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Effects of Garlic Supplementation on Fasting Blood Sugar, HbA1c and Lipid Profile in Type 2 Diabetics Receiving Metformin and Glyburide

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***ABSTRACT**: Diabetes mellitus is a metabolic disorder characterized by failure of glucose homeostasis with disturbances of carbohydrate, fat and protein metabolism caused by defects in insulin secretion, insulin action, or both. The aim of this study was to evaluate the effects of natural substances such as garlic on fasting blood sugar, HbA1c and lipid profile in patients with type 2 diabetes who were treated with metformin and glyburide. The study lasted for 12 weeks, the patients (n = 96) were divided into 2 groups. Group G (n = 51) was given garlic capsules at a dose of 50 mg/day in combination with their treatment. While, group C received their treatment alone (n = 45). We measured fasting blood sugar (FBS), Glycated hemoglobin (HbA1c), triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) at the beginning of the study (week 0) and at the end of the study (week 12). Our results showed a decrease in fasting blood glucose in garlic group when compared from week 0 to week 12, but this reduction was statistically insignificant and no significant change in HbA1c was observed. On the other hand, there was a significant decrease in TG levels in garlic group at week 12 in comparison with the baseline values at week 0. There was also a decrease in TC and LDL-C levels from week 0 to week 12 in garlic group, but this reduction was statistically not significant. While, no significant change in HDL-C levels was observed. Conclusively, the combination of garlic with antidiabetic agents (metformin and glyburide) has shown hypoglycemic and hypolipidemic effects. So garlic may be a good addition in the management of patients with type 2 diabetes.*

***Keywords**: Fasting blood sugar, garlic, HbA1c, lipid profile, type 2 diabetes*

I. INTRODUCTION

Diabetes mellitus is a metabolic disorder of multiple etiology characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Abnormalities in the metabolism of carbohydrate, protein, and fat are also present [1, 2]. If blood glucose levels remain high over a long period of time, this can result in long term damage of organs such as the kidneys, eyes, nerves, heart and blood vessels. Complications in some of these organs can lead to death [3-5].

The treatment of diabetes mellitus constitutes lifestyle management, exercise, weight control and antihyperglycemic drugs like sulfonylureas, biguanides, alpha-glucosidase inhibitors, thiazolidinediones, and meglitinide [1]. The prevalence of type 2 diabetes (T2D) is increasing globally [6, 7]. It is anticipated that by the year 2025, over 75% of all people with diabetes will belong to the developing countries. In Syria, diabetes mellitus is one of the most common diseases, that the diabetic patients comprise 10% of population [8].

When patients are diagnosed with diabetes, a large number of medications become appropriate therapy. These include medications for dyslipidemia, hypertension, antiplatelet therapy, and glycemic control agents. So many medications can be overwhelming, and it is imperative that patients are thoroughly educated about their drug regimen [9].

Despite the availability of medication for management of diabetes, the interest in alternative traditional remedies is increasing [10]. The use of natural substances has become more extensive over the past few years, motivated certainly by the faith that they may have fewer side effects as compared to pharmaceuticals

and by their effortless accessibility to the populace without prescriptions or visits to the health providers [11], and more interestingly as the natural substances may enhancing the effect of some medications leading to reduce their doses when they are taken concurrently [12].

More than 400 traditional plant treatments for diabetes mellitus have been recorded, but only a small number of these have received scientific and medical evaluation to assess their efficacy. A hypoglycemic action for some plant treatments has been confirmed in animal models and non-insulin-dependent diabetic patients, and various hypoglycemic compounds have been identified [13]. A botanical substitute for insulin seems unlikely, but traditional treatments may provide valuable clues for the development of new oral hypoglycemic agents and simple dietary adjuncts [13]. Garlic has a reputation because of its widespread health use around the world as a dietary as well as therapeutic supplement. It contains a variety of effective compounds, such as allicin, a sulfur-containing compound that exhibits anticoagulant, antithrombotic, antioxidant, hypocholesterolemic, hypoglycemic, and hypotensive activities [14, 15]. Many clinical trials on garlic showed a hypoglycemic and hypolipidemic effects in non-treated patients with T2D [11, 16, 17]. The clinical studies on garlic in treated patients are limited [18-20], and more researches are needed to further explore the role of garlic in those patients.

