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EFFECT OF GARLIC (ALLIUM SATIVUM) WATER EXTRACT AND VITAMIN E ON ALLOXAN-NICOTINAMIDE ADULT MALE DIABETIC RAT

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ABSTRACT

Background: Garlic contains a variety of effective compounds that exhibit variable activities. **Aim of work:** This study was carried out to assess the effect of treatment with I.P. injection of water garlic extract (500mg/kg BW) and/or vitamin E orally (500mg/kg BW) on blood glucose, insulin levels and lipid profile in diabetic male albino rats. **Materials and Methods:** Fifty four rats of local strain were used. The animals were divided into six equal groups: Normal control group, normal garlic-treated group, normal vitamin E-treated group, diabetic control group, diabetic garlic-treated group, and diabetic garlic- and vitamin E-treated group. Diabetes mellitus was induced by a single IP injection of alloxan (160 mg/kg). This was preceded by single IP injection of nicotinamide (110 mg/kg) to alleviate alloxan toxicity. The procedure was continued for 5 weeks. Blood samples were taken at the beginning of the experiment and at the end of 3rd and 5th week. **Results:** Diabetic control group showed significant elevation of blood glucose and lipid profile, whereas insulin levels and body weight significantly reduced. Diabetic group treated with garlic extract showed significant improvement in blood glucose, insulin, lipid profile and body weight. Diabetic group treated with garlic extract and vitamin E showed significant improvement in blood glucose and lipid profile. Also, there was progressive detectable improvement through the experiment in both insulin levels and body weight. **Conclusion**: Garlic therapy has a marked effect on improvement of blood glucose, insulin level and lipid profile in adult male albino diabetic rats.

INTRODUCTION

Garlic (Allium sativum) has been used medicinally since antiquity. The current state of knowledge does not recognize garlic as a true alternative to established methods of disease prevention or treatment, but it will likely find a place for garlic as a complement to established methods of disease prevention and treatment **(Rivlin, 2005)**. Garlic contains a variety of effective compounds that exhibit antioxidant, antiplatelet, anti-coagulant, hypocholesterolemic, hypoglycemic, antibiotic, anticancer, as well as hypotensive activities **(Thomson et al., 2007).**

Tissue damage associating diabetes occurs through five major mechanisms: **(1)** increased flux of glucose and other sugars through the polyol pathway; **(2)** increased intracellular formation of AGEs (advanced glycation end products); **(3)** increased expression of the receptor for AGEs and its activating ligands; **(4)** activation of protein kinase (PK)C isoforms; and **(5)** overactivity of the hexosamine pathway. All these five mechanisms are activated by a single upstream event which is mitochondrial overproduction of reactive oxygen species "ROS" **(Giacco and Brownlee, 2010).**

Vitamin E is the most important lipid-soluble antioxidant. Vitamin E occurs in nature in at least eight different isoforms: α-, β-, γ- and δ-tocopherols and α-, β-, γ- and δ-tocotrienols. Humans absorb all forms of vitamin E **(Lester et al., 2001).** In addition to being antioxidant and supporting fertility, α-tocopherol inhibits smooth muscle cell proliferation, decreases protein kinase C activity, increases phosphoprotein phosphatase 2A activity, and controls expression of the α-tropomyosin gene **(Regina and Traber, 1999).**

This work was directed to study the effect of aqueous garlic extract and vitamin E on blood glucose, insulin level

and lipid profile in alloxan-nicotinamide-induced diabetes mellitus.

