

## Effect of *Salvia officinalis* L. (Sage) Aqueous extract on Liver and Testicular Function of Diabetic Albino Male Rats.

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### Abstract

The study was current to examine the antidiabetic effects of administration of aqueous extracts of *Salvia officinalis* leaves in alloxan (100 mg/kg) induced diabetic rats and reveal the effect of *Salvia officinalis* in the the liver and testicular function. The present study aimed to evaluate the effects of aqueous extracts of Sage leaves (*Salvia officinalis* L., *Lamiaceae*), on the levels of blood glucose, plasma lipids profiles such as triglycerides (TG), total cholesterol (TC), high-density lipoproteins (HDL), low-density lipoproteins (LDL) and very low-density lipoproteins (VLDL) in diabetic rats. The animals were rendered diabetic by a single intraperitoneal injection alloxan (100 mg/kg).

Twenty eight adult male albino rats of 7-9 weeks old weighting (240± 10 gm) were used for this study. They were kept for one week for proper acclimatization before starting the experiment under the same controlled laboratory conditions of illumination period (12h light/12h darkness), temperature at 22±2°C and maintained on standard diet and water. The aqueous *Salvia officinalis* extracts were injected intraperitoneally at a dosage of 300 mg/kg for five weeks since the day after diabetes confirmation blood samples were obtained from heart. The results showed that i.p. injection with alloxan induced very highly significant elevation in mean of blood glucose levels of diabetic animals as compared with control group and sage administration groups. Diabetic rats also revealed highly significant elevation in, total cholesterol (TC), triacylglyceride (TAG), low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) concurrent with highly significant reduction in high-density lipoprotein cholesterol (HDL-C) as compared with control group. administration of sage tea had no effect on normal rats. Animals treatment with sage to diabetic rats induced significant improvement in all testicular function parameters (total count, viability, motility and morphology), it reduced significantly blood glucose levels as well as induced significantly amelioration in lipid profile parameters as compared with non treated diabetic group. Therefore, it could be concluded that sage had a potent hypoglycemic activity, this effect may be attributed to its antioxidant activities. Results showed a significant decrease in Testosterone, LH, FSH levels in diabetic male rats compared with control male and sage with diabetic groups after 5 weeks from treated. The results obtained a significant increase in dead sperm, morphology abnormalities in diabetic male rats compared with control male, Sage extract and Sag extract with diabetic

**Key words:** *Salvia officinalis* L, Diabetes mellitus, Hyperglycaemia, Lipid profile, Rat. Alloxan monohydrate.

### الخلاصة

صممت هذه التجربة لاختبار التأثيرات المضادة لمرض داء السكري بواسطة التجريب بالمستخلص المائي لنبات الميرمية في الجرذان المستحدث فيها داء السكري باستخدام مادة الالوكسان وبجرعة مقدارها 100 ملغم/كيلوغرام ودراسة تأثير الميرمية على وظائف الكبد والخصية. الدراسة الحالية تهدف الى تقييم تأثيرات المستخلص المائي لنبات الميرمية على مستوى الكلوكرز بالدم ومستوى الدهون التي تشمل الدهون الثلاثية، الكوليسترول، البروتينات الدهنية عالية الكثافة والبروتينات الدهنية واطئة الكثافة في الجرذان المستحدث فيها داء السكر.

استخدم في هذه التجربة ثمانية وعشرون من الجرذان الذكور البالغه بعمر 7-9 اسابيع وبوزن 240 + 10 غم تركت لمدة اسبوع للتكيف تحت نفس الظروف المختبريه وهي 12ساعة ضوعو 12 ساعة ظلام ودرجة حراره 22م وجهزت بغذاء قياسي وماء جرع