According to the global tendency for using natural remedies in order to reduce the side effects associated with drugs, we investigated in this study the role of garlic in contributing with antidiabetic agents in controlling various bioclinical parameters in patients with T2D. Therefore, the present study is focusing on the effects of garlic supplementation on fasting blood sugar (FBS), HbA1c and lipid profile in T2D patients receiving both metformin and glyburide, and this is the first time that the garlic is studied along with the combination of two antidiabetic agents (metformin and glyburide), which is the most commonly used in treatment of T2D [21-24].

II. MATERIALS AND METHODS

This was a 12 weeks study. The research protocol has been approved by the University of Aleppo, Syria. Kits used in this study: Kits for the assay of glucose, TC, HDL cholesterol, LDL cholesterol and TG were purchased from BioSystems (Reagents & Instruments) Barcelona, Spain. Kits for the assay of HbA1c were purchased from iChromα.

Patients with previously diagnosed type 2 diabetes mellitus (n = 96), visiting the Center of Comprehensive Medical Clinics in Aleppo, were divided randomly into two groups: G and C, Group G (garlic group) was comprised of 51 patients who were given soft gelatin capsules containing 25 mg garlic twice a day in combination with their treatment that they were previously receiving (500 mg metformin once a day and 4 mg glyburide twice a day). Group C (control group) was comprised of 45 patients who were given only the treatment that they were previously receiving (500 mg metformin once a day and 4 mg glyburide twice a day) without garlic.

On the first day of the study (week 0), venous blood was taken. Whole blood was used to determine HbA1c percentage by using immunofluorescence method. After centrifugation, plasma was used to quantify: fasting blood sugar (FBS) using the enzymatic method (glucose oxidase), triglyceride (TG) using the enzymatic method, total cholesterol (TC) using the enzymatic method, high-density lipoprotein cholesterol (HDL-C) using the precipitation method and low-density lipoprotein cholesterol (LDL-C) using the precipitation method. On the final day of the study (week 12), venous blood was taken and the previous mentioned steps were followed.

1.1. Inclusion criteria of patients

- Patients with diagnosed type 2 diabetes mellitus who were receiving metformin and glyburide
- Patients of both sexes
- Patients aged between 30 to 70 years

1.2. Exclusion criteria of patients

- Patients with type 1 diabetes mellitus
- Patients with a history of allergy to garlic
- Patients having a history of myocardial infarction
- Patients with a history of hepatic or renal failure
- Pregnant or lactating women

III. RESULTS AND DISCUSSION

1.3. Effects of administration garlic capsules with metformin and glyburide on FBS & HbA1c:

Fig. 1 shows the change in fasting blood sugar levels at week 12 comparing with week 0 in garlic group (G) and in control group (C). The results showed a decrease in FBS in garlic group (G) from 216.16 ± 10.34 at week 0 to 188.44 ± 17.45 at week 12, but this reduction was statistically insignificant ($p > 0.05$). While there was a slightly increase in FBS in group C from 173.38 ± 9.28 at week 0 to 192.24 ± 18.92 at week 12 ($p > 0.05$). The comparison between both groups showed that garlic could contribute with antidiabetic agents (metformin and glyburide) in enhancing the hypoglycemic effect.

