

Effect of Garlic on Serum Lp-PLA2, Blood Pressure and Blood Glucose Levels

Roza Talaat Yaseen¹, Badraddin Hamad², Harmand Hama³ Abdulrahman Jawdat², Raid Duraid⁴,
Mohammed Merza^{2,3,4,5}

¹ Department of Nursing, Faculty of Nursing, Tishk International University, Erbil, Kurdistan Region of Iraq

² Department of Clinical Analysis, College of Pharmacy, Hawler Medical University, Erbil, Kurdistan, Iraq

³ Department of Biology, Faculty of Education, Tishk International University, Erbil, Kurdistan Region of Iraq

⁴ Department of Medical Biochemical Analysis, College of Health Technology, Cihan University-Erbil, Kurdistan Region of Iraq

⁵ Department of Pharmacy, Gasha Technical Institute, Erbil, Kurdistan Region of Iraq.

Corresponding author: Mohammed Merza, mohammed.merza@hmu.edu.krd

ABSTRACT

Background: There are many investigations on the effect of garlic on the body and its potential therapeutic roles, which makes garlic a useful addition to our diet either as food or as supplements. Lp-PLA2 is a novel biomarker for the prediction of getting Cardio-Cerebro vascular accident. High blood pressure is an important cardiovascular risk factor and is a major health problem. Diabetes mellitus, is categorized to the world's major diseases considering that affects high population on earth. It is complications include cardiac arrest and stroke. **Objective:** There are three objectives attained via conducting this study; first is to investigate the effect of garlic on Lp-PLA2 second is its influence on blood pressure, and lastly on blood glucose level. **Material and Method:** Data was collected from twenty students of different age groups within a period of one week; using Paired Sample T-Test (dependent sample t-test) to determine the mean difference between two sets of observations. **Results:** Lp-PLA2 and blood pressure levels were reduced but no affect was observed in blood glucose levels. **Conclusion:** Garlic supplements can be used to prevent and reduce the risk for cardiovascular diseases and hypertension (excluding contraindications). Garlic can be beneficial in reducing the risk of heart attacks and stroke in young and adults.

Keyword: Garlic, Blood glucose, Blood pressure, and Lp-PLA2

INTRODUCTION

Lipoprotein-associated phospholipase A2 (Lp-PLA2), also known as platelet-activating factor acetylhydrolase (PAF-AH), is a calcium-independent serine lipase that hydrolyzes oxidized phospholipids. The Lp-PLA2 test is a novel and unique biomarker of cardiovascular diseases.¹ Lp-PLA2 is formed from hematopoietic and inflammatory cells and is associated with apolipoprotein B-containing particles. Most of the circulating Lp-PLA2 level is found in the LDL lipid fraction and only a small percentage is in HDL lipid fraction.² Lp-PLA2 has been recommended as an adjunct to traditional risk factors in assessing future cardiovascular risks. The Lp-PLA2 test may be used along with a CRP test to evaluate a person's level of underlying inflammation associated with cardiovascular risk. However, unlike CRP, the Lp-PLA2 test is not affected by conditions other than cardiovascular that can cause general inflammation, so it may be used when someone has an inflammatory condition, such as arthritis. However, hypertension is a major public health problem resulting from pressure on the main arteries for long duration and is called the silent killer because it does not have any symptoms and takes a long time before it is diagnosed, thereby causing major cardiovascular complications such as myocardial infarction, stroke, renal failure, and death.^{2,3,4}

Hypertension among the adult population is increasing, and it affects more than 1 billion people worldwide, with higher prevalence in low-income countries compared to high-income countries as the access to healthcare and awareness of the disease are inadequate.⁵

Garlic has played important dietary and medicinal roles. Garlic has been found to have antihypertensive effects as well as lowering plasma lipid and antiplatelet effect. Blood pressure lowering effects may be linked to its hydrogen sulphide production and allicin liberated from alliin and the enzyme alliinase. Hypertensive patients may take garlic to lower the blood pressure and non-hypertensive patients may take garlic as a preventive strategy to reduce the risk of other cardiovascular complications.⁶

Hyperglycemia produces reactive oxygen species and free radicals; the resulting oxidative stress plays a key role in the pathogenesis and progression of diabetes and its complications. Garlic has antioxidant and hypoglycemic effects. Diet containing 5% of garlic powder decreases serum glucose and total cholesterol.⁷

The aim of this study is to investigate effect of garlic on Lp-PLA2, blood pressure, and blood glucose levels. Measuring serum Lp-PLA2 level is a quite informative parameter and is regarded as an independent risk factor of cardio-cerebro vascular accident (cerebral infarction and myocardial infarction). Lp-PLA2 analysis is set up and conducted in this study which is regarded as a new investigation for the first time in Iraq.