MATERIAL AND METHODS

Animals: Fifty four adult male albino rats of local strain, 8 weeks of age and weighing from 150 to 180 g, were chosen as an animal model for this study. They were kept in suitable cages (20x32x20 cm for every 4 rats) at room temperature with the natural light-dark cycle. They were maintained on a standard diet of commercial rat chow and tap water. They were kept for 10 days for the adaptation to the new environment before the start of the experiment in the department of Physiology, Al-Azhar Faculty of Medicine. The animals were divided into six equal groups:

1. **Normal control group:** Each rat has been injected intraperitoneally (I.P.) by 0.5ml of normal saline daily.
2. **Normal garlic-treated group:** Each rat has been injected I.P. with 500mg/kg BW aqueous garlic extract daily (Thomson et al., 2007).
3. **Normal vitamin E-treated group:** Each rat has received 500mg/kg BW of vitamin E by gavaging daily (Siman and Erikson, 1997).
4. **Diabetic control group:** After induction of diabetes, each rat has been injected I.P. by 0.5ml of normal saline daily.
5. **Diabetic garlic-treated group:** After induction of diabetes, each rat has been injected I.P. with 500mg/kg BW aqueous garlic extract daily.
6. **Diabetic garlic- and vitamin E-treated group:** After induction of diabetes, each rat has been injected I.P. with 500mg/kg BW aqueous garlic extract and also given 500mg/kg BW of vitamin E by gavaging daily.

The procedure was continued for 5 weeks.

Induction of diabetes: Rats were starved for 24 hours in specific cages with a perforated floor, in order to avoid coprophagia. In the next day, nicotinamide was dissolved in 0.9% NaCl. Each rat was weighed and injected with the nicotinamide intraperitoneally at a dose of 110 mg/kg BW **(Madkor et al., 2011).** After about 20 minutes, alloxan was dissolved in 0.9% NaCl and injected intraperitoneally at a dose of 160 mg/kg BW **(Szkudelski, 200).** Just before alloxan injection, 2ml of glucose (5%) were given orally. After 48 hours, blood samples were taken from tail vein for blood sugar estimation. Rats with blood sugar higher than 200mg/dl were considered diabetic.

Aqueous extract of garlic: Aqueous garlic extract was prepared from locally available fresh garlic bulbs. The garlic bulbs were peeled on crushed ice. Fifty grams of the peeled garlic were cut into small pieces and homogenized in 70 ml of cold sterile 0.9% NaCl in the presence of some crushed ice. Homogenization was carried out in a blender using twenty bursts each in about 30 seconds (total time of homogenization was about ten minutes). The homogenized mixture was filtered three times through cheesecloth. The filtrate was then centrifuged at 4000 rpm for 10 minutes and the clear supernatant was diluted to 100 ml with normal saline. The concentration of this garlic preparation was considered to be

500 mg/ml on the basis of the weight of the starting material (50 g/100 ml). The aqueous extract of garlic was stored in small aliquots at -20°C **(Thomson et al., 2007).**

Vitamin E (Pharco Pharmaceuticals Company): Vitamin E oily content was evacuated from capsules and dissolved in a small volume of sunflower oil. Each 2 grams of vitamin E (5 capsules each contained 400mg vitamin E.) were dissolved in 8ml of sunflower oil. The total volume of the solution after addition of the capsules content to the oil was 10 ml. Depending on the basis of the weight of the starting material (2 g/10 ml), the concentration was considered to be 100mg/ml **(Traber, 2007).**

Changes in food consumption and body weight were measured.

At the beginning of the experiment and at the end of 3rd and 5th weeks, blood samples were collected from the retro-orbital venous plexus by using a heparinized capillary tube (about 0.75 - 1.0mm internal diameter) inserted in the medial canthus medial to the eye globe. The collected blood samples were kept in dry clean graduated plastic centrifuge tubes until coagulated, then centrifuged at 5000 rotations per minute for about 15 minutes to separate the serum. Most of the serum was sucked out into Eppendorf tubes and stored frozen at -20°C till used for the determination of:

- Total Cholesterol (TC).
- Tri acyle glycrols (TAG_s).
- High density lipoproteins (HDL).
- Low density lipoproteins (LDL).
- Glucose.
- Insulin.

One way ANOVA test followed by post-hoc test was used through the computer SPSS version "17". Significance was considered when $P < 0.05$.