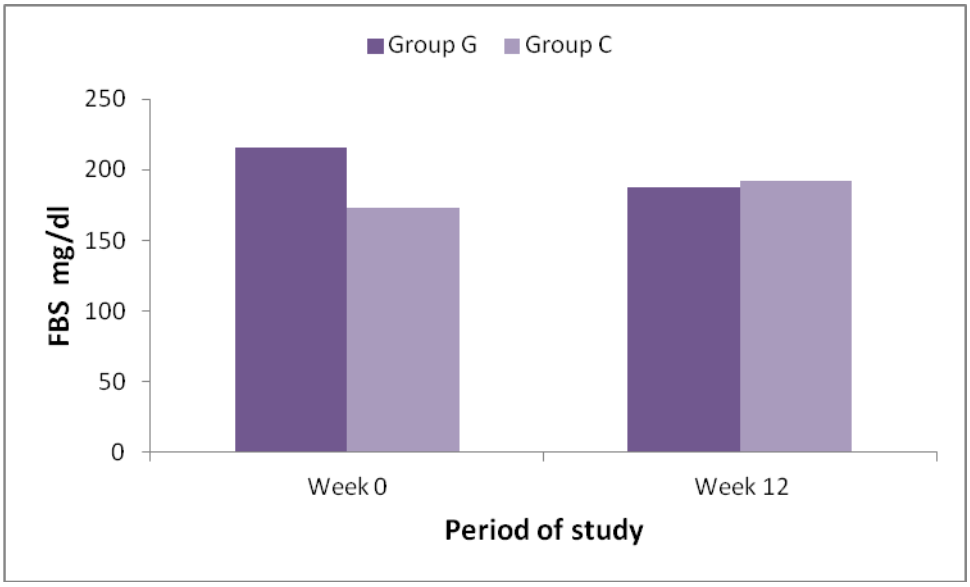

Figure 1. Changes in mean FBS from week 0 to week 12 in patients receiving garlic supplementation with metformin and glyburide (group G), and patients receiving only metformin and glyburide (group C).

Measuring glycated hemoglobin (HbA1c) assesses the effectiveness of therapy by monitoring long-term serum glucose regulation. The HbA1c level is an indicator of average blood glucose concentrations over the preceding three months [25]. Fig. 2 shows the change in HbA1c percentage from week 0 to week 12 in garlic group (G) and in control group (C). The results showed no significant change in HbA1c percentage ($p > 0.05$) from week 0 to week 12 in both groups.

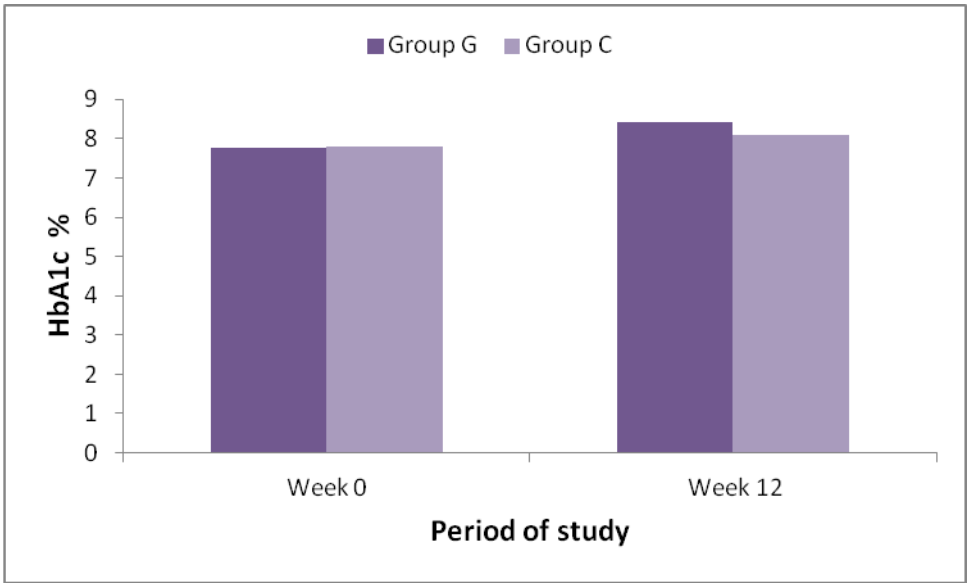

Figure 2. Changes in mean HbA1c from week 0 to week 12 in patients receiving garlic supplementation with metformin and glyburide (group G), and patients receiving only metformin and glyburide (group C).