المستخلص المائي لنوات الميرمية بجرعه مقدارها 300ملغم/كيلوغرام ولمدة خمسة اسابيع بعد يوم واحد من استحداث داء السكر، تم جمع عينات الدم مباشرة من القلب لاجراء الفحوصات. اظهرت النتائج ان الحقن تحت البريتون لمادة الالوكسان سببت ارتفاع معنوي لمعدل مستوى السكر بالدم في الجرذان المستحدث بها داء السكر مقارنة مع مجموعة السيطرة والمجموعه التي جرعت مستخلص الميرمية. الجرذان المستحدث بها داء السكر اظهرت ارتفاعا في مستويات الكوليسترول والدهون الثلاثيه والدهون واطئة الكثافه وانخفاض عالي في الدهون عالية الكثافه مقارنة مع مجموعة السيطرة وان تجريب مستخلص الميرمية لم يظهر اي تأثيرات على الحيوانات الطبيعیه. الحيوانات التي جرعت بالمستخلص اظهرت تحسنا معنوبافي جميع الوظائف الخصويه(العدد الكلي للنفط، العيوشيه، الحركه والمظهر العام) وانخفاض في مستوى السكر بالدم كما سببت تغييرات معنويه في مستويات الدهون مقارنة مع مجموعة الحيوانات المستحدث بها داء السكر وغير المعامله بالمستخلص المائي للميرمية. اظهرت النتائج بان المستخلص المائي له تأثيرات ايجابيه على انخفاض مستوى السكر والتي قد تعود بسبب تأثير المستخلص المضاد للاكسده. بينت النتائج وجود انخفاض في مستوى هرمونات الشحمون الخصوي والمحفز للجريبات وهرمون الجسم الاصفر في الحيوانات المستحدث بها داء السكر مقارنة مع مجموعة السيطرة والجرذان المستحدث بها داء السكر والمعامله بالمستخلص المائي بعد خمسة اسابيع من المعامله. اظهرت النتائج وجود زياده في عدد النفط الميتة وغير السويه مقترنة مع حيوانات السيطرة والحيوانات التي جرعت بالمستخلص المائي كذلك الحيوانات المصابه بداء السكري والتي جرعت بالمستخلص المائي .

**الكلمات المفتاحيه :** الميرمية، داء السكري، ارتفاع السكر في الدم، تحليل الدهون، الجرذان، مادة الالوكسان.

## Introduction

Plant constitutes consider important sources of active natural products which differ widely in terms of structures, biological properties and mechanisms of actions, various phytochemical components, especially polyphenols (such as flavonoids, phenyl propanoids phenolic acids, tannins, etc) are known to be responsible for the free radical scavenging, inhibition of peroxidation, chelating transition metals and antioxidant activities of plants (Melo *et al.*, 2005). In recent years, the extracts of many plants have been screened for their antioxidant and hypoglycemic activities. Among these, sage is well-known for their antioxidant properties and most of its active components have been identified. It has been established that the antioxidant effects are mainly due to the phenolic compounds of the plant (Tepe *et al.*, 2006). *Salvia officinalis* L. (Sage), a member of the family of Lamiaceae, has been reported to have a wide range of biological activities, such as antioxidant, antibacterial, hypoglycemic and anti-inflammatory properties. Recent studies have found that the Sage has positively physiological effects on heart, liver, kidney and testes (Chien *et al.*, 2011).

The constituents reported in this plant are rosmarinic acid, phenolic acids, carnosic compounds and flavonoids cinel, borneol, pinene, flavonoids, saponin, glycoside, resin, tannin, vitamin C and E, anti-inflammatory, antifungal, antimicrobial, antioxidant and anti-hypoglycemic properties (Kennedy, D.O. 2006 ; Oniga *et al.*, 2007). Since sage extract has a prominent effect, so it is conceivable that can improve male reproductive function (Lindi *et al.*, 2005) It has been proposed as effective against cardiovascular diseases, brain and nervous disorders, various infections (such as throat infections, dental abscesses, and mouth ulcers) and among the plants that are claimed to be beneficial to diabetic patients. Lima *et al.*, 2006 showed that a sage methanolic extract given intraperitoneally significantly reduced serum glucose level in fasted streptozotocin-induced diabetic rats without change in insulin level. Carla *et al.*, 2009 reported that Sage (*Salvia officinalis* L.) reducing malonaldehyde level and releasing the inhibitory effect of azathioprine on the activities of glutathione, catalase and superoxide dismutase enzymes. In addition, (Lima *et al.*, 2005) demonstrated that the replacement of drinking water with sage tea in rats resulted in an improvement of the antioxidant status of rat. Therefore, the purpose of the current study was to examine the hypoglycemic effects of oral administration of sage infusion on diabetic male rats. Diabetes mellitus is one of the most common endocrine metabolic disorders, characterized by hyperglycemia due to defects in insulin secretion, action or both (Hajzadeh *et*