RESULTS

During the experiment, changes in body weight and food consumption in different groups were more or less concomitant together. There were significant difference in body weight and food consumption of group V when compared with the corresponding values of group IV. Increase in body weight was associated with increase in food consumption and vice versa (Table1).

Table (1): Changes in body weight and food consumption (Mean ± SD).

Parameters	Group / Time	Group "1" normal receiving saline I.P.	Group"2" normal receiving garlic extract I.P.	Group"3" normal receiving vitamin E orally	Group "4" diabetic receiving saline I.P.	Group"5" diabetic receiving garlic I.P.	Group"6" diabetic receiving garlic I.P. & vitamin E orally
Body weight (grams)	At the beginning of the experiment	123.3 ± 10.5	140.3 ± 11.9	148.2 ± 31.6	132.6 ± 24.4	141.9 ± 15.3	136.7 ± 18.7
	At the end of the 3rd week	166.6 ± 17.7	170 ± 26.1	175 ± 21.4	122.6 ± 24.1	144.1 ± 15.8	133.3 ± 18.2
	At the end of the 5th week	166.6 ± 16.5	161.8 ± 25	159.2 ± 28.8	122.3 ± 15.5	149.4 ± 16.3	135.1 ± 16.8
Food Consumption (grams)	At the end of the 5th week	112.9 ± 23.4	108.6 ± 30.1	97.1 ± 20.6	48.6 ± 15.4	72.6 ± 15.4	71.4 ± 14.3

There were significant difference in blood glucose and insulin levels of group V when compared with the corresponding values of group IV. There was a concomitant inverse relationship between blood glucose and insulin. Decrease in blood glucose was associated by increase in insulin level and vice versa (Table 2).

Table (2): Changes in blood glucose and insulin levels (Mean±SD).

Parameters	Group / Time	Group "1" normal receiving saline I.P.	Group"2" normal receiving garlic extract I.P.	Group"3" normal receiving vitamin E oral	Group "4" diabetic receiving saline I.P.	Group"5" diabetic receiving garlic I.P.	Group"6" diabetic receiving garlic I.P. & vitamin E oral
Glucose level (mg/dl)	At the beginning of the experiment	110.1 ± 25.1	98.3 ± 14.1	113.3 ± 21	420.6 ± 25.9	407.9 ± 16.5	406.6 ± 17.9
	At the end of the 3rd week	113 ± 9.8	120.2 ± 12.5	116.6 ± 12.5	426 ± 20.4	380.2 ± 50.8	396.9 ± 28.8
	At the end of the 5th week	100.7 ± 14.6	108.9 ± 8.8	105.9 ± 9.1	431.8 ± 15.5	351.9 ± 71.7	373.4 ± 15.5
Insulin level (ng/dl)	At the beginning of the experiment	29.3 ± 3.3	31.9 ± 3.5	29.7 ± 2.9	5.9 ± 1.1	5.5 ± 1.1	5.3 ± 1.5
	At the end of the 3rd week	30.5 ± 2.1	33.9 ± 3.6	31.7 ± 2.2	5.1 ± 0.9	7.4 ± 2.2	6.7 ± 1
	At the end of the 5th week	32.1 ± 3.3	34.1 ± 4.1	35.3 ± 3.6	5.4 ± 0.7	9.4 ± 4.3	7.5 ± 1.2

Diabetic group injected with saline IP (group IV) showed significant elevation of total cholesterol, TAGs and LDL. Diabetic group treated with garlic extract IP (group V), or with garlic extract IP and oral vitamin E (group VI) showed significant improvement in cholesterol, TAGs, and LDL. (Table 3).

Table (3): Changes in lipid profile (Mean ± SD).