These results showed statistically an insignificant decrease in fasting blood glucose levels in garlic group (patients who were treated with metformin and glyburide along with garlic) when compared from week 0 to week 12, and no significant change in HbA1c was observed in patients in both groups (G & C).

Our result is almost in accordance with the result obtained in a previous clinical study of Kumar et al., 2013, which studied the effects of garlic in T2D obese patients receiving metformin and observed that metformin with garlic reduced FBS significantly; however, the change in HbA1c levels was not significant [20]. On the other hand, in a study on patients with T2D who were not-treated with antidiabetic agents for a certain period of time showed that garlic in low doses didn't reduce FBS and HbA1c significantly in the period of 0 – 12 weeks. However, by using a higher dose of garlic or a longer duration of study (24 weeks), a significant decrease was obtained [16].

Chhatwal et al., 2012 [18], conducted a study that evaluated the hypoglycemic effect of garlic as an adjunct to metformin in obese patients of T2D and reported that both metformin and garlic reduced HbA1c significantly. This result was contradictory to the result obtained in present study in which no significant change in HbA1c were observed in both groups.The contradictory effects of garlic seen in different studies may be attributed to the differences in garlic preparations, doses or duration of study.

The probable mechanism underlying garlic's hypoglycemic effects is increasing either the pancreatic secretion of insulin from the beta cells or insulin sensitivity [20, 26]. Garlic has been reported to spare insulin from sulfhydryl group (which is known to inactivate insulin) by some compounds identified in garlic such as allicin; which can effectively combine with cysteine residues and enhance insulin sensitivity [27].

1.4. Effects of administration of garlic capsules with metformin and glyburide on lipid profile:

Due to the disturbed levels of glucose in T2D patients, hyperlipidemia could occur as a secondary complication [17]. So we measured the parameters of lipid profile in T2D patients.Fig. 3 shows the change in triglyceride levels from week 0 to week 12 in garlic group (G) and in control group (C). The results showed significant decrease in triglyceride levels in group G from 183.16 ± 12.06 at week 0 to 117.04 ± 14.51 at week 12 ($p < 0.05$). This decrease was more in garlic group than in control group, that in group C the triglyceride concentration was decreased from 194.20 ± 12.57 at week 0 to 143.28 ± 13.99 at week 12, and this reduction

was not statistically significant ($p > 0.05$). The comparison between both groups showed that garlic could contribute with antidiabetic agents (metformin and glyburide) in lowering TG levels.

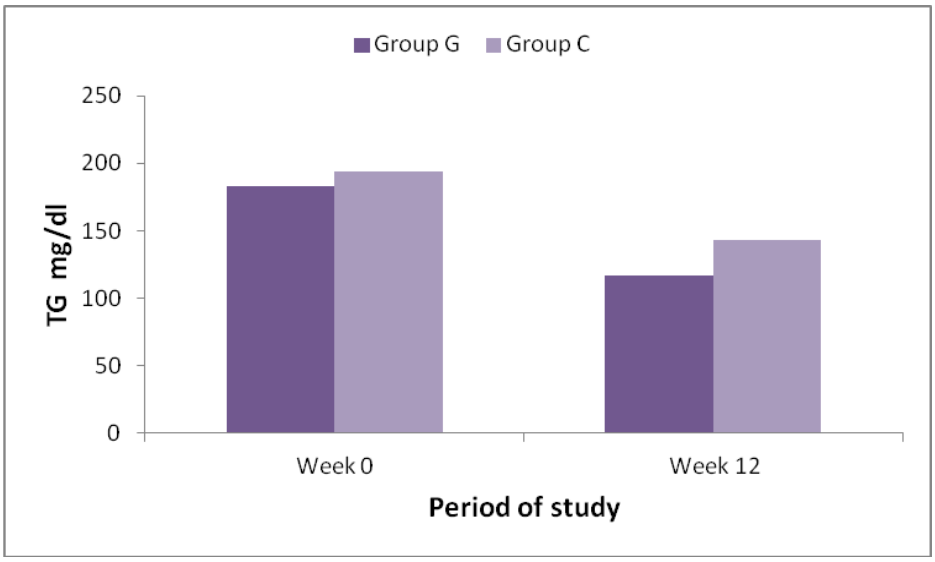

Figure 3. Changes in mean TG from week 0 to week 12 in patients receiving garlic supplementation with metformin and glyburide (group G), and patients receiving only metformin and glyburide (group C).