*al.*,2011) it has caused a significant morbidity and mortality due to microvascular (retinopathy, neuropathy and nephropathy) and macrovascular (heart attack, stroke and peripheral vascular disease) complications (Patel *et al.*,2011). Diabetes mellitus is characterized by hyperglycemia and is associated with disturbances in carbohydrate, protein and fat metabolism which occurs secondary to an absolute (type I) or relative (type II) lack of insulin (Alberti and Zimmet, 1998). Oxidative stress occurs when the balance between oxidant and antioxidant systems shifts in favor of the former leading to the generation of free oxygen radicals. Reactive oxygen species are involved in the pathogenesis of many diseases including hypoxia, hypercholesterolemia, atherosclerosis, hypertension, ischemia reperfusion injury and heart failure (Wilcox and Gutterman, 2005).

## Materials and methods

### Preparation of sage tea:

Considering the Sage is traditionally used as a tea an infusion of Sage tea was freshly prepared by pouring 250 ml of boiling water onto 50 gm dried leaves plant, covering and allowing it to steep for 5 min according to (Lima *et al.*,2005).

### Induction of diabetes:

Diabetes was experimentally induced in overnight fasted rats by subcutaneous injection of Alloxan monohydrate (100 mg Kg<sup>-1</sup>, Sigma, St. Louis, MO, USA), dissolved in citrate buffer (pH = 4.5), according to a previously described method (Kumar.,2008).

Diabetic rats were supplied with 5% sucrose solution orally for the first 48 hrs, after alloxan injection to minimize death from hypoglycemia. Seventy-two hrs. later, blood samples were obtained by heart puncture with a needle and blood glucose levels were determined to confirm induction of diabetes. Surviving rats with a fasting blood glucose level higher than 250 mg/dl, were considered diabetic and then included in this study. Animals blood glucose was estimated by using one touch glucometer (Peschke *et al.*,2000).

### Experimental design:

Twenty eight adult albino male rats of 7-9 weeks old weighting (240± 10 gm) were used for this study. Rats were randomly divided into four groups, each of seven rats as follows: **Group 1:** Control group, healthy control rats received 0.3 ml isotonic saline solution intraperitoneally (negative control). **Group 2:** Diabetic rats, injected i.p. with 100 mg/kg body weight alloxan, **Group 3:** Sage group, rats i.p. injected with the same method as in group (1), 72 hrs, later they received Sage tea 300mg/kg b.wt. as a single dose/day. **Group 4:** Diabetic rats as in group (2), 72 hrs, later they treated with Sage at the same route as in group (3). Rats were given standard diet and tap water *ad libitum*. The experiment lasted for five weeks starting from sage administration. At the end of the experimental period, rats were deprived of food overnight and sacrificed under ether anesthesia. Blood samples were collected by heart puncture with a fine needle. Collected blood was stored for 30 min at room temperature and centrifuged with 3000 rpm for 15 min. The supernatant kept in - 20 °C until use. At the end of treatment period, fertility parameters such as sperm motility, viability, abnormality and count, blood testosterone, FSH and LH levels and lipid profile were measured.

