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***BIOLOGICAL ACTIVITIES OF VITEX AGNUS-CASTUS (L.) LEAVES  
IN DIABETES CONTROL IN HIGH FAT/HIGH FRUCTOSE FED FEMALE RATS***

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**BIOLOGICAL ACTIVITIES OF VITEX AGNUS-CASTUS (L.) LEAVES  
IN DIABETES CONTROL IN HIGH FAT/HIGH FRUCTOSE FED FEMALE RATS**

*Hanaa F. El-Mehiry\**

**Abstract**

The aim of the current study is to investigate the effect *Vitex agnus castus* leaves on oxidative stress, glucose level and lipid profile in rats fed on high fat/ high fructose (HF/HFr) diet. The phenolic content as well as the antioxidant activity of the vitex leaves extract was analyzed. Rats were divided into four groups, group I received basal diet (control), group II received basal diet containing 20 g vitex leaves /kg., groups III received high fructose high fat diet and group IV received high fructose high fat diet containing 20 g vitex powder /kg diet. After 6 weeks, body weight, BMI, blood glucose, serum insulin, HOMA-index, lipid profile, leptin, resistin, TNF- $\alpha$  , total antioxidant capacity and total oxidant capacity were analyzed in the study male rats.

Results showed high phenolic content as well as antioxidant activity of the vitex leaves extract. Vitex leaves showed significant decrease in blood glucose, serum insulin, HOMA-index, leptin, resistin, TNF- $\alpha$ , total oxidant capacity while increasing the total antioxidant capacity in addition to lipid profile normalization in group IV that received high fructose high fat diet containing 20 g vitex powder /kg diet as compared to high fructose high fat diet group (group III). It can be concluded that consumption of vitex leaves can improve the lipid profile, reduce insulin resistance, blood glucose level and inflammatory cytokines as well as it can protect the body from the oxidative stress, related to their phenolic compounds. Thus, vitex leaves consumption has a beneficial effect in control and management of diabetes and diabetes associated complications with no risk of hypoglycemic effect.

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**Key words:** Hypoglycemic- Vitex leaves - Hypolipidmic-Inflammatory Cytokines

## **INTRODUCTION**

Diabetes mellitus (DM) is considered as one of the most serious diseases which that linked to hyperglycemia which occurs either when the pancreas cannot produce enough insulin, or when the body cannot effectively use the produced insulin (**Ramachandran *et al.*, 2010**). Several types of diabetes are known including type I DM, type II DM and Gestational diabetes (GDM). Millions of people worldwide are suffering from diabetes and the number of diabetics may double by the next 15 years. Diabetes have several acute and chronic complications that greatly affect human health and some of them considering as life threatening such as diabetic ketoacidosis (DKA) and hyperosmolar coma. World Health Organization (WHO) indicates diabetes as one of the major killers nowadays (**Maridass and John De Britto, 2008 and Zhang and Gao, 2016**).

Visceral obesity one of the main risks of metabolic disorders due to chronic inflammation. of metabolic disorders as result of chronic inflammation. Dysregulated production of certain inflammatory cytokines such as tumor necrosis factor alpha and interleukin - 6 by adipose tissues that exceeding the anti-inflammatory adipose tissue-derived mediators (adipokines as adiponectin) is known to stimulate a condition known as insulin resistance (**Nishimura *et al.*, 2009**).

Insulin and oral hypoglycemic drugs are commonly used for lowering blood glucose level in diabetics. However, they have numerous adverse effects including hypoglycemia, weight gain, and lactic acidosis as well as hepatic and renal dysfunction (**Tripathi and Singh, 2000**). Thus, many herbal products are commonly used as traditional medicine for diabetes treatment throughout the world (**Pushparay *et al.*, 2000**). However, no sufficient proof of the antidiabetic effect of certain medicinal plants that associated with fewer side effects. Herbal products may improve not only

glucose metabolism but also it improve antioxidant status, lipid metabolism as well as the capillary function (**Bailey and Day, 1989**).