Fig. 4 shows the change in total cholesterol levels from week 0 to week 12 in garlic group (G) and in control group (C). The results showed a decrease in TC in garlic group (G) from 201.78 ± 6.53 at week 0 to 186.84 ± 7.95 at week 12, but this reduction was statistically insignificant ($p > 0.05$). Without garlic (group C), the decrease in TC was less than group G, that the TC was decreased from 201.44 ± 11.64 at week 0 to 197.24 ± 9.09 at week 12 in group C ($p > 0.05$). The comparison between both groups showed that garlic could contribute with antidiabetic agents (metformin and glyburide) in lowering TC levels.

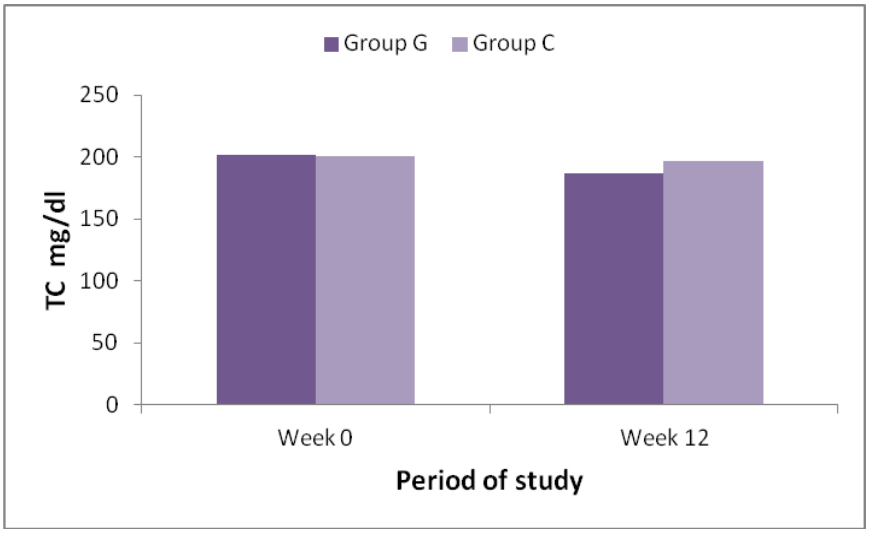

Figure 4. Changes in mean TC from week 0 to week 12 in patients receiving garlic supplementation with metformin and glyburide (group G), and patients receiving only metformin and glyburide (group C).

Fig. 5 shows the change in HDL cholesterol levels from week 0 to week 12 in garlic group (G) and in control group (C). The results showed no significant change in HDL-C levels ($p > 0.05$) from week 0 to week 12 in both groups.