METHODS

This study was conducted in Hawler Medical University-College of Pharmacy, Erbil, Kurdistan region of Iraq, from September 2019 to March 2021. Using interview questionnaires with clinical and laboratory measures. A total number of 60 cases were collected. For each case blood pressure, and blood was withdrawn to calculate Lp-PLA2 and glucose level. The subjects were asked to rest for 5 minutes before measuring the blood pressure in a sitting position. Then 3 mL blood was withdrawn from them and centrifuged. For each case asked to take garlic capsules three times daily for duration of a week, in total 21 capsules for each subject. The serum was stored in -4 degree Celsius in the refrigerator. Lp-PLA2 and blood sugar was measured from the serum the day after. After a week the same procedure was repeated for each of the cases.

Lp-PLA2 test

The Lp-PLA2 was measured by the UPT Immunoassay Analyzer, which is a photoelectric detection instrument, based on Up-converting Phosphor Technology (UPT). The analyzer calculates the concentrations of the target analyte in the sample through measuring, analyzing and processing the distribution of Up-Converting Phosphor (UCP) particles on the immuno-chromato-graphic strip, to make the testing rapid, accurate and quantitative. The serum of the subjects was mixed with the special solution for the measurement, then put into the analyzer. Each test takes 15 minutes. The POCT analyzer and the kits of Lp-PLA2 was provided from Beijing Hotgen Biotech Company from china to the Hawler Medical University-College of Pharmacy in Kurdistan region of Iraq.

LP-PLA2 Operation

1. Connect the power cable on the instrument rear, then press the "Power on" key on the front panel



2. Enter into the working interface after pre-heating process. Press "Setting" and then press "read para"



3. Insert the calibration card to the bottom as prompted.



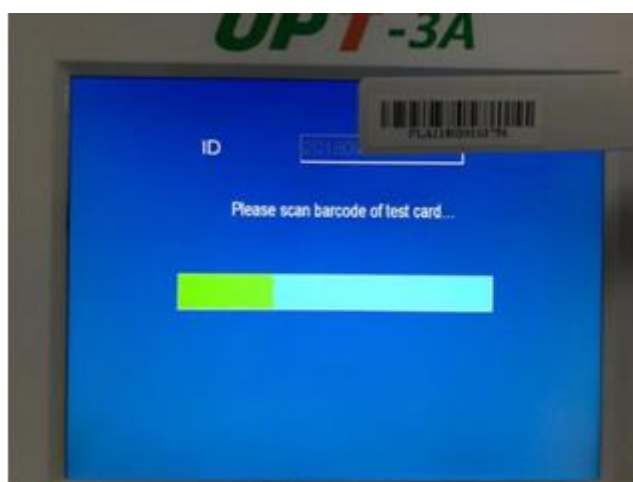
4. After read parameters successfully, press “exit” to return to the main interface.



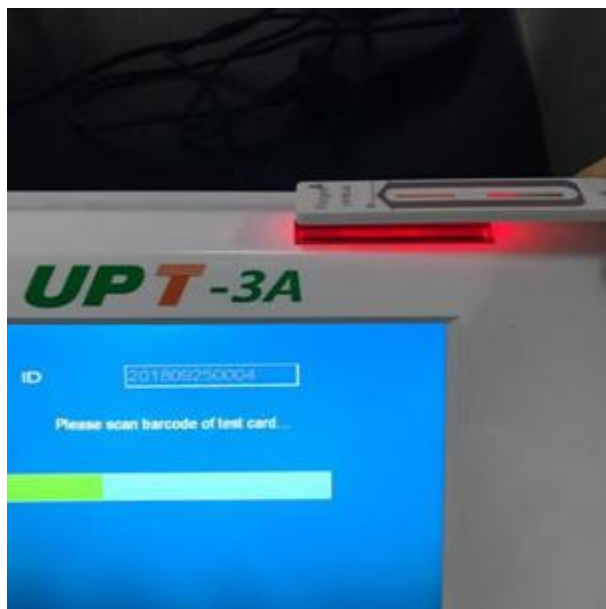
5. Dilute the sample and add the sample process: Take 150ul sample dilution, and add 100ul sample, mixed well and take 100ul of the mixed into the sample well of Lp-PLA2 test card, time 15min. then Detection: After 15 minutes when time is up, press “Manu test” on the main interface and continue to press “Enter”.