There are many evidences that indicate the role of reactive oxygen species in different disturbance and pathological symptoms. Recently, naturally occurring antioxidant components have proved to be effective in scavenging free radicals and protecting health (**Katirae et al., 2015**). Vitex is known with different common names including chasteberry, vitex, chaste tree, Abraham's balm, lilac chastetree, or monk's pepper (**Mabberley, 2008**). Also it is a native plant to the Mediterranean costal region and central Asia and belongs to the botanical family Verbenaceae, *Vitex agnus-castus* contain rich phytochemicals such as flavonoids, alkaloids, diterpenoids, agnuside, p-hydroxybenzoic acid and precursors for steroidal hormones (**Hoberg et al., 2000**). It was used in ancient Rome and Greece as anaphrodisiac (minify sexual desire) and traditionally used as digestive aid, anti-infective, sedative, cure acne, insect repellent (**Mehlhorn et al., 2005 and Jeong-Hyun et al., 2016**), antihistaminic, anti inflammatory and antioxidant (**Meena et al., 2010**) as well as treatment of differnt female disorders including endometriosis, menopausal conditions, abnormal menstrual cycles, insufficient lactation as well as acne (**Azarnia et al., 2007 and Kannathasan et al., 2007**). Therefore, consumption and treatment with vitex agnus-castus making it a popular alternative therapy (**Diab et al., 2015**).

This study was therefore undertaken to analyze the *Vitex agnus castus* leaves effect on blood glucose level, insulin sensitivity, lipid profile, antioxidant capacity and inflammatory cytokines in experimental animals.

## **MATERIALS AND METHODS**

### ***a-Materials:***

**Vitex (*Vitex agnus-castus L.*) leaves:** Vitex leaves were obtained from Agriculture Research Center, Giza, Egypt.

**Fructose:** Fructose was purchased from the International Company for Scientific and Medical Supplies, Cairo, Egypt.

**Chemicals:** Kits for measurements of lipid profile were purchased from Diagnosticum Zrt, Budapest and those for measurements of TOC and TAC were obtained from Labor Diagnostika Nord GmbH and Co, Germany. Insulin, resistin, leptin and TNF- $\alpha$  enzyme immunoassay kits were purchased from IBL Co., Japan.

**Experimental rats:** thirty six weanling female Sprague-Dawley rats weighing 60-70 g in aged of 3 weeks were used. The animals were acclimatized for 1 week before dietary manipulation and were housed individually in cages under laboratory healthy conditions.

***b-Methods:***

**Total antioxidant capacity:** *Vitex (Vitex agnus-castus L.)* leaves extract were determined according to the method outlined in (Pellegrini *et al.*, 2003), ferric reducing antioxidant power (FRAP) and total radical-trapping antioxidant parameter (TRAP) assay (Benzie and Strain, 1999) and (Ghiselli *et al.*, 1995). The TRAP and TEAC values were expressed as micromoles of Trolox per g of plant extract while FRAP values were expressed as micromoles of Fe<sup>2+</sup> equivalents per g of plant extract.

**HPLc analysis of polyphenols and flavonoids:** 30-50 mg of extract sample (depending on the sample) was dissolved in acidified methanol (10 mL, 1% formic acid). The extract was kept at -20 °C in dark. The content of phenolic content was determined using the Folin-Ciocalteu method which based on the reduction of phosphotungstate-phosphomolybdate complex by phenolic compounds to a blue product and the absorbance was measured at 760 nm according to (Singleton and Rossi, 1965). The data were calculated according to standard curve of catechin (0.01–0.20 mg/mL), and were expressed as mg of catechin equivalents (CE) per gram of extract.

**Diets:** Two types of diets were used in this study: 1- basal diet was prepared according to (Reeves *et al.*, 1993). 2- HF/HFr diet, consisted of basal diet contain 20% fat (15% beef tallow + 5% corn oil) combined with

fructose added in drinking water at 13% w/v which is the range of concentration that reported for soft drinks (**Light et al., 2009**).

**Experimental Design:** Female rats were randomly assigned into four groups (6 rats) as follow:

Group (I): Normal control rats (ve-), received basal diet.

Group (II): Vitex group (ve+): Vitex powder treated rats, received basal diet contained 20 g vitex powder /kg/ diet according to (**Gruenwald et al., 2010**).

Group (III): High fat & high fructose-fed group (HF/HFr): fat-fructose fed rats, received high fat diet and fructose in drinking water.

Group (IV): High fat & high fructose + vitex powder group (HF/HFr + VL): vitex leaves treated fat-fructose fed rats, received high fructose high fat diet contain 20 g vitex powder /kg diet.