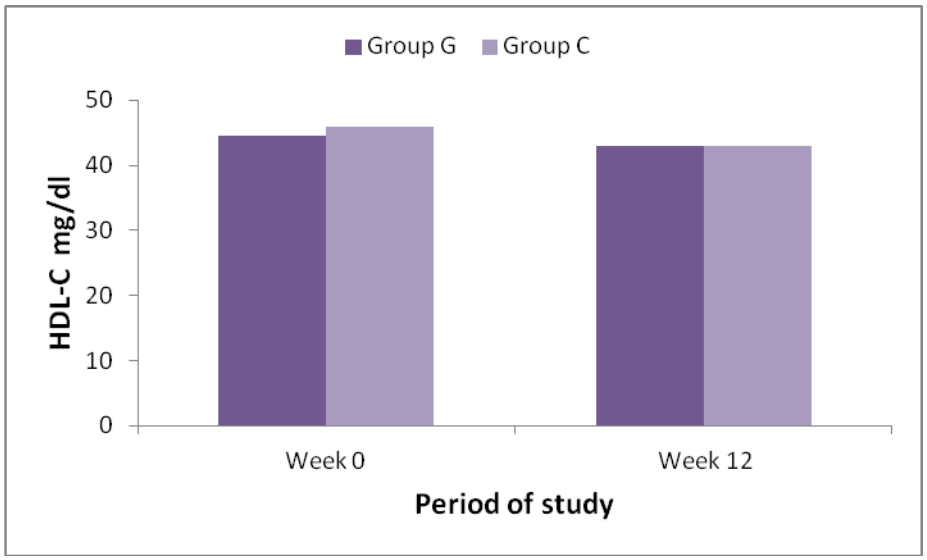

Figure 5. Changes in mean HDL-C from week 0 to week 12 in patients receiving garlic supplementation with metformin and glyburide (group G), and patients receiving only metformin and glyburide (group C).

Fig. 6 shows the change in LDL cholesterol levels from week 0 to week 12 in garlic group (G) and in control group (C). The results showed a decrease in LDL-C in garlic group (G) from 159.54 ± 6.9 at week 0 to 146.92 ± 8.24 at week 12, but this reduction was statistically insignificant ($p > 0.05$). While there was an insignificant increase in LDL-C in group C from 150.02 ± 8.66 at week 0 to 159.60 ± 9.79 at week 12 ($p > 0.05$). The comparison between both groups showed that garlic could contribute with antidiabetic agents (metformin and glyburide) in lowering LDL-C levels.

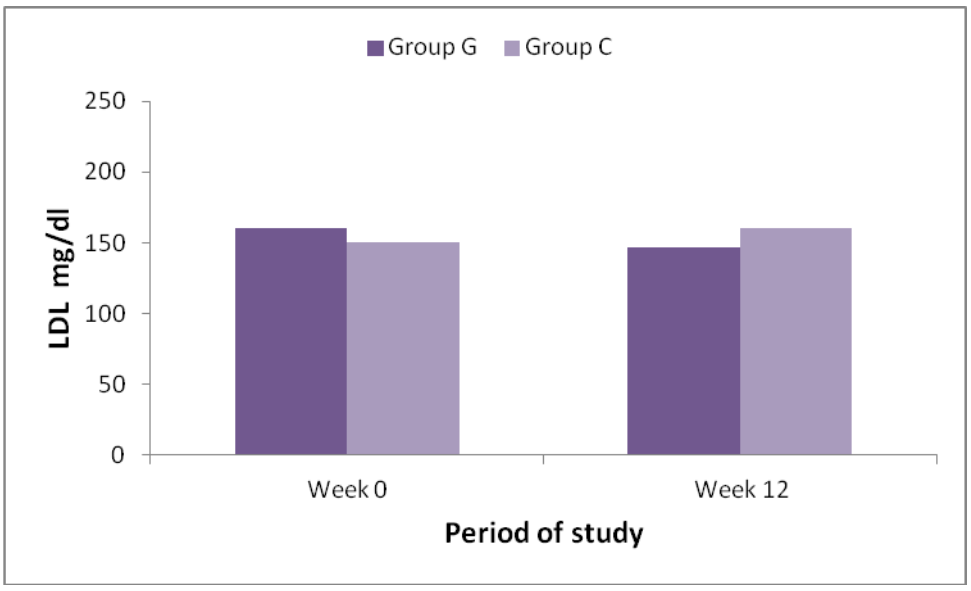

Figure 6. Changes in mean LDL-C from week 0 to week 12 in patients receiving garlic supplementation with metformin and glyburide (group G), and patients receiving only metformin and glyburide (group C).

These results demonstrate that garlic could improve the lipid profile, which is frequently affected in patients with T2D. There was a significant decrease in TG levels in garlic group (patients who were treated with metformin and glyburide along with garlic) when compared from week 0 to week 12. There was also a decrease in TC and LDL-C levels from week 0 to week 12 in garlic group, but this reduction was not statistically significant. While, no significant change in HDL-C was observed in patients in both groups (G & C).