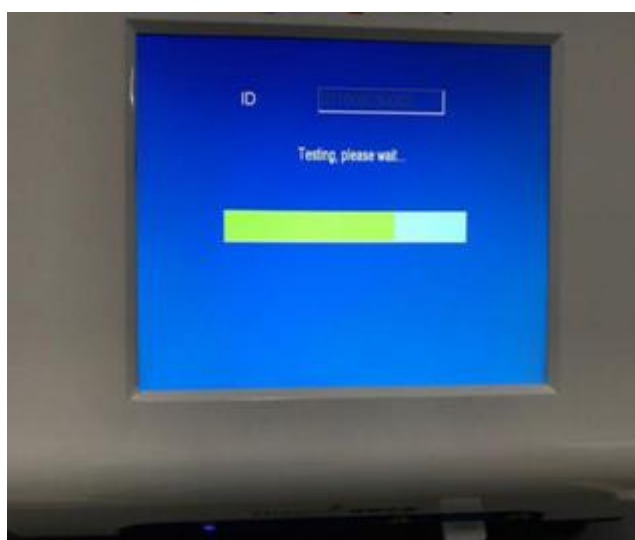
6. There is a barcode on the back of the test card, and you can see the instrument interface prompt to scan the barcode.



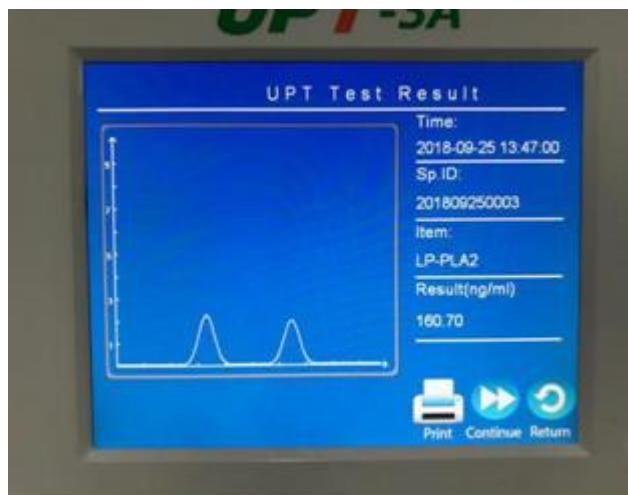
7. Scan the barcode on the back of the test card in the infrared area at the upper right corner of the instrument according to the prompt;



8. After the scan is completed, insert the test card to the bottom according to the prompt;



9. The test results can be read out later on the instrument interface. (Press the “Return” or “Continue” in the lower right corner to test the next sample).



10. When the instrument is not in use, you can click “Power on” in the lower left corner of the main interface to shut down;



Blood pressure

The device used for blood pressure measurement was an electronic sphygmomanometer (smart angel- automatic blood pressure monitor).

Blood glucose

Random blood glucose tests were obtained. Glucose was measured from the serum of each subject by a glucometer (SEJOY, BG-202 Blood Glucose Monitoring System).

Garlic capsules

Supplements of garlic compared to raw garlic have the advantage of reducing garlic breath, body odor, and prevents possible destruction of active compounds in the cooking process. The capsules used were an easy swallow, odorless garlic capsules which we got in a local pharmacy.

RESULTS

The effect of garlic on serum Lp-PLA2

Table (1) illustrate the effect of garlic on Lp-PLA2 levels. The Lp-PLA2 was measured before and after taking garlic capsule for one-week duration. As demonstrated in the table, garlic capsule when given to the students shows a substantial effect on the novel cardiovascular biomarker.

Table (1): Effect of garlic on serum Lp-PLA2 level in students

Variable	Group Mean (SE)		P value *
	Group 1 (n=30)	Group 2 (n=30)	
RBG (mg/dL)	118 (14)	108 (10)	0.04

Values are denoted as Mean \pm standard error. *P value is significant at <0.05 . Group 1 (students before treatment). Group2 (students after one-week treatment)

The effect of Garlic on RBG in normal individuals

Table (3) illustrate the effect of garlic on blood glucose level in students; RBG is measured before and after taking garlic capsule for one-week duration. As demonstrated in the table, garlic capsule when given to the students didn't show influence on blood glucose level.

Table (3): Effect of garlic on random blood glucose levels in students

Variable	Group Mean (SE)		P value *
	Group 1 (n=20)	Group 1 (n=20)	
RBG (mg/Dl)	112(15.27)	114.11(14.20)	0.0749

Values are denoted as Mean \pm standard error. *P value is significant at <0.05 . Group 1 (students before treatment). Group2 (students after one-week treatment)

DISCUSSION

The results of this study revealed that garlic has significant effect on Lp-PLA2 and blood pressure levels. With respect to the former, the work of this study verified that garlic is more likely to cause a substantial reduction of Lp-PLA2 in the volunteers. The reason behind the reduction effect of garlic on the Lp-PLA2 can be elucidated as below. First Garlic can have Preventive effects on oxidative stress and oxidative stress could be a cause of release of Lp-PLA2 from leukocyte. In addition, the second reason would be that garlic has lipid lowering properties, having impact on blood cholesterol and LDL levels. Additionally, LDL would enter tunica intima blood vessel via combination with Lp-PLA2. Hence it is likely that any decrease in LDL level could lead to a decrease in LDL deposition in the blood vessel wall.

