

EFFECT OF *ALLIUM SATIVUM* ESSENTIAL OIL ON THE GLYCEMIC CONTROL AND HYPERLIPIDEMIA IN TYPE 2 DIABETES MELLITUS SUBJECTS¹Dr. Ali Naseer, ²Dr. Suhail Ahmed Almani*, ³Dr. Saad Abdul Quddus, ⁴Dr. Pir Maroof, ⁵Dr. Raza Naseer,¹MBBS, Postgraduate Student, Department of Medicine, Liaquat University of Medical and Health Sciences, Jamshoro, Sindh, Pakistan.²MBBS, MD, Professor, Department of Medicine, Liaquat University of Medical and Health Sciences, Jamshoro, Sindh, Pakistan.^{3,4}MBBS, House Officer, Department of Medicine, Liaquat University of Medical and Health Sciences, Jamshoro, Sindh, Pakistan.⁵MBBS, House Officer, Department of Medicine, Abbasi Shaheed Hospital, Karachi, Sindh, Pakistan.***Corresponding Author: Dr. Suhail Ahmed Almani**

MBBS, MD, Professor, Department of Medicine, Liaquat University of Medical and Health Sciences, Jamshoro, Sindh, Pakistan.

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ABSTRACT

Background: *Allium sativum* (AS) is used as herbal medicine since time immemorial. *Allium sativum* has shown anti-hyperglycemic, anti-oxidant, anti-cancer, and anti-atherogenic activity. **Objective:** To analyze the glycemic improving potential and anti-hyperlipidemia effects of *Allium sativum* essential oil (ASEO) in type 2 Diabetes mellitus (T2DM). **Methods:** The present interventional study was conducted at the Department of Medicine, Liaquat University of Medical and Health Sciences Jamshoro/Hyderabad from December 2014 to May 2015. 100 diagnosed T2DM were enrolled for study protocol through non-probability sampling according to inclusion and exclusion criteria. *Allium sativum essential oil* (ASEO) was purchased from Pharmacy of the Isra university hospital. 13.5 mg of ASEO was given orally daily for six months. Blood samples were centrifuged to separate sera which were stored at -20°C frozen. Blood glucose, glycated HbA1c, and blood lipoproteins were measured by standard laboratory methods. Data was analyzed on SPSS 21.0 version using student t-test. P-value of ≤0.05 was taken statistically significant. **Results:** Diastolic blood pressure, random blood glucose, Glycated HbA1c, total cholesterol, triglycerides, low and very low density lipoproteins showed significant reduction at third and sixth months compared to baseline ($p < 0.001$). While HDLc showed significant rise at third and sixth months ($p < 0.001$). **Conclusion:** The present study reports *Allium sativum* essential oil improves glycemic control and exerts anti-hyperlipidemic effect. A decrease in Diastolic blood pressure was also noted.

KEYWORDS: *Allium sativum* Glycemic control Hyperlipidemia Diabetes mellitus.**INTRODUCTION**

Allium sativum (AS) is publicly known as the *Garlic*. AS is a herbal root bulb commonly used as taste enhancer and food spice. Its use as herbal medicine is known since time immemorial. It has been used as home remedy for the infections, flu, cardiac diseases, etc. AS has been used for both prevention and treatment.^[1] Anti-microbial activity of AS has also been reported.^[2] AS is confidently acknowledged of its anti-hyperglycemic, anti-oxidant, anti-cancer and anti-atherogenic activity. It is confidently used for the cardiovascular diseases (CVD).^[3,4] Its effectiveness in CVD may be due to its blood cholesterol lowering effect.^[4,5] Previous reviews showed that the AS decreases blood lipids hence it may be prescribed as anti-hyperlipidemic agent.^[5-7] AS protects against CVD by lowering blood triglycerides (TAG), total cholesterol (TC), Low density lipoprotein-cholesterol (LDLc) and boosting effect on the high density lipoprotein-cholesterol (HDLc). An increase in good cholesterol