**Induction of diabetes:** Oral glucose tolerance tests (OGTT), twelve hours prior to day 40, rats were fasted and were subjected to OGTT. Fructose added in drinking water in HF/HFr and HF/HFr + VL groups was replaced with water for the overnight fasting period for the measurement of basal blood glucose concentrations. Basal blood glucose levels were measured in the tail vein blood using a Medisense Precision Q.I.D glucose meter (Abbott Laboratories). The rats were given 2 g/kg body weight of glucose via oral gavage as a 40% solution. Tail vein blood samples were withdrawn at 0, 30, 60, 90, and 120 min following glucose administration.

At the end of the period (6 weeks), rats were fasted overnight and the blood samples were collected directly from portal vein into non-heparinized centrifuge tubes. Serum were separated by centrifugation and then were frozen at -20 °C for biochemical analysis.

**Anthropometric measurements:** The body weight and the amount of food consumed for each animal were measured three times a week. The length of the animals was determined once a month according by

**Jeyakumar *et al.*, 2006**). Body mass index (BMI) was calculated once a month by the formula:  $BMI = \text{body mass (g)} / (\text{naso-anal distance (cm)})^2$

***Biochemical Parameters:***

**Determination of serum insulin:** Fasting serum insulin level was measured using the ultrasensitive rat insulin ELISA according to (**Thorell and Lanner, 1973**). Determined of insulin resistance was by the homeostasis model assessment (HOMA-IR) calculated as following formula:  $\text{insulin } (\mu\text{U/mL}) \times \text{glucose (mg/dl)} / 405$  (**Matthews *et al.*, 1985**) (**Matthews *et al.*, 1985**).

**Determination of serum lipids:** Serum TG, TC and HDL levels were determined by enzymatic method that had previously described by (**Fossati and Prencipe, 1982, Allain, 1974 and Burstein *et al.*, 1970**), respectively. Serum LDL levels were calculated according to the equation of **Friedwald *et al.* (1972)**.

**Determination of serum resistin, tumor necrosis factor alpha (TNF- $\alpha$ ) and leptin levels:** Fasting serum resistin, TNF- $\alpha$  and leptin were measured by enzyme-linked immunosorbent assay according the methods that had previously described by (**Thorell, 1973, Beutler *et al.*, 1985 and Maffei *et al.*, 1995**), respectively.

**Determination of antioxidant parameters:** Serum total antioxidant and oxidant capacities were measured according to (**Cao *et al.*, 1993 and Flohe and Gunzler, 1984**), respectively.

***Statistical Analysis:***

The obtained data were statistically analyzed using computerized SPSS (Statistic Program Sigmastat, Statistical Soft-Ware, SAS Institute, Cary, NC). Effects of different treatments were analyzed by one way ANOVA (Analysis of variance) test using Duncan's multiple range test and  $p < 0.05$  was used to indicate significance between different groups (**Snedecor and Cochran, 1967**).

## RESULTS

The results of the antioxidant activity of vitex leaves methanolic extract (Table 1) reveals that they have potent antioxidant activity that represented by FRAP (1278.52  $\mu\text{mol Fe}^{++}/\text{g}$ ) and TRAP (612.90  $\mu\text{mol TE}/\text{g}$ ) assays. The phytochemical screening of vitex leaves methanolic extract using HPLc analysis showed the presence of different phenolic compounds including gallic, pyrogallol, 4-amino-benzoic, catechol, caffeine, caffeic, vanillic and P-conmaric compounds as indicated by the maximum absorption ( $\lambda_{\text{max}}/\text{nm}$ ) and retention times (tR/min) of the phenolic standards (Table 2).

Analysis of the nutritional status indicators (Fig 1 & 2) revealed that the differences in feed intake, body weight gain and body mass index (BMI) between rats belonging to different study groups were insignificant except for group III (High fat high fructose-fed (HF/HFr) group) which showed significant reduction in feed intake in addition to significant increase in body weight gain as well as the final BMI when compared to the control and group II. Although, the final BMI of group III was significantly higher than group IV, the difference in both feed intake, body weight gain was insignificant indicating slight effect of vitex leaves in decreasing the BMI in overweight rats.