### Collection and sperms parameters

Rats were killed and dissected directly, the testes were removed and placed in a sterile disposable Petri dish containing 3ml RPMI-1640 medium at 37 °C, the sperms were collected from the epididymis of rats by the caudal vas cut and placed in a Petri dish containing 1ml of RPMI-1640 medium and minced by using microsurgical scissor and forces (Bearden and Faquay, 1992)

### Sperm motility

Sperm motility was assessed according to the method reported by (Bearden and Faquay, 1992)

Fifty  $\mu\text{l}$  of the sperm suspension was placed over a slide and covered by a cover slide. Using light microscope, several fields were examined to estimate the percentage of individual motility of sperms.

### Sperm viability and abnormalities

The percentages of dead and abnormal sperms were measured as following according to the method reported by (Bancroft and Steven, A. 1982).]. A drop of the sperm suspension was placed over the slide and, then a drop of Eosin-Nigrosin stain was added and mixed. The mixture was spread using another slide and left to dry. Using light microscope, 200 sperms were counted to calculate the percentages of dead and abnormal sperm.

### Biochemical analysis

Separated serum samples were used for determination of glucose enzymatically, total cholesterol (TC) high density lipoprotein cholesterol (HDL-C) and triglycerid (TG) were spectrophotometrically measured using appropriate kits [Demacker *et al.*,1980] (SPINREACT,S.A-Ctra.Santa Coloma,7-17176 SANT DE BAS cholesterol kit -(Girona)SPAIN. cholesterol (LDL-C) and very low-density lipoprotein(VLDL-C) were calculated according to the equation [Friedwald *et al.*,1972]. and testosterone,FSH and LH levels were performed depends on kit assay procedure of ELISA kit(Germany) antibodies to Ag.

### Results

Effect of aqueous extracts of Sage (*Salvia officinalis*) on serum glucose levels in diabetic rats is presented in Table (1). Results showed that the glucose level showed significant elevation ( $p < 0.05$ ) in diabetic rats by  $304.39 \pm 12.63$  mg/dl when compared to control, Sag and Sag+ diabetic groups ( $98.94 \pm 4.31$ ,  $96.39 \pm 4.79$ ,  $122.53 \pm 5.22$ ) mg/dl respectively. Data illustrated in Table (1) revealed the effect of oral administration of Sage tea treatment on serum lipid profile parameters in normal and diabetic rats. Diabetic rats showed significant increase ( $p < 0.05$ ) in TC, TG, LDL and VLDL respectively concurrent with significant reduction in HDL ( $p < 0.05$ ) as compared with control and Sag groups. Injection of Sage tea to normal rats had no effect on glucose levels, their values tended to match with the control value, indicating its safe use under the experimental conditions, while treatment with sage to diabetic rats significantly ( $p < 0.05$ ) ameliorated the elevation in glucose concentration compared to diabetic +sage group). The obtained result was similar to these obtained by [Eidi and Eidi,2009] who reported that oral administration of Sage extract for five weeks exhibited a significant reduction in serum glucose, triglycerides, total cholesterol, LDL and VLDL, in diabetic rats but not in normal rats. The hypoglycemic effect may be attributed to increase the hepatocyte glucose consumption, decrease fasting gluconeogenesis and inhibit the stimulation of hepatic glucose production by glucagon [7].The present results are in agreement with that of [Plana *et al.*,2008] who reported that defects in insulin action and hyperglycemia could lead to these changes, the characteristic features of diabetic dyslipidemia are a high triglyceride concentration, low HDL-C concentration and increased concentration of LDL-C. Normal rats received Sage tea showed no significant changes in these parameters compared with control rats, meanwhile diabetic rats treated with Sage exhibited significant decrease in TC, TAG, LDL and VLDL by respectively. On the other hand a significant increase was observed in HDL when compared with non treated diabetic group ( $p < 0.05$ ). Testosterone, LH, FSH level no significant decrease in diabetic male rats ( $1.02 \pm 0.13$ ,  $0.86 \pm 0.21$ ,  $1.13 \pm 0.23$ ) respectively, compared with control male ( $2.62 \pm 0.12$ ,  $1.84 \pm 0.02$ ,  $2.12 \pm 0.11$ ) Sage extract ( $3.21 \pm 0.11$ ,  $1.99 \pm 0.04$ ,  $2.96 \pm 0.15$ ) and Sag+ diabetic groups ( $2.76 \pm 0.11$ ,  $1.29 \pm 0.03$ ,  $2.31 \pm 0.11$ ). after five weeks from treated. The results obtained a significant increase in dead and morphological abnormalities sperm ( $17.29 \pm 1.78$ ,  $16.32 \pm 1.21$ )% respectively in diabetic male rats compared with control male ( $6.44 \pm 0.43$ ,  $5.42$