(HDLc) and a reduction in bad cholesterol (LDLc) prevent atheroma formation thus protecting against the coronary artery disease (CAD) and peripheral arterial diseases (PAD).^[8,9] Efficacy of AS as anti-hyperlipidemic agent has been debated owing to diverging views of previous studies^[10-15] in the CAD and PAD. However, recently published studies^[10-12] have reported positive efficacy of AS against the CAD by cutting down the elevated blood cholesterol and lipids. Data from developing countries is lacking although AS is frequently used as food additive even in Pakistan.^[11,13] Previous studies^[13,14] had applauded its anti-hypertensive effects of ASE. A previous study^[15] reported that the AS essential oil (ASEO) was effective in mobilizing the fat from fatty liver. *Allicin* is believed to be the active ingredient of AS. Biochemically, the allicin is a “*diallyl-disulfide-oxide*” which is reported to dilate the blood vessels (vasodilator).^[16] AS is reported to reduce the Diastolic blood pressure (DBP) in subjects with

uncontrolled arterial hypertension.^[17] Ether extract of AS has been reported to inhibit platelet aggregation in an *in-vitro* experimental study.^[18] Immune enhancing effects of AS had been reported.^[19,20] Human studies have reported hypolipidemic effect of raw extract of AS, but none researcher have evaluated the effects of AS essential oils against the hyperlipidemia in type 2 DM (T2DM) from Pakistan. As the DM is increasing in the country, and is a major risk factor for the hyperlipidemia and coronary artery disease, hence it is worth to analyze the easily available and cost effective herbs. Most of previous studies have used raw extract of *Allium sativum*. The present study used the essential oil of *Allium sativum* for the first time. The present small scale study was conducted to analyze the efficacy of *Allium sativum* essential oil (ASEO) against hyperlipidemia in type 2 DM subjects presenting at our tertiary care hospital.

SUBJECTS AND METHODS

The present interventional study was conducted at the Department of Medicine, Liaquat University of Medical and Health Sciences Jamshoro/Hyderabad from December 2014 to May 2015. 100 diagnosed type 2 Diabetes mellitus (T2DM) were enrolled for study protocol according to inclusion and exclusion criteria. Non-probability purposive sampling technique was used. Type 2 DM subjects, age 30- 70 years, DM duration of ≥ 5 years, taking oral sulfonylurea drugs and both genders were included. T2DM subjects with concomitant chronic liver disease (CLD), diabetic kidney disease (DKD), bone disease, female with menopause, patients taking vitamin pills and HMG-co A reductase inhibitor drugs were exclusion criteria. T2DM subjects with previous history of coronary artery disease and peripheral arterial disease were also excluded. Subjects were communicated about the purpose of study. The advantages and disadvantages were informed and were asked for willingness of blood sampling. They were informed for 3 times blood sampling at baseline, at third and sixth months respectively. Subjects who gave volunteer consent were allowed to enter study protocol. Patient's vitals were recorded by nursing staff. A medical officer was assigned to take full history for the exclusion of patients. Medical officers were trained for the relevant history of the patients as in inclusion and exclusion criteria. This was followed by examination by the Consultant Physician. Written consent was signed by the volunteer participants. Body weight was measured on a weighing machine. Systemic blood pressure was noted after 5 minutes rest as per standard criteria. Diabetes mellitus was defined as per criteria of American Diabetes Association (ADA). Fasting blood glucose (FBG) ≥ 126 mg/dl or postprandial blood glucose (RBG) ≥ 200 mg/dl was taken as DM.^[21]

- **Allium sativum essential oil**

Allium sativum essential oil (ASEO) was purchased from Pharmacy of the Isra university hospital (Garlish oil

soft gel, High Q international Pharmaceutical, Pakistan). 13.5 mg of ASEO was given orally daily for six months.

- **Blood sampling**

Patients were informed to come overnight fasting or a fasting of at least 8-12 hours for blood sampling. Blood samples were taken through Venepuncture after antiseptic measures were taken. Sampling was performed by senior technician staff. Centrifugation of blood was performed for 10 minutes at 3000 rpm. Ser were separated out. Care was taken for hemolysis prevention. Sera were stored at -20°C frozen for analysis.

- **Glucose estimation**

Blood glucose was estimated by "*glucose oxidase*" enzymatic method. Automated Chemistry analyzer (Hitachi 902, Roche diagnostics, USA) was used.

- **Glycated Hb A1 (HbA1c) estimation**

HbA1c assay was carried as per criteria of DCCT trial assay. HbA1c assay was carried out on an automated Chemistry analyzer (Hitachi 902, Roche diagnostics, USA).^[22]

- **Blood lipids determination**

Serum TC, TAG and VLDL were estimated by colorimetric method, HDLc by precipitant method and LDLc was measured by Friedewald's formula.²³ Hyperlipidemia was defined as per ATP III criteria; TC >200 mg/dL, TAG >150 mg/dL, VLDL > 30 mg/dL, LDLc >130 mg/dL and HDLc < 40 mg/dL.