The results in (Fig. 3) showed that the blood glucose level in both group III and group IV was significantly higher than that in group II and the control group. However, the blood glucose level in group IV it was significantly lower than that of group III indicating the antihyperglycemic effect of the vitex leaves. The Serum insulin level was significantly reduced only in group IV (Fig. 4), despite the presence of high glucose level when compared to the other groups while no significant difference in HOMA-index when compared to group II and the control group (Fig 5). In addition, HOMA-index was significantly higher in group III when compared to the other groups which indicate the effect of vitex leaves on increasing the insulin sensitivity.

Lipid profile analysis (Fig. 6) revealed that group III has significantly the highest levels of triacylglycerols, total cholesterol, LDL-C and VLDL-C while having the lowest level of HDL-C which indicate the negative effect of HF/HFr diet on the lipid profile. On the other hand, group IV has significantly the lowest levels of triacylglycerols, total cholesterol and VLDL-C while having the highest level of HDL-C although the LDL-C level was similar to that in group II and the control group (insignificant difference). The results indicate the great effect of vitex leaves in control of dyslipidemia.

Group III has significantly the highest Leptin, resistin, TNF- $\alpha$  levels and total oxidant capacity while has the lowest Total antioxidant capacity compared to the other groups. Although the resistin and TNF- $\alpha$  levels in groups IV were found to be the lowest among the study groups, the reduction was insignificant when compared with group II and the control group (Table 3). These results confirm the antioxidant effect of vitex leaves.

## **DISCUSSION**

Diabetes mellitus is a chronic disease that associated with a higher blood glucose level in the peoples (**Duncan et al., 2003**). It was reported that the leaves, flowers and fruits of *Vitex agnus-castus* L. contained flavonoids, tannins, diterpenoids and iridoids which showed different pharmacological properties (**Hoberg et al., 2000 and Eugenio et al., 2012**). In the present study, vitex methanolic extract contained high concentration of phenolic components and possessed high potent antioxidant activity that represented by FRAP and TRAP assays. The phytochemical screening revealed the presence of different phenolic compounds including gallic, pyrogallol, 4-amino-benzoic, catechol, caffeine, caffeic, vanillic and P-conmaric compounds. The correlation between the antioxidant activity and the total phenolic content was reported previously (**Van Acker et al., 2000 and Sarikurkcu et al., 2009**). Tannins are the most antioxidants present in the human diet and they are involved in protection against degenerative diseases and oxidative stress, gallic acid showed potent antioxidant activity

by preventing lipid per-oxidation (**Shahrzad et al., 2001**). Based on the obtained data, the vitex has antioxidant activity, related to the phenolic content which promoting possible health benefits, thus it can serve as an excellent natural source of antioxidant agents.

The effect of vitex leaves on the BMI and weight gain is controversial, results showed significantly low final BMI in HF/HFr fed rats treated with vitex leaves (group IV) when compared to the HF/HFr fed rats (group III) although the weight gain difference was insignificant. This indicates the minor effect of vitex leaves on lowering the BMI and weight gain. On the other hand, weight gain was reported as a rare side effect for vitex consumption (**Brown, 1994**)

Feeding the rats on HF/HFr diet for 6 weeks led to development of hyperglycemia with high significant increase in serum glucose, insulin and HOMA-index (group III). The obtained data a showed a significant decrease in blood glucose, serum insulin and HOMA-index in vitex leaves treated rats (group IV), when compared with the hyperglycemic rats (group III) while no hypoglycemic effect was observed in normal glycemc rats (group II and the control group). The possible mechanism of vitex leaves antihyperglycemic action may be through variety of mechanisms such as acting like insulin, modifying glucose utilization (**Sezik et al., 2005**) and enhance blood glucose transport to the peripheral tissues (**Bopanna et al., 1997**). There are different approaches for quantitative determination of insulin resistance as well as beta-cell function, however, HOMA-index is found to be the most suitable mode (**Wallace and Matthews, 2002**). Maybe to positive effect of antioxidants on HOMA-index has been shown in healthy people (**Vincent et al., 2009**). Administration of vitex leaves can decrease HOMA- index and improve the metabolism of glucose which confirm its role in controlling hyperglycemia.