Parameters	Groups / Time	Group "1" normal receiving saline I.P.	Group"2" normal receiving garlic extract I.P.	Group"3" normal receiving vitamin E oral	Group "4" diabetic receiving saline I.P.	Group"5" diabetic receiving garlic I.P.	Group"6" diabetic receiving garlic I.P. & vitamin E oral
Cholesterol level (mg/dl)	At the beginning of the experiment	105.6 ± 13	99.7 ± 12.2	99.3 ± 15.2	113.2 ± 10	103.4 ± 13.6	102.4 ± 11.5
	At the end of the 3rd week	100.9 ± 15.1	88.6 ± 7.3	96.8 ± 9.8	122.1 ± 8.7	106.2 ± 11.9	100.9 ± 19.4
	At the end of the 5th week	100.2 ± 21.5	92.7 ± 10	93.3 ± 15.2	122 ± 12.3	92.3 ± 14.5	98.8 ± 16.4
TAG_s level (mg/dl)	At the beginning of the experiment	93.6 ± 14.7	87.8 ± 13.2	92.3 ± 16.3	100.9 ± 8.9	102 ± 14.3	102.8 ± 16.7
	At the end of the 3rd week	96.8 ± 15	93.8 ± 7	92.8 ± 5.7	113.6 ± 11	86.4 ± 9.4	94.8 ± 15.3
	At the end of the 5th week	97 ± 11.4	91.9 ± 12.5	90.4 ± 7.9	116.8 ± 15.5	87.4 ± 12.8	87.9 ± 12.3
HDL level (mg/dl)	At the beginning of the experiment	38.2 ± 3.5	39.7 ± 2.9	39.1 ± 3	37.8 ± 2.3	37.2 ± 2.4	38.1 ± 3.8
	At the end of the 3rd week	38.3 ± 2.5	37.8 ± 4.2	38.1 ± 2.8	38.6 ± 3.8	38.9 ± 3.3	39.9 ± 4.3
	At the end of the 5th week	39.1 ± 4.7	39.3 ± 5	38.1 ± 4.9	36.3 ± 2.4	36.6 ± 2.3	39.6 ± 3.4
LDL level (mg/dl)	At the beginning of the experiment	48.6 ± 15.5	42.4 ± 10.9	41.8 ± 14.2	54 ± 9.3	45.8 ± 13.4	43.8 ± 6.8
	At the end of the 3rd week	43.2 ± 16.7	32 ± 9.2	40 ± 9.1	60.8 ± 9.7	50 ± 10.7	42 ± 19.9
	At the end of the 5th week	41.7 ± 23.5	35 ± 7.3	37.1 ± 15.6	62.3 ± 15.2	38.2 ± 14.8	41.6 ± 17.1

DISCUSSION

Insulin is an anti-lipolytic and anabolic hormone besides being the main regulator of blood glucose. Also, when insulin is deficient, cells are starved from glucose and this lead to breakdown of fat and proteins to supply cells with fuel and hence body weight decreases. With garlic treatment, insulin level and sensitivity increase and glucose utilization by the cells improves and this will restrain the breakdown of body proteins and fats with subsequent increase in body weight.

Severe hypoglycemia occurs after alloxan injection as a result of release of insulin from injured β-cells which may cause death of the animal and this was prevented by giving oral glucose just before injection of alloxan **(Zobali et al., 2002).** To alleviate its toxicity on β cells, a single intraperitoneal injection of nicotinamide was given before alloxan. The inhibitor of poly ADP-ribose synthase, nicotinamide, is effective in attenuating alloxan- and streptozotocin-induced β-cell toxicity **(Wilson, 1984).** Fragmentation of

DNA of pancreatic islets takes place in β cells exposed to alloxan. DNA damage stimulates poly ADP-ribosylation. Inhibitors of poly ADP-ribosylation, including nicotinamide, can partially restrict alloxan toxicity. This effect is, however, suggested to be due to the ability to scavenge free radicals rather than to a restriction of poly ADP ribosylation initiated by alloxan **(Ebelt et al., 2000).**