- **Ethical clearance and confidentiality**

Ethical clearance was approved by the ethical committee of the institute. Pre structured proforma was used for data collection. Patient confidentiality was maintained by securing patient data. Only authorized persons were allowed to access the patient record.

- **Data analysis**

Data was entered on excel sheet and copied to the sheet of SPSS 21.0 version (IBM Corporation, USA). Normality of data was checked by "Shapiro Wilk test". Student's t-test was used for age and chi square for gender distribution. Continuous variables data taken at baseline, 3rd and 6th months were analysed by Students paired sample t-test. P-value of ≤ 0.05 (CI 95%) was taken statistically significant.

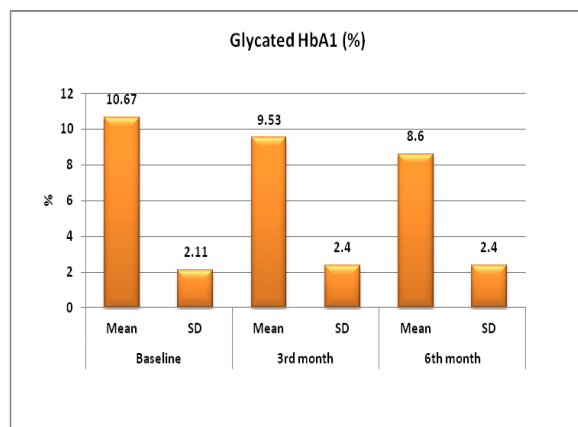
RESULT

Mean \pm SD of age was noted as 42.8 ± 8.5 years. Male dominated in the present study. Of 100 subjects, 61 were male and 39 were female patients. Male to female ratio was 1.56:1. Research variables were noted at baseline, 3rd and 6th month. Diastolic BP, RBG, Glycated HbA1, TC, TAG, LDLc and VLDL showed statistically significant reduction at 3rd and 6th month compared to baseline as shown in table 1 ($p < 0.001$). While HDLc showed significant rise at 3rd and 6th month compared to baseline as shown in table 1 ($p < 0.001$). However, body

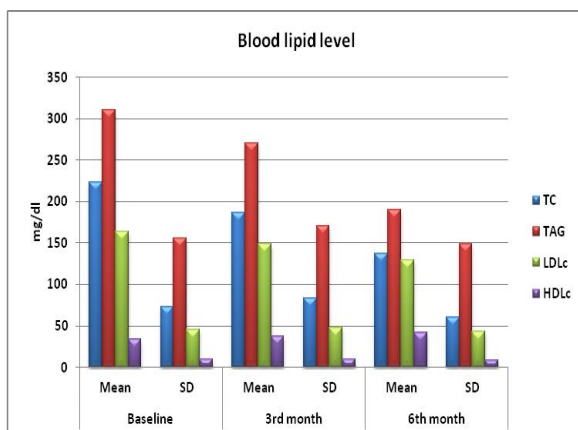
weight, systolic BP and TAG showed non-significant differences at baseline versus 3rd month analysis ($p > 0.05$).

Table: 1. Glycemic control and blood lipids in type 2 Diabetic subjects (n=100)

	Baseline (Mean± SD)	3 months (Mean± SD)	6 months (Mean± SD)	p-value
Age (years)	42.8±8.5	-	-	0.48
Body weight (kg)	76.8±11.6	▶ 76.0±11.4 ▶	71.6±9.4	0.01
Systolic BP (mmHg)	144.4±20.9	▶ 139.2±20.2 ▶	133.7±18.6	0.001
Diastolic BP (mmHg)	85.2±14.6	78.7±14.2	76.5±13.2	0.001
Random Blood glucose (mg/dl)	227.4±66.8	203.2±72.9	175.1±63.1	0.0001
Glycated HbA1 (%)	10.67±2.11	9.53±2.4	8.6±2.4	0.0001
Blood glucose (F) (mg/dl)	143.9±41.7	139.9±19.7	129.7±15.7	0.0001
Fasting insulin (μIU/ml)	15.5±4.5	14.9±5.5	13.7±2.3	0.0001
HOMA-IR (%)	7.47	6.11	5.91	0.0001
Total cholesterol (TC) (mg/dl)	223.6±72.9	186.1±83.7	137.1±60.4	0.0001
Triglycerides (TAG) (mg/dl)	310.4±155.1	▶269.9±170.9 ▶	189.8±149.1	0.001
LDLc (mg/dl)	163.5±44.9	148.6±47.4	128.8±43.1	0.001
HDLc (mg/dl)	34.2±10.3	37.7±10.3	41.5±8.9	0.001
VLDL (mg/dl)	34.3±7.1	32.0±7.8	29.4±7.5	
		Baseline versus 3 rd month p-value Non-significant		