In the present study, feeding the rats on HF/HFr diet for 6 weeks (group III) led to development of dyslipidemia with obvious high significant increase in serum triacylglycerol, total cholesterol, LDL-Cholesterol, VLDL-Cholesterol while significantly decrease the HDL-Cholesterol level

when compared to normal lipidemic groups (group II and control group) that fed on normal standard diet. These changes may be related to that HF/HFr diet can induce dyslipidemia by demodulating lipid metabolism, mainly by decreasing  $\beta$ -oxidation, increasing cholesterol synthesis and oxidative stress (**Rui *et al.*, 2008** and **Jeong-Hyun *et al.*, 2016**). In addition, it was reported that high fat diet can induce abnormal increases in serum concentrations of triacylglycerol, total cholesterol, low-density lipoprotein cholesterol and lipid peroxidation, in addition to depressed antioxidant defense system (**Yan *et al.*, 2006**). The serum lipid profile in group IV was normalized using vitex leaves despite feeding on HF/HFr diet in comparison with non-treated group (group III) and even found to be better than that of the control group indicating the positive effect of vitex leaves in the control of dyslipidemia. This effect may be due to certain chemical constituents such as polyphenols or terpens in vitex leaves which possess good oxygen radical scavenging potential (**Mu and Porsgaard, 2005**). Flavonoids can dramatically lower cholesterol levels and the rate of formation of oxidized (LDL) (**James aand Anderson, 1994**).

There are many evidences concerning the role of inflammation in the pathophysiology of diabetes (**Yudkin, 2003**). Abnormal production of inflammatory cytokines such as TNF- $\alpha$  and IL-6 by adipose tissues over the anti-inflammatory humoral mediators (adipokines) is known to induce insulin resistance (**Nishimura *et al.*, 2009**). Insulin resistance is defined as a state in which certain concentration of insulin leads to a lower biological effect than-expected. Thus, controlling diabetes and insulin resistance can be achieved via modulation of inflammatory cytokines and adipokines (**Garcia-Diaz *et al.*, 2010** and **Zhang and Gao, 2016**). Free radicles generation cause exhaustion in the endogenous antioxidants (**Pessayre *et al.*, 2002**) and can cause hepatic inflammation by activation the inflammatory cytokines (**Weisberg *et al.*, 2008**).

Leptin is a peptide hormone as an adipokine that regulate energy intake and expenditure (**Brennan and Mantzoros, 2006**). Leptin could inhibit the development of obesity via stimulation of the satiety centers in

brain (DePaoli, 2014). Leptin is synthesized primarily in the adipocytes and its level is proportional to the total body fat (Fischer *et al.*, 2002). Most of obese peoples have deficiency in leptin receptors, which lead to leptin resistance (Tartaglia *et al.*, 1995). Several investigations have shown that high leptin level is associated with increased risk of developing diabetes (Tong *et al.*, 2005). It was reported that leptin level in diabetic patients is higher than normal. This confirmed the positive correlation between insulin resistance and leptin level (Fischer *et al.*, 2002). The results showed that administration of vitex leaves significantly could decrease serum leptin level (group IV) when compared to group III and its level has reached slightly less than that in both the control group and group II.

TNF- $\alpha$  is an adipocytokine that involved in systemic inflammation (Moller, 2000) and is secreted by macrophages and variety of cells including adipocytes (Gimeno and Klamann, 2005). TNF- $\alpha$  inhibits insulin transduction and affect on glucose metabolism (Zou and Shao, 2008). The correlation between insulin resistance and TNF- $\alpha$  in type 2 DM has been reported. The TNF- $\alpha$  concentration in diabetic patients and impaired glucose tolerance was found to be higher than in normal individuals (Yudkin, 2003 and Swaroop *et al.*, 2012). The obtained results showed that vitex leaves could decrease serum level of TNF- $\alpha$  as in group IV when compared to group III and its level has nearly reached that in the control group and group II.

Resistin, a cysteine-rich adipokine which is induced during adipogenesis, and can modulate numerous steps in the insulin-signaling pathway leading to insulin resistance (Asano *et al.*, 2010). In vitro studies in adipocytes showed that resistin neutralization with resistin antiserum led to enhanced glucose uptake and decreased insulin resistance. Studies in high-fat diet-induced obese mice showed increased levels of resistin while immunoneutralization of resistin in these animals resulted in improved insulin sensitivity (Steppan and Lazar, 2002). Resistin can also function as a proinflammatory molecule in vitro as well as in vivo and can modulate several molecular pathways involved in inflammatory responses, such as

increasing the production of the proinflammatory cytokines (**Jamaluddin et al., 2012**). The current data showed that vitex leaves could decrease serum level of resistin (IV) when compared to group III and its level has nearly reached that in both the control group and group II. With regard to the above-mentioned facts, vitex leaves administration is able to diminish serum levels of leptin TNF- $\alpha$  and resistin could be important in the control of diabetes, indicating its role in controlling diabetes and diabetic complication by increasing insulin sensitivity and decreasing the levels of the inflammatory cytokines.