In the present study, there was a significant increase of glucose level and a significant decrease in insulin level in diabetic group (IV) when compared with the control group (I). This was due to production of excess ROS in β-cells of the pancreas in alloxan-treated animals. These ROS produced damage of these cells. This was compatible with **Bromme et al. (2001)** who stated that β-cell damage induced by alloxan occurs through the noxious oxygen free radicals such as O^{-}_{2}, H_2O_2 and malondialdehyde (MDA). This was also in agreement with **Green et al. (2004)** who mentioned that reactive oxygen species produced by alloxan treatment lead to breakdown of DNA strands. Such damaged DNA activates nuclear poly-synthetase which depletes the cellular pool of NAD^+, resulting in β-cell damage. **Szkudelski (2001)** stated that the toxic action of alloxan on pancreatic β cells is the sum of several processes such as generation of free radicals, DNA damage, oxidation of essential SH groups, inhibition of glucokinase and disturbances in intracellular calcium homeostasis.

In the present study, there was a significant increase of cholesterol, TAGs and LDL in diabetic group (IV) when compared with the control group (I). These results were compatible with the findings of **Chaiulo and Kirienko (1980), Abd el Mohsen et al. (1997), Thomson et al. (2007) and Ali & Agha (2009)** who found that cholesterol, TAGs and LDL levels showed significant elevations in diabetic animals when compared with normal ones. Also, **Bennion and Grundy (1977)**, **Abbat & Brunzell (1990)** and **Laakso (1996)** reported that elevated serum cholesterol and TAGs levels occur in both type I and type II diabetes, and tend to fall toward normal with control of hyperglycemia.

Free fatty acids (FFA) are stored as triglycerides in adipocytes and serve as an energy source during fasting conditions. Insulin is a potent anti-lipolytic hormone and restrains the release of FFA (lypolysis) from the adipocyte by inhibiting the enzyme hormone sensitive lipase. So, insulin deficiency causes enhancement of lipolysis within the adipose tissue. This in turn results in increase of free fatty acids flux to the liver and drives cholesterol, TAGs and LDL synthesis and secretion **(Arvindan, 2005).** Also, cholesterol synthesis is found to be greater in the gut of diabetic animals than in controls. This enhancement of sterol synthesis occurs soon after the onset of the disease and causes elevation in plasma cholesterol concentrations **(Lee et al., 2004).**

Cholesterol acyltransferase activity in intestinal mucosa is increased in diabetic rats. Therefore, an enhancement of cholesterol acyltransferase-dependent cholesterol esterification in the intestine might be one of the major factors that are responsible for hypercholesterolemia in diabetes **(Jiao et al., 2003). Niall et al.**

(1990) found that intestinal HMG-CoA reductase activity, a key enzyme in biosynthesis of cholesterol, significantly increases in poorly controlled compared with moderately controlled alloxan-induced diabetic animals.

There was a significant decrease in BW in the diabetic group (IV) when compared with the control group (I). This result was compatible with **Al-Shamaony et al. (1994)) and Pari & Mahiswari (1999), Stanely et al. (2000)** and **Ene et al. (2007)** who reported that body weight decreases in alloxan diabetic rats. **Frier and Fisher (2006)** stated that profound insulin deficiency causes unrestrained lipolysis and proteolysis result in weight loss. This is because insulin is not only a glucose lowering hormone but it is also a fat storage hormone. If there is marked insulin deficiency, there is no fat storage. So, it is impossible to gain weight. Added to that, without insulin, the cells are not able to use glucose which the bodies prefer it as a fuel. Because cells are starving with no insulin to let glucose in, the body begins breaking down fat and muscle in an attempt to feed the cells. Obviously, this causes weight loss. **Cooke and Plotnick (2008)** reported that, with further insulin deficiency, there is an increase in lipolysis from fat cells as well as protein breakdown, an exaggeration of the normal fasting state designed to provide alternative sources of fuel. These mechanisms, along with the caloric loss from glucosuria, result in weight loss.