Our results are on one hand in agreement with other clinical trials as TG levels was reduced significantly with garlic, but on the other hand the present results are not statistically in accordance with other clinical trials concerning of other parameters (TC, HDL-C and LDL-C) [18, 19]. This statistical disagreement could be due to the duration of garlic administration as shown by Ashraf et al., 2011 [19], who found that the effects of garlic along with antidiabetic agent (metformin) on lipid profile in patients with T2D, may be dependent on the duration of study.However, our results contradicts with a clinical study conducted by Ashraf et al., 2005 [11], that evaluated the effects of garlic on dyslipidemia in patients with T2D mellitus and showed no significant difference in the triglyceride level from week 0 to week 12.

The probable mechanism of the antilipidemic effect of garlic could be contributed to allicin, a sulfur – containing compound, which is believed to act as natural form of statin (an agent commonly used to lower cholesterol levels by competitively inhibiting HMG – CoA reductase that determine the rate of cholesterol synthesis). Allicin could situate itself into the active site of HMG – CoA reductase, leading to delay the reaction of cholesterol formation and thus, less cholesterol is produced [28-32].

IV. CONCLUSION

The clinical studies which evaluate the effects of garlic on patients with T2D treated with antidiabetic agents are limited. Our study is supporting these studies, and present results showed that garlic had additive effects to antidiabetic agents (metformin and glyburide) on improving fasting blood glucose levels and lipid profile in patients with T2D.

More clinical studies about the role of garlic with antidiabetic agents in patients with T2D are recommended to confirm the positive effects of garlic in order to obtain potential reduce in drugs doses, thus reduce side effects associated with them and delay the shift to insulin treatment in type 2 diabetics.

V. ACKNOWLEDGEMENTS

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VI. REFERENCES

1. Report of a WHO Consultation. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications: World Health Organisation 1999.
2. R. Defronzo, Pathogenesis of diabetes, *Diabetes Rev*, *5(177)*, 1997.
3. I.B. Hirch, Glycemic control and complications of diabetes mellitus, *West J Med*, *162(5,)* 1995, 430-8.
4. M. Brownlee, Biochemistry and molecular cell biology of diabetic complications, *Nature*, *414(6865)*, 2001, 813-20.
5. J.S. Weiss and B.E. Sumpio, Review of prevalence and outcome of vascular disease in patients with diabetes mellitus, *Eur J Vasc Endovasc Surg*, *31(2)*, 2006, 143-50.
6. P. Zimmet, KG. Alberti and J. Shaw, Global and societal implications of the diabetes epidemic, *Nature*, *414*, 2001, 782-787.
7. AH. Mokdad, BA. Bowman, ES. Ford, F. Vinicor, JS. Marks and Koplan, The continuing epidemics of obesity and diabetes in the United States, *JAMA*, *286*, 2001, 1195-200.
8. sy.aliqtisadi.com/ 2013, Ministry of health.
9. C. Triplitt, Drug Interactions of Medications Commonly Used in Diabetes, *Diabetes Spectrum*, *19(4)*, 2006, 202-211.
10. L. Pari and J. Umamaheswari, Antihyperglycaemic activity of Musa sapientum flowers: effect on lipid peroxidation in alloxan diabetic rats, *Phytother Res*, *14*, 2000, 1-3.
11. R. Ashraf, K. Aamir, AR. Shaikh and T. Ahmed, Effects of Garlic on Dyslipidemia in Patients with Type 2 Diabetes Mellitus. *J Ayub Med Coll*, *17(3)*, 2005, 60-64.
12. Diabetes Spectrum 2001, *14*, 199-208.
13. C. Bailey and C. Day, Traditional Plant Medicines as Treatments for Diabetes. *Diabetes care*, *12(8)*, 1989, 553-564.