Free radicals have variety of adverse effects on cells, resulting in many disorders. Phenolic components in plants can act as free radical scavengers that resulted in delay or prevention of oxidative stress caused by free radicals. Recently, plant materials that proved to be rich in phenolic components are widely used as foods therapies, because of their protective role and enhancing well being and health (**Kahkonen et al., 1999**). The present results revealed that group III has significantly the highest total oxidant capacity while has the lowest total antioxidant capacity as compared to the other groups. On the other hand, vitex leaves could significantly decrease the total oxidant capacity and increasing the total antioxidant capacity as shown in group IV when compared to group III and their level has nearly reached that in both the control group and group II. These results confirm the antioxidant effect of *Vitex agnus-castus* L. leaves. As mentioned previously, the free radical scavenging activity of vitex may be due to certain chemical constituents such as polyphenols or terpenes which possess good oxygen radical scavenging potential (**Mu and Porsgaard, 2005**).

### **CONCLUSION**

In conclusion, according to the obtained results, it seems that vitex leaves could induce inhibitory effects on inflammatory cytokines such as TNF- $\alpha$ , and leptin in addition to resistin level. It also can improve the lipid profile, insulin sensitivity, hyperglycemia control and the total antioxidant capacity with relieving of the oxidative stress. Therefore, consumption of Vitex leaves could be beneficial for control of diabetes and diabetes associated complications.

**Table 1:** Antioxidant activity of plant extract of vitex leaves

Antioxidant assay	FRAP ( $\mu\text{mol Fe}^{++}/\text{g}$ )	TRAP ( $\mu\text{mol TE}/\text{g}$ )
Vitex leaves	1278.52	612.90

FRAP: Ferric reducing antioxidant power

TRAP: total radical-trapping antioxidant parameter

**Table 2:** Retention times (tR/min) and maximum absorption ( $\lambda_{\text{max}}/\text{nm}$ ) of the phenolic standards and their correlation with the compounds of in vitex leaves.

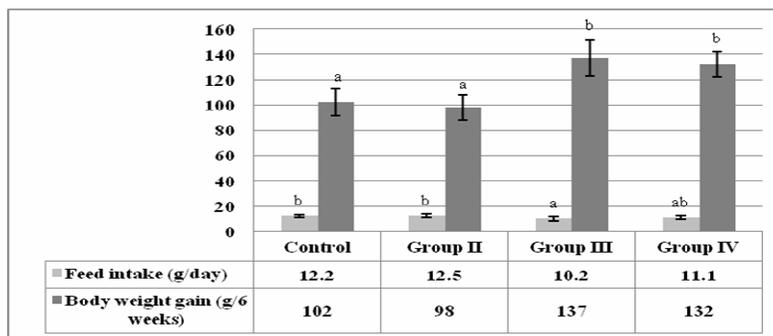
phenolic compound	RT /min	$\lambda_{\text{max}}/\text{nm}$
Gallic	6.9	10.96
Pyrogallol	9.3	31.47
4-Amino-benzoic	15.3	4.99
Catechol	17.9	27.11
Caffeine	18.5	21.21
Caffeic	19.3	290.20
Vanillic	20.1	218.16
P-conmaric	21.3	3.11

**Table 3:** Effect of vitex leaves on serum leptin, resistin, TNF- $\alpha$ , total antioxidant capacity and total oxidant capacity in female rats