Food consumption of the diabetic control group (group IV) was low at the beginning of the experiment, then it increased later in the second half of the experiment. The reveres occurred in the normal control group (group I), i.e. food consumption was high then lowered at the end of the experiment. This finding was in agreement with **Thomas (1976)** who stated that, with alloxan-induced diabetes after an initial decline in food intake lasting several days, meal size increased steadily for 2–3 weeks, while meal frequency remained very near to pre-injection level. When food intake again stabilizes, rats were eating meals 2–3 times as large as those they eat prior to injection. **Booth (1972)** stated that increased food consumption in surviving alloxan-induced diabetic rats takes several days to develop and then continues to increase. **Robin & Kanarek (1984)**, **Badole et al. (2006) and Shan et al. (2006)** found that there is no initial decline in food consumption in diabetic rats, and food consumption increases in diabetic animals when compared with normal ones from the start of the experiment. On another hand, **Niall et al. (1990)** noticed that the diabetic animals consume less food than the normal animals from the beginning till the end of his experiment.

The initial decrease in food consumption in diabetic animals may be due to the effect of alloxan toxicity on different body organs and the large amount of ROS formed after its injection. These ROS affect mainly the pancreas, but still have injurious effects on other systems including the GIT. Also, severe hyperglycemia is associated with loss of large amounts of water and electrolytes in the urine causing dehydration and electrolyte abnormalities which in turn disturb the GIT functions and alter its motility, particularly hypokalemia. These factors together may lead to marked loss

of appetite with subsequent decrease in food consumption **(Fowler, 2009)).** The later increase in food consumption occurring in diabetic animals later in the experiment is mostly due to deficiency in insulin and leptin hormones. In the CNS, insulin and leptin reduce food intake, closing a negative feedback loop, whereby an increase of energy intake lead to increase the release of these hormones with subsequent reduction of energy intake. Both hormones circulate at levels proportionating to body fat stores and recent energy intake **(Havel et al., 2000).** Insulin regulates leptin production and the fall of leptin in insulin-deficient diabetes is likely to be mediated by decreased insulin-mediated glucose metabolism in adipose tissue **(Mueller et al., 1998).**

This study showed that IP injection of diabetic group "V and VI" with aqueous extract of garlic led to significant reduction of blood glucose level when compared with group "IV" (diabetic received saline intraperitoneally). This result was consistent with the finding of **Sher et al. (20012)** who found that, in diabetic animals, garlic extract produced hypoglycemia as well as hypolipidemia like metformin, but the hypoglycemic effect was more pronounced with metformin, whereas garlic extract was more effective in causing hypolipidemia as compared to metformin. **Eidi et al. (2006)** stated that the administration of the garlic extract at doses of 0.25, 0.5 g/kg body weight lower serum glucose significantly in diabetic rats.

Mahmoud & Abdalla (2012), Kumar et al. (2013) and Thomson et al. (2013) mentioned that garlic has anti-hyperglycemic and lipid-lowering properties. The additional lowering of C-reactive protein and serum adenosine deaminase levels with garlic suggests that garlic can be a valuable agent in providing good glycemic control and in the prevention of long-term complications. Also, **Tripathi et al. (2013)** reported that allium sativum extract (ASE) administered alone at a dose of 500 mg/kg I.P. causes reduction of blood glucose and synergizes the action of metformin when co administered with it. **EL-Demerdash and his Coworkers (2004)** showed that garlic exerted antioxidant and anti-hyperglycemic effects and consequently may alleviate liver and renal damage caused by alloxan-induced diabetes. **Thomson and Coworkers (2007)** found that garlic extract-treated diabetic rats show significant reduction in serum glucose levels during the treatment period when compared to the control diabetic rats. The hypoglycemic effect of garlic was also proven by **Sheela & Augasti (1992), Sheela et al. (1995), Kasuga et al. (1999), Eisenbarth & Kotzin (2003) and Jelodar et al. (20005).** In these studies, it is found that, in comparison with the positive control group, the group which consumes garlic shows significant low mean blood sugar.