$\pm 0.58$ )%respectively. Sag extract( $4.63 \pm 0.23$ ,  $2.45 \pm 0.09$ )%While Sag extract +diabetic( $9.35 \pm 0.67$ ,  $8.52 \pm 0.22$ ).

**Statistical analysis:**

Results were expressed as mean  $\pm$  SE. Data were statistically analyzed for variance and the least significant difference using one way analysis of variance (ANOVA) according to [Snedecor and Cochran, 1989]. An IBM computer with a software system SPSS version 20 was used for these calculations.

**Table-1-. Effect of *Salvia officinalis* L.(300mg/kg b.wt.) on serum triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) in Alloxan-diabetic male rats, after five weeks of treatment.**

Experimental parameters	Control Means $\pm$ SE	Diabetic Means $\pm$ SE	Sage Means $\pm$ SE	Diabetic +Sage Means $\pm$ SE
Glucose mg\dl	98.94 $\pm$ 4.31 a	304.39 $\pm$ 12.63 b	96.39 $\pm$ 4.79 a	132.53 $\pm$ 5.22 c
Cholesterol mg\dl	90.94 $\pm$ 2.32 a	149.92 $\pm$ 6.72 b	87.77 $\pm$ 1.88 a	98.72 $\pm$ 4.78 c
TG mg\dl	85.20 $\pm$ 1.19 a	135.499.02 b	85.46 $\pm$ 1.12 a	90.68 $\pm$ 2.09 c
HDL mg\dl	44.12 $\pm$ 1.38 a	30.37 $\pm$ 1.24 b	31.20 $\pm$ 1.01 b	33.29 $\pm$ 1.84 b
LDL mg\dl	29.04 $\pm$ 0.24 a	92.10 $\pm$ 0.22 b	39.69 $\pm$ 0.22 c	47.54 $\pm$ 0.42 d
VLDL mg\dl	17.78 $\pm$ 1.96 a	27.45 $\pm$ 5.70 b	17.88 $\pm$ 1.98 a	18.89 $\pm$ 2.82 c

Values are Means  $\pm$  Standard Error.

Different letters refer to significant differences ( $p < 0.05$ ) compared between groups.

**Table- 2- Effect of *Salvia officinalis* L.(300mg/kg b.wt.) on sperm characterize (Count , Motility, Dead sperm and Abnormality)in Alloxan-diabetic male rats after five weeks of treatment.**

Groups	Count(million/ml) Means $\pm$ SE	Motility% Means $\pm$ SE	Dead sperm% Means $\pm$ SE	Abnormality % Means $\pm$ SE
Control	78.22 $\pm$ 0.75 a	89.19 $\pm$ 1.04 a	6.44 $\pm$ 0.43 a	5.42 $\pm$ 0.5 a
Aqueous Sage(300mg/kg)	88.21 $\pm$ 1.2 b	95.37 $\pm$ 0.32 b	4.63 $\pm$ 0.23 a	2.45 $\pm$ 0.09 b
Diabetic+ sage	80.13 $\pm$ 1.6 a	87.41 $\pm$ 1.34 a	10.35 $\pm$ 0.67 b	9.52 $\pm$ 0.22 c
Diabetic	65.18 $\pm$ 0.56 d	80.17 $\pm$ 0.48 c	17.29 $\pm$ 1.78 c	16.32 $\pm$ 1.21 d

Values are Means  $\pm$  Standard Error.