Graph 1. Glycated hemoglobin A₁ at baseline, third and sixth months



Graph: 2. Blood lipid levels at baseline, third and sixth months

DISCUSSION

The present study was conducted to analyze the efficacy of the ASEO for the glycemic control and

hyperlipidemia in type 2 DM subjects. To the best of knowledge, the *Allium sativum* essential oil (ASEO) is the first time being reported from our tertiary care hospital. In the present study, DBP, RBG, HbA_{1c}, TC, TAG, LDLc and VLDL were decreased at third and sixth month compared to baseline ($p < 0.001$). The HDLc was increased at third and sixth month compared to baseline ($p < 0.001$). However, body weight, systolic BP and TAG showed non-significant differences at baseline versus third month ($p > 0.05$). The present study observed a significant improvement in glycemic control and anti hyperlipidemia by the ASEO. A significant decrease in blood lipoproteins with simultaneous increase in HDLc were observed at high doses of ASEO particularly at sixth month. The findings of a decrease in TC, TAG, LDLc, and VLDL, body weight and systolic BP are consistent with previous studies^[19,20] Previous studies^{11,12} reported decrease total cholesterol in subjects with hypercholesterolemia after raw garlic extract (RGE). The finding of reduction in serum total cholesterol (table 1) is in keeping with previous studies.^[24,25] The previous studies concluded that the ASEO might be reducing the HMG-CoA reductase enzyme activity^[24,25], as it is the regulatory enzyme of cholesterol biosynthesis particularly in the liver. The finding of a decrease in LDLc and an increase in HDLc by ASEO is a worth finding of the present study which may be exploited for the prevention of coronary artery disease in type 2 diabetics. ASEO has anti hyperlipidemic effects, is proved in the present similar to previously reported studies.^[11-14] The ASEO may be prescribed for the prevention of atherogenesis in its earlier stages. How the ASE reduces LDLc and increases HDLc. As regards mechanism and site of action by ASEO; it is not clear. However, the most probable underlying mechanism seems to be the HMG-co A reductase inhibition as

reported.^[20,24] Anti-hyperlipidemic effect and improved glycemic control by ASEO is consistent with previous studies.^[20,24] Inhibition of lipoprotein lipase is another suggested mechanism by which ASEO exerts its anti-hyperlipidemic effect,^[20, 24-26] but the mechanisms are not more than an speculation until further studies are conducted at the molecular level. A recent study²⁷ reported mean cholesterol levels were reduced from baseline 265 ± 16.7 mg/dL to 232.7 ± 11.2 mg/dL 3rd month (90th day) by 3 gram raw garlic dose orally daily ($P < 0.001$). Finding of above study are in parallel to present study (table 1). A meta-analysis of 39 studies showed a significant decrease in TC, TAG, LDLc, VLDL and a rise in HDLc.^[28] This supports the findings of the present study. The findings of improved glycemic control and anti hyperlipidemic effects of ASEO are also consistent with previous studies.^[29-31] Animal studies have also reported anti hyperlipidemic effects of garlic extract.^[32,33] Interventional studies have similarly shown anti hyperlipidemic effects of total plasma lipids in humans.^[34-36] The strength of study lies in its participants who showed regular follow ups, regular use of drug and prospective study design. Side effects of ASEO were not observed in the present study. Another important strength of study lies in the use of *Allium sativum essential oils* (ASEO) which is more purified compared to raw garlic extract. Limitations of study include small sample size and dietary habits which might have changed the results towards alternative hypothesis. However, the findings are worth to report as the *Allium sativum essential oil* is easily available, palatable and inexpensive.

CONCLUSION

The present study reports positive efficacy of *Allium sativum* in improving glycemic control and anti hyperlipidemia effects. Diastolic blood pressure, random blood glucose, glycated HbA1, total cholesterol, triglycerides, low density lipoprotein and very low density lipoproteins showed a significant decrease, while high density lipoprotein was increased.

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Ethical Committee

Approval from ethical review committee of Liaquat University of Medical and Health Sciences vide letter No. 121/78/Res/LUMHS/2014.

Footnotes

Source of Support: None

Conflict of Interest: None

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