There was a significant elevation in insulin level in diabetic group "V" treated with garlic when compared with the diabetic untreated group "IV". Also, group "VI" treated with garlic and vitamin E showed detected gradual elevation in insulin level across the experiment. There are many mechanisms which have been suggested for the hypoglycemic effect of garlic and increasing insulin level is one of them. This finding was in agreement with **Liu et al. (2005)**, **Shahidul &**

Haymie (2008) and **Ashour et al. (2011)** who stated that insulin level improved in the diabetic rats when treated with garlic. This finding was also consistent with the results of **Eidi et al. (2006)** who found that administration of garlic extract leads to significant elevation of insulin level in diabetic rats treated with the extract in comparison to the diabetic untreated group. **Augusti and Sheela (1996)** reported that garlic produces its hypoglycemic effect by acting as an insulin secretagogue in diabetic rats. The hypoglycemic effect of aqueous extract of garlic may be attributed to the presence of SAC in it which significantly increased the insulin level, and it should be considered reliable compliance maker for human clinical studies involving garlic intake **(Harunobu, 2006). Sarvanan and his Coworkers (2009)** studied the action of S-allylcysteine, a major component in the aqueous extract of garlic, on diabetic animals in vivo and they found that insulin level increased in the blood of diabetic animals treated with this substance. Many of the health benefits of garlic are attributed to S-allylcysteines (SAC); a substance derived from γ-glutamyl-S-allyl-L-cysteines, organosulfur compounds in the raw garlic, through an enzymatic transformation with γ-glutamyl transpeptidase when garlic is extracted with an aqueous solution **(Harunobu, 2006).** The hypoglycemic potency of garlic has been attributed to its content of sulphur compounds. These compounds might enhance glucose utilization because it significantly decreased the blood glucose level in glucose-loaded rats. Also, this hypoglycemic potency may be due to restoration of delayed insulin response and release of bound insulin **(Eidi et al., 2006). El-Demerdash and his Coworkers (2004)** stated that the hypoglycemic effect of garlic is due to spare insulin from sulfhydryl group. Inactivation of insulin by sulfhydryl group is a common phenomenon. Garlic can effectively combine with endogenous thiol containing molecule such as cysteine, glutathione, and serum albumins and enhance serum insulin.

In the present study, cholesterol, LDL cholesterol and TAGs levels were significantly lower in group V (diabetic receiving garlic extract intraperitoneally) and in group VI-(diabetic receiving garlic extract intraperitoneally and vitamin E orally) when compared with group IV (diabetic receiving saline intraperitoneally). These findings were in agreement with **Yeh and Liu (2001)** who stated that administration of garlic extract led to significant reduction in cholesterol, TAGs and LDL levels. Also, **Eidi et al. (2006)** reported that the administration of garlic extract significantly decreased serum triglycerides and cholesterol in diabetic rats. **Thomson et al. (2007)** found that, after treatment with garlic extract, the lipid profile of garlic-treated diabetic rats was significantly lower in comparison with the control diabetic rats and this reduction elicited by garlic was sustained throughout the course of treatment. **El-Sabban and Abouazahra (2008)** stated that different garlic preparations have been valued as lipid lowering agents. In addition, garlic is also known for its benefit against the atherosclerotic disease process.