Different letters refer to significant differences ( $p < 0.05$ ) compared between groups

Table- 3- Effect of *Salvia officinalis* L.(300mg/kg b.wt.) on Testosterone, FSH and LH levels in Alloxan-diabetic male rats after five weeks of treatment.

Groups	Testosterone ng/ml Mean $\pm$ SE	FSH(mIU/ml) Mean $\pm$ SE	LH(mIU/ml) Mean $\pm$ SE
Control	2.0 2 $\pm$ 0.12 a	2.12 $\pm$ 0.11 a	1.84 $\pm$ 0.02 a
Diabetic	1.02 $\pm$ 0.13 b	1.13 $\pm$ 0.23 b	0.86 $\pm$ 0.21 b
Aqueous Sage(300mg/kg)	3.21 $\pm$ 0.11 c	2.96 $\pm$ 0.15 c	1.99 $\pm$ 0.04 a
Diabetic +sage	2.1 6 $\pm$ 0.11 a	2.31 $\pm$ 0.11 a	1.6 9 $\pm$ 0.03 a

Values are Means  $\pm$  Standard Error.

Different letters refer to significant differences ( $p < 0.05$ ) compared between groups.

## Discussion

It has been shown that patients with diabetes mellitus have increased oxidative stress and impaired antioxidant defense systems, which appear to contribute to the initiation and progression of diabetes-associated complications [Maritim *et al.*, 2003]. There is convincing experimental and clinical evidence that the generation of reactive oxygen species is increased in both types of diabetes. Normally, the level of oxidative stress is modulated by antioxidant defense systems. Diabetes-linked alterations in antioxidant defense system enzymes such as catalase, glutathione peroxidase, superoxide dismutase have been demonstrated. [Orasanu and Plutzky 2009]. However, Lipid peroxidation and antioxidant status of hepatic tissue were studied by Feillet-Coudray and associates in experimental diabetes [Feillet-Coudray *et al.*, 1999]. Herbal medicines derived from plant extracts are being increasingly utilized to treat a wide variety of clinical disease. More attention has been paid to the protective effects of natural antioxidants against chemically induced toxicities. Herbal formulations with a simultaneous antioxidant effect would thus be more useful in the management of diabetes mellitus.

Their use alone or in combination with oral hypoglycemic agents or insulin may help in the better control of blood glucose level in diabetic subjects. Natural antioxidants strengthen the endogenous antioxidant defenses from reactive oxygen species (ROS) and

restore and optimal balance by neutralizing the reactive species [Feillet-Coudray *et al.*,1999]. Consistent with the present study [Frei and Higdon,2003] reported that sage modulated antioxidant pathways to minimize stress by scavenging free radicals. This may be due to the active constituents of sage polyphenols, especially, phenolic and rosmarinic acid in sage which has potent antioxidant effect, thus protecting membrane lipids of fatty acids and phospholipids from oxidative stress. Elida *et al.* ,2010 reported that *Salvia officinalis* tea consumption is accountable for the improvement of the lipid profile inducing a decrease on the highly atherogenic LDL-C particles (which are easily oxidizable and less readily cleared) and an increase in the HDL-C, these effect may be due to the ability of *Salvia officinalis* to suppress cholesterol biosynthesis,. Moreover, demonstrated that *Salvia officinalis* L. leaves methanolic extract have a significant inhibitory effect on serum triglyceride elevation [Kianbakht *et al.*, 2001]. However, sage modulating results may attributed to several sage natural components that have been shown to act on cholesterol metabolism by reducing its absorption or its synthesis, such as catechins [Plana *et al.*,2008]. Thujone is a monoterpene that occurs mainly as a mixture of alpha and  $\beta$  diastereoisomers in many plants such as *Artemisia absinthium* L. and *Salvia officinalis* L., it lowers cholesterol and triglyceride levels. and induces oxidative stress which in turn causes lipid peroxidation [Ninomiya *et al.*,2004; Kee *et al.*,2009]. Decreased antioxidant enzymes levels and enhanced lipids peroxidation have been well documented in Alloxan-induced diabetes [Kaleem *et al.*,2006].