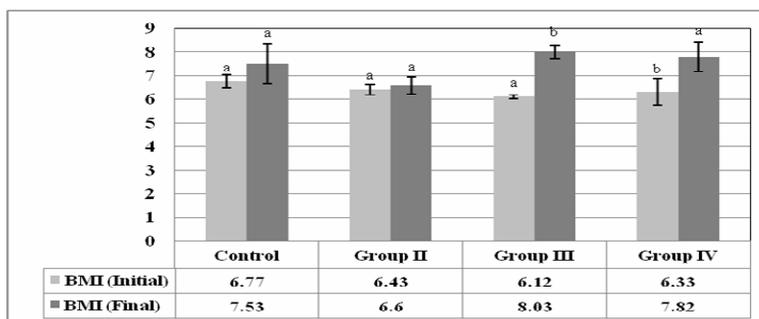
Parameters Groups	Leptin (pg/ml)	Resistin (ng/ml)	TNF- $\alpha$ (pg/ml)	Total antioxidant capacity (mmol/L)	Total oxidant capacity (mmol/L)
Control	2.83 $\pm$ 0.1a	3.85 $\pm$ 0.04ab	3.8 $\pm$ 0.11a	1.76 $\pm$ 0.04c	0.236 $\pm$ 0.012a
Group II	2.98 $\pm$ 0.31ab	3.81 $\pm$ 0.06ab	3.73 $\pm$ 0.17ab	1.78 $\pm$ 0.06c	0.235 $\pm$ 0.01a
Group III	4.63 $\pm$ 0.066d	4.45 $\pm$ 0.04c	4.7 $\pm$ 0.126cd	1.14 $\pm$ 0.013a	0.365 $\pm$ 0.014c
Group IV	3.05 $\pm$ 0.11ab	3.51 $\pm$ 0.47a	3.296 $\pm$ 0.05ab	1.64 $\pm$ 0.02c	0.286 $\pm$ 0.01ab

The values are expressed as mean  $\pm$  SEM (n= 6 rats/ group).

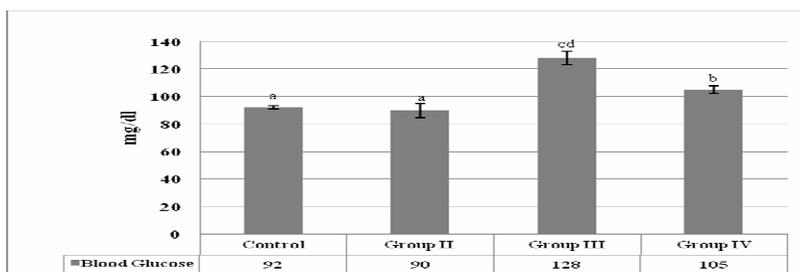
Values with the same letters indicate insignificant difference and vice versa.



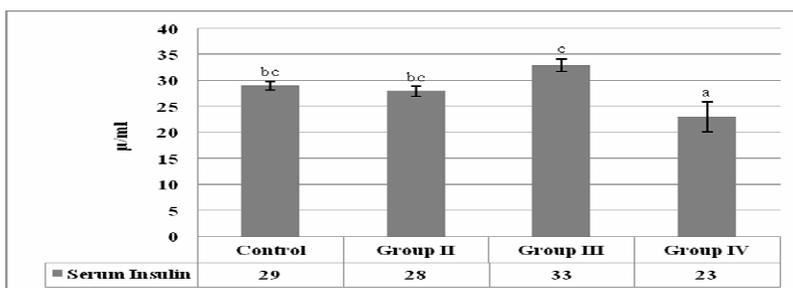
**Fig. 1:** Effect of vitex leaves on feed intake and body weight gain in female rats, the values are expressed as mean  $\pm$  SEM (n= 6 rats/ group). Values with the same letters indicate insignificant difference and vice versa.



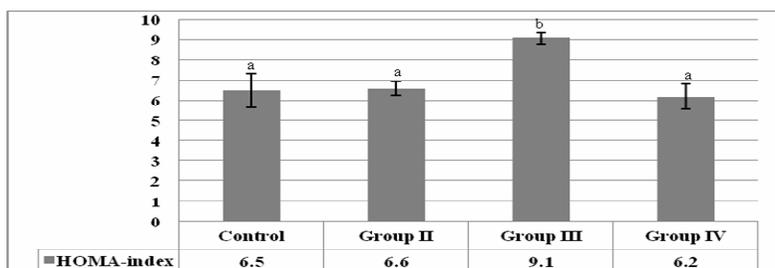
**Fig. 2:** Effect of vitex leaves on BMI (g/cm<sup>2</sup>) in female rats, the values are expressed as mean  $\pm$  SEM (n= 6 rats/ group). Values with the same letters indicate insignificant difference and vice versa.