The lipid lowering effect of garlic was also proved by **Stevenson et al. (2000), Lawson et al. (2001), Steiner & Li**

(2001), Rizwan et al. (2005) Gorinstein et al. (2006), and **Jastrzebski et al. (2007)** who stated that garlic positively influences the plasma lipid levels and plasma antioxidant activity. The data from their investigations confirm that garlic possesses significant hypolipidemic properties. Administration of fresh garlic or etheric garlic extracts improves lipid profile **(Knipschild and Ter-Riet, 1989). Yeh and Yeh (1994)** proved the anti-cholesterogenic properties of garlic and confirmed its cholesterol and lipid lowering effects through in vitro experiments using primary hepatocyte cultures. The lowering of total cholesterol observed with garlic is believed to be largely due to inhibition of hydroxyl methyl glutaryl-CoA reductase, an important enzyme in the biosynthesis of cholesterol **(Rizwan et al., 2005).**

Eidi et al. (2006) stated that the triacylglycerol lowering effect of garlic appears to be due to inhibition of fatty acid synthesis in the liver. With respect to the cholesterol lowering property of garlic, it has been suggested that some constituents of garlic may act as inhibitors for some enzymes such as hydroxyl methyl glutaryl CoA reductase, which participates in cholesterol synthesis. **Mathew et al. (2003)** mentioned that the hypolipidemic effect of garlic is attributed to its content of organo-sulfer compounds. These organosulfur compounds can inhibit HMG-CoA reductase and other lipogenic enzymes in the liver.

CONCLUSION

Garlic therapy has a marked effect on improvement of blood glucose, insulin level and lipid profile in male Albino rats. This was most probably due to increasing insulin secretion, increasing tissue sensitivity to the hormone and decreasing hepatic fat biosynthesis. These hypoglycemic and hypolipidemic effects of garlic beside other studied effects such as antioxidant, antiplatelet and anti atherosclerotic could improve diabetic relate mortality and morbidity.

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تأثير خلاصة الثوم المائية وفيتامين E على الجرذان البيضاء الذكور البالغين المصابين بمرض الداء السكرى المحدث بالألوكزان والنيكوتيناميد

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خلفية البحث: يحتوى الثوم على مجموعة فعالة متباينة تحدث تأثيرات صحية متنوعة.

الهدف من البحث: تقييم تأثير العلاج بخلاصة الثوم المائية بالحقن البريتونى وفيتامين E بالفم على مستويات السكر والإنسولين ونمط الدهون فى االجرذان البيضاء الذكور البالغة المصابة بمرض الداء السكرى المحدث بالألوكزان والنيكوتيناميد.

مواد وطرق البحث: تم إختيار أربعة وخمسين جرذا أبيضا بالغا لهذه التجربة، تم تقسيمها إلى ست مجموعات متساوية: مجموعة ضابطة، ومجموعة تم حقنها بالخلاصة المائية للثوم، ومجموعة تم إعطاؤها فيتامين E ، ومجموعة ضابطة مصابة بمرض الداء السكرى، ومجموعة مصابة بمرض الداء السكرى تم معالجتها بالخلاصة المائية للثوم، ومجموعة مصابة بمرض الداء السكرى تم معالجتها بالخلاصة المائية وفيتامين E . وقد تم إحداث مرض الداء السكرى بالحقن بالألوكزان المسبوق بالحقن بالنيكوتيناميد للوقاية من التأثير السمى للألوكزان. وإستمرت التجربة لمدة خمسة أسابيع. وقد تم أخذ عينات من الدم لكل مجموعة فى بداية التجربة، وفى نهاية الأسبوعين الثالث والخامس.

النتائج: أحدثت الخلاصة المائية للثوم تحسنا ذو قيمة معيارية فى مستوى السكر فى الدم والإنسولين ونمط الدهون ووزن الجسم. كذلك أحدث العلاج بالخلاصة المائية للثوم مع فيتامين E تحسنا فى مستوى السكر فى الدم ونمط الدهون وأيضا تحسنا ملموسا فى مستوى الإنسولين ووزن الجسم طوال مدة التجربة.

الإستنتاج: العلاج بالثوم له تأثير واضح فى تحسين مستويات السكر فى الدم والإنسولين ونمط الدهون فى االجرذان البيضاء البالغة المصابة بالداء السكرى.

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