In the enzymatic antioxidant defense system, Superoxide dismutase (SOD )is one of the important enzymes and scavenges the superoxide radicals by converting them to H<sub>2</sub>O<sub>2</sub> and molecular oxygen. The observed decrease in SOD activity in diabetic control rats could result from inactivation by H<sub>2</sub>O<sub>2</sub> or by glycosylation of the enzyme, which have been reported to occur in diabetes. Catalase (CAT) and Glutathione peroxidase (GPX) are involved in the elimination of H<sub>2</sub>O<sub>2</sub> [Monavar-Feshani *et al.*,2010]. Saponins found in the plants extracts are suggestive of their antihyperlipidemic properties. It was shown that saponins have hypocholesterolemic activities [Oakenfull, 1996]. These results might be due to the effect of *Salvia* components, in particular vitamins C and E, flavonoids, phenolic compounds and antioxidants. These components leads to regulation of signal transduction pathway of cell growth and proliferation, induction of apoptosis, modulation of enzyme activity related to detoxification, oxidation and reduction, stimulation of the immune system and DNA repair and regulation of hormone metabolism [Oakenfull, 1996].

The results may be due to the effect of plant extract on testosterone,FSH and LH which affects the formation of type A spermatogonia and conversion of spermatocyte into a secondary spermatocyte and on intestinal cell stimulating hormone (ICSH) or spermatogenic cell stimulating hormone (SSH) responsible for the final steps of maturation of spermatids. *Salvia* plant which contains steroidal saponins. Also, essential oil of *Salvia* was shown to have certain effect on fertility and that is why many parameters under study gave positive result for *Salvia* effects [Aron and Kennedy 2008]. Other studies have shown that antioxidants within *Salvia* extract can stimulate the normal function of Leydig cells [Perry,2000]. Moreover, the presence of vitamins C and E also has a beneficial effect in the treatment of male infertility. It was concluded from this study that the use of *Salvia officinalis* might be increase fertility in male mice [Agrwal *et al.*,2005].

The improving effects of *Salvia* on male reproductive system may come from the effects of *Salvia* component –in particular vitamins C and E ,flavonoids and antioxidant

.Studies have shown that antioxidants can enhance Leydig cells normal function the use of vitamins C and E has also beneficial effects in treatment of male infertility[Lindi *et al.*,2005].It is conceivable that salvia extract administration in our study in improvement of testicular function and increased serum testosterone ,FSH and LH levels. The aqueous extract of salvia was indicated that alkaloids, terpenes, flavonoids, saponins, glycosides and steroids were present. Results exhibited that Salvia leaves extract caused a significant increase in testosterone FSH and LH level, sperm activity and total count; moreover a significant decrease in sperm mortality and abnormalities was recorder. This result reported that the presence of saponine, alkaloids in rocket extract caused a significant increase in sperm activity. This increase might be due to ability of *Salvia officinalis* extract to stimulate the growth of testes and enhance the proliferation, maturation and differentiation of spermatozoa as compared with the control group . the presence of saponine, alkaloids in salvia extract caused a significant increase in sperm activity. Results This increase might be due to ability of salvia extract to stimulate the growth of testes and enhance the proliferation ,maturation and differentiation of sperm as compared with the control group[Lima and Femandes-Ferreira ,2007, Merz and Brain ,2000].

Conclusion of this study, oral administered of *Salvia officinalis* revealed significant hypoglycemic activity in alloxan-induced diabetic rats. This effect may be attributed to its antioxidant activity and its high content of polyphenols. Therefore, it could be recommended that sage tea should be ingested to diabetic and hypercholesterolemic patients beside the usual therapy. From the observation in this study, we conclude that the aqueous extract of *Salvia officinalis* caused a positive effect on some fertility parameters and pituitary-testicular hormone axis.

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