, S., Blair, A.R., Deluca, N., Fam, B.C. and Proietto, J. (2008). Evaluating the glucose tolerance test in mice. *American Journal of Physiology-Endocrinology and Metabolism*, 295(6),1323-1332.

5. Babu, V., Gangadevi, T. and Subramoniam, A. (2002). Anti-hyperglycaemic activity of *Cassia kleinii* leaf extract in glucose fed normal rats and alloxan-induced diabetic rats. *Indian journal of pharmacology,* 34(6), 409-415.

6. Busattaa, C., Vidala, R.S., Popiolskia, A.S., Mossia, A.J., Darivab, C., Rodriguesc, M.R.A., Corazzaa, F.C., Corazzaa, M.L., Vladimir Oliveiraa, J. and Cansian, R.L. (2008). Application of *Origanum majorana* L. essential oil as an antimicrobial agent in sausage, *Food Microbiology*, 25(1), 207–211.

7. Deshmane, D.N., Gadgoli, C.H. and Halade, G.V. (2007). Anticonvulsant effect of *Origanum majorana* L. *Pharmacologyonline*, 1.64-78.

8. Dineshkumar, B., Mitra, A. and Manjunatha, M., (2010). A comparative study of alpha amylase inhibitory activities of common anti-diabetic plants at Kharagpur 1 block. *International Journal of Green Pharmacy*, *4*(2)115-121.

9. Erenler, R., Sen, O., Aksit, H., Demirtas, I., Yaglioglu, A.S., Elmastas, M. and Telci, I. (2016). Isolation and identification of chemical constituents from *Origanum majorana* and investigation of antiproliferative and antioxidant activities. *Journal of the Science of Food and Agriculture*, 96(3), 822-836.

10. Faleiro, L., Miguel, G., Gomes, S., Costa, L., Venâncio, F., Teixeira, A., Figueiredo, A.C., Barroso, J.G. and Pedro, L.G. (2005). Antibacterial and antioxidant activities of essential oils isolated from *Thymbra capitata* L.(Cav.) and *Origanum vulgare* L. *Journal of Agricultural and Food Chemistry*, 53(21), 8162-8168.

11. Firenzuoli, F. and Gori, L. (2007). Herbal medicine today: clinical and research issues. *Evidence-Based Complementary and Alternative Medicine*, 4(S1), 37-40.

12. Fowler, M.J. (2008). Microvascular and macrovascular complications of diabetes. *Clinical diabetes*, 26(2), 77-82.

13. Inzucchi, S.E., Bergenstal, R.M., Buse, J.B., Diamant, M., Ferrannini, E., Nauck, M., Peters, A.L., Tsapas, A., Wender, R. and Matthews, D.R. (2012). Management of hyperglycemia in type 2 diabetes: a patient-centered approach: position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Spectrum*, 25(3),154-171.

14. Kitabchi, A.E., Umpierrez, G.E., Fisher, J.N., Murphy, M.B. and Stentz, F.B. (2008). Thirty years of personal experience in hyperglycemic crises: diabetic ketoacidosis

and hyperglycemic hyperosmolar state. *The Journal of Clinical Endocrinology & Metabolism*, 93(5), 1541-1552.

15. Lee, M.G., Choi, Y.H. and Lee, I. (2008). Effects of diabetes mellitus induced by alloxan on the pharmacokinetics of metformin in rats: restoration of pharmacokinetic parameters to the control state by insulin treatment. *Journal of Pharmacy & Pharmaceutical Sciences*, 11(1), 88-103.

16. Mealey, B.L. and Oates, T.W. (2006). Diabetes mellitus and periodontal diseases. *Journal of periodontology*, 77(8), 1289-1303.

17. Novak, J., Langbehn, J., Pank, F. and Franz, C.M. (2002). Essential oil compounds in a historical sample of marjoram (*Origanum majorana* L., Lamiaceae). *Flavour and Fragrance Journal*, 17(3), 175-180.

18. Oliveira, H.C., dos Santos, M.P., Grigulo, R., Lima, L.L., Martins, D.T., Lima, J.C., Stoppiglia, L.F., Lopes, C.F. and Kawashita, N.H. (2008). Antidiabetic activity of *Vatairea macrocarpa* extract in rats. *Journal of ethnopharmacology*, 115(3), 515-519.

19. Pareek, H., Sharma, S., Khajja, B.S., Jain, K. and Jain, G.C. (2009). Evaluation of hypoglycemic and anti-hyperglycemic potential of Tridax procumbens (Linn.). *BMC complementary and alternative medicine*, *9*(1), 48-54.

20. Paul, D.S., Hernández-Zavala, A., Walton, F.S., Adair, B.M., Dědina, J., Matoušek, T. and Stýblo, M. (2007). Examination of the effects of arsenic on glucose homeostasis in cell culture and animal studies: development of a mouse model for arsenic-induced diabetes. *Toxicology and applied pharmacology*, 222(3), 305-314.

21. Pimple, B.P., Kadam, P.V. and Patil, M.J., (2012). Comparative antihyperglycaemic and antihyperlipidemic effect of Origanum majorana extracts in NIDDM rats. *Oriental pharmacy and experimental medicine*, 12(1), 41-50.

22. Rao, S., Timsina, B. and Nadumane, V.K. (2014). Evaluation of the anticancer potentials of *Origanum marjorana* on fibrosarcoma (HT-1080) cell line. *Asian Pacific Journal of Tropical Disease*, 4(1), 389-394.

23. Robertson, R.P., Harmon, J., Tran, P.O., Tanaka, Y. and Takahashi, H. (2003). Glucose toxicity in β-cells: type 2 diabetes, good radicals gone bad, and the glutathione connection. *Diabetes*, 52(3), 581-587.

24. Saravanamuttu, S. and Sudarsanam, D. (2012). Antidiabetic plants and their active ingredients: A review. *International journal of Pharmaceutical sciences and research*, 3(10), 3639-3650.

25. Tripathy, B., Satyanarayana, S., Khan, K.A. and Raja, K. (2018). Evaluation of Anti-Diabetic and Anti-Hyperlipidemic Activities of Ethanolic Leaf Extract of *Origanum Majorana* in Streptozotocin Induced Diabetic Rats. *International Journal of Pharmaceutical Sciences and Research,* 9(4), 1529-1536.

26. Vagi, E., Simándi, B., Daood, H.G., Deak, A. and Sawinsky, J. (2002). Recovery of pigments from *Origanum majorana* L. by extraction with supercritical carbon dioxide. *Journal of agricultural and food chemistry*, 50(8), 2297-2301.

27. Yazdanparast, R. and Shahriyary, L. (2008). Comparative effects of Artemisia dracunculus, Satureja hortensis and *Origanum majorana* on inhibition of blood platelet adhesion, aggregation and secretion. *Vascular pharmacology*, 48(1), 32-37.

28. Zimmet, P., Alberti, K.G.M.M. and Shaw, J., (2001). Global and societal implications of the diabetes epidemic. *Nature*, 414(6865), 782-787