14. K. Agarwal, Therapeutic actions of garlic constituents. *Med Res Rev, 16(1),* 1996, 111–124.
15. YY. Yeh and SM. Yeh, Garlic educes plasma lipids by inhibiting hepatic cholesterol and triacylglycerol synthesis. *Lipids, 29(3),* 1994, 189–193.
16. Rizwan Ashraf M. Phil1, Rafeeq Alam Khan and Imran Ashraf, Effects of garlic on blood glucose levels and HbA1c in patients with type 2 diabetes mellitus. *J Med Plant Res, 5(13),* 2011, 2922-2928.
17. Z. Hussien, Effect of Garlic on Dyslipidemi Patients with Diabetes Mellitus (Type 2). *Diyala Journal of Medicine, 6(1),* 2014, 100-104.
18. S. Chhatwala, R K. Sharmaa, G. Sharmaa and A. Khuranab, To study the antihyperglycaemic and lipid lowering effect of garlic as an adjunct to metformin in patients of type 2 diabetes mellitus with obesity, *Int J Basic Clin Pharmacol, 1(1),* 2012, 22-26.
19. R. Ashraf, R. Alam Khan and I. Ashraf, Garlic (Allium Sativum) Supplementation with Standard Antidiabetic Agent Provides Better Diabetic Control in Type 2 Diabetes Patients. *Pak J Pharm Sci, 24(4),* 2011, 565-570.
20. R. Kumar, S. Chhatwal, S. Arora, S. Sharma, J. Singh, N. Singh and V. Bhandari1, Antihyperglycemic, antihyperlipidemic, anti-inflammatory and adenosine deaminase–lowering effects of garlic in patients with type 2 diabetes mellitus with obesity. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 6,* 2013, 49–56.
21. RA. DeFronzo and AM. Goodman, Efficacy of metformin in patients with non-insulin-dependent diabetes mellitus. *The Multicenter Metformin Study Group. N Engl J Med, 333,* 1995, 541–9.
22. R. DeFronzo, Pharmacologic therapy for type 2 diabetes mellitus. *Ann Intern Med, 131,* 1999, 281–303.
23. H. Lebovitz, Stepwise and combination drug therapy for the treatment of NIDDM. *Diabetes Care, 17,* 1994, 1542–4.
24. G. Erle, S. Lovise, C. Stocchiero, L. Lora, A. Coppini, P. Marchetti and D. Merante, A comparison of preconstituted, fixed combinations of low-dose glyburide plus metformin versus high-dose glyburide alone in the treatment of type 2 diabetic patients. *Acta Diabetol, 36,* 1999, 61–5.
25. D M. Matheka, J M. Kilonzo, C M. Munguti and P W. Mwangi, Pattern, knowledge and practices of HbA1C testing among diabetic patients in a Kenyan tertiary referral hospital. *Globalization and Health, 9(55),* 2013.
26. RC. Jain and CR. Vyas, Garlic in alloxan-induced diabetic rabbits. *Am J Clin Nutr, 28,* 1975, 684-685.
27. PT. Mathew and KT. Augusti, Studies on the effect of allicin (diallyl disulphide-oxide) on alloxan diabetes I. Hypoglycaemic action and enhancement of serum insulin effect and glycogen synthesis. *Indian J Biochem Biophys, 10,* 1973, 209-212.
28. G. Siegel, A. Walter, S. Engel, A. Walper and F. Michel, Pleiotropic effects of Garlic. *Wien Med Wochenschr, 149,* 1999, 217-224.
29. Adler A et al., Effect of garlic and fresh oil supplementation on serum lipids and lipoproteins concentration in hypercholesterolemic men. *Am J Clin Nut, 65,* 1997, 445-450.
30. AK. Jain, R. Varger, S. Gotzkowsky and FG. Mcmahon, Can garlic reduce levels of serum lipids. A Controlled Clinical Study. *Am J Med, 94,* 1993, 632 – 635.
31. K. Rhman and G. Lowe, Garlic and cardiovascular Disease: A Critical Review. *The Journal of Nutrition, 136,* 2006, 736 – 740.
32. C. Stevinson, H. Pitter and E. Edzard, Garlic for treating hypercholesterolemia. *Ann Intern Med, 133,* 2000, 420 – 429.