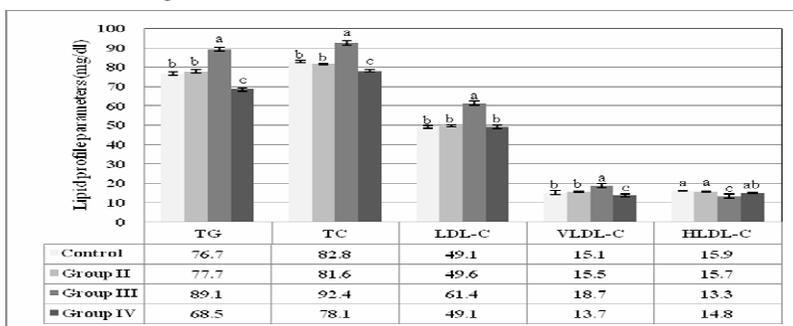
**Fig. 3:** Effect of vitex leaves on blood glucose in female rats, the values are expressed as mean  $\pm$  SEM (n= 6 rats/ group). Values with the same letters indicate insignificant difference and vice versa.



**Fig. 4:** Effect of vitex leaves on serum insulin in female rats, the values are expressed as mean  $\pm$  SEM (n= 6 rats/ group). The different letters means that there is a significant difference between groups at  $p < 0.05$  and vice versa.



**Fig. 5:** Effect of vitex leaves on HOMA-index in female rats, the values are expressed as mean  $\pm$  SEM (n= 6 rats/ group). Values with the same letters indicate insignificant difference and vice versa.



**Fig. 6:** Effect of vitex leaves on serum lipid profile in female rats, the values are expressed as mean  $\pm$  SEM (n= 6 rats/ group). Values with the same letters indicate insignificant difference and vice versa, TG: Triglycerides, TC: Total cholesterol, HDL-c: High density lipoprotein cholesterol, LDL-c: Low density lipoprotein cholesterol.

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## التأثيرات الحيوية لأوراق نبات كف مريم في السيطرة على مرض السكري في إناث الفئران المغذاه على حمية عالية في الدهون والفركتوز

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### الملخص العربي

يهدف هذا البحث إلى دراسة تأثيرات أوراق نبات كف مريم على الأكسدة، مستوى السكر في الدم ومستوي الدهون في الفئران وتحليل المركبات الفينولية المتواجدة في أوراق النبات. تم تقسيم الجرذان إلى ٤ مجموعات وتغذت لمدة ٦ أسابيع كالاتي:

- المجموعة الأولى تم تغذيتها بالوجبة القياسية، كمجموعة الضابطة السالبة.
- المجموعة الثانية تم تغذيتها بالوجبة القياسية، وتحتوى على ٢٠ جرام/كجم من أوراق نبات كف مريم.
- المجموعة الثالثة تم تغذيتها بالوجبة القياسية بالإضافة إلى دهون عالية و الفركتوز .
- المجموعة الرابعة تم تغذيتها بالوجبة القياسية بالإضافة إلى دهون عالية والفركتوز وإضافة ٢٠ جرام/كجم من أوراق نبات كف مريم.

وقد أظهرت النتائج احتواء أوراق نبات كف مريم على نسب عالية من المركبات الفينولية المضادة للأكسدة. كما أدى تناول الحمية العالية في الدهون والفركتوز إلى زيادة الوزن وارتفاع مستوى السكر وكذلك مستوى الأنسولين في الدم مع ارتفاع مؤشر مقاومة الأنسولين HOMA وكذلك ارتفاع مستوى الجلوسريدات الثلاثية والكوليسترول الكلي وكوليسترول البروتين الشحمى منخفض الكثافة والليبتان والريسيسيتين وعامل نخر الورم و إجمالي قدرة الأكسدة مع انخفاض في نسبة كوليسترول البروتين الشحمى عالي الكثافة وإجمالي القدرة المضادة للأكسدة مقارنة بالمجموعة الضابطة. ومن جهة أخرى فإن إضافة أوراق نبات كف مريم إلى الحمية العالية في الدهون والفركتوز قد أدى الي تحسن ملحوظ في جميع القياسات السابقة.

**توصي الدراسة :** بتناول أوراق نبات كف مريم حيث أنه غني بالمركبات الفينولية والمضادة للأكسدة. كما أنه فعال في تحسين مستوى الدهون وتقليل مقاومة الأنسولين مما يعمل على ضبط نسبة السكر بالدم ، كما ان لها تأثير ملحوظ في تقليل نسبة السيتوكينات الالتهابية وحماية الجسم من مخاطر الأكسدة .

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