The detailed role of both endogenous substance and their role in atherosclerosis can be explicated as follows. Arterial inflammation is the principal driving force responsible for

atherosclerotic plaque development and destabilization. Lp-PLA2 when released binds to the apolipoprotein B moiety on low-density lipoprotein (LDL) particles and remains latent until LDL is oxidized.⁸ Hence, it is likely that when Oxidized phosphatidylcholine contained in the oxidized LDL acts as a substrate for Lp-PLA2. Lp-PLA2 hydrolyzes oxidized phosphatidylcholine to generate two bioactive compounds lysophosphatidylcholine (lyso-PC) and oxidized non-esterified free fatty acids both which are considered proinflammatory mediators.⁹ This causes migration of macrophages and this form of LDL can be internalized by macrophages by means of the scavenger receptors on the surfaces of these cells. The internalization leads to the formation of lipid peroxidase and facilitates the accumulation of cholesterol esters, resulting in the formation of foam cells, which accumulates to form plaque.¹⁰ Hence, Lipoprotein-associated phospholipase A2 (Lp-PLA2) is a marker of inflammation in the vessel wall. Elevated level of Lp-PLA2 are indicative of vascular inflammation associated with the formation of plaque and rupture within the arteries.¹¹ this may play an important role in triggering cardio-cerebrovascular accident. Garlic has preventive effect from cardiovascular events due to its ability to reduce lipid content at the artery wall and in turn reducing Lp-PLA2 or via reducing oxidative stress that can be a cause of LP-PLA2 level.

The possible mechanism for hypotensive effect of garlic as assumed by Rashid and Khan to be due to its prostaglandins like- effect, which decreases peripheral vascular resistance.¹² Another study suggests that the gamma-glutamyl cysteines are the compounds in garlic that may lower blood pressure, as indicated by their ability to inhibit angiotensin-converting enzyme in in vitro.¹³ Another study on characteristics of garlic induced relaxation in pulmonary arteries concluded that garlic influences the production and function of endothelium derived relaxing and constricting factors which contribute to its protective effect against hypoxic pulmonary vasoconstriction.¹⁴ The vasodilatory effect of garlic is due to the activation of endothelial nitric oxide synthase and smooth muscle cell membrane hyperpolarization, which could decrease pulmonary vascular.¹⁵ Moreover, another study reported that the pulmonary vasodilatory effect of garlic is independent of the synthesis of NO.^{16,17}

Lastly, in our study garlic did not have effect on glucose levels, it could be due to the fact that blood glucose was a random test, and the participants were not fasting on both days of the sample collection.

CONCLUSION

Garlic supplements decrease Lp-PLA2 and blood pressure levels in normal individuals. Our data indicated that garlic supplements did not affect blood glucose levels. However, garlic can have a potential role in preventing sudden cardio-cerebro vascular accidents through reducing LP-PLA2 level.

Recommendation

To further investigate the effects of garlic (as whole or its ingredients) on Lp-PLA2 on bigger sample size with different age groups and young adults who are at higher risk for heart attacks and stroke.

To study effect of garlic on Lp-PLA2 in patients with acute cardio-cerebro vascular attack risk factors regardless of age for instance, hypertensive, and diabetics.

Due to an alarming rise in both morbidity and mortality rate of cardiovascular diseases worldwide, new strategies can be implemented for the investigation and treatment of the diseases.

Conflicts of Interest

No conflicts of interest.

Funding

Not funded

REFERENCES

1. Kearney, P.M., Whelton, M., Reynolds, K., Muntner, P., Whelton, P.K. and He, J., 2005. Global burden of hypertension: analysis of worldwide data. *The lancet*, 365(9455), pp.217-223.
2. Ibekwe, R.U., 2015. Modifiable risk factors of hypertension and socio demographic profile in Oghara, Delta state; prevalence and correlates. *Annals of medical and health sciences research*, 5(1), pp.71-77.
3. James, S. P.A., Oparil, S., Carter, B.L., Cushman, W.C., Dennison-Himmelfarb, C.,
4. Handler, J., Lackland, D.T., LeFevre, M.L., MacKenzie, T.D., Ogedegbe, O. and Smith, S.C., 2014. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *Jama*, 311(5), pp.507-520.
5. Vlachopoulos, C. and Terentes-Printzios, D., 2019. Global interventions in hypertension. *Heart and Metabolism*, p.25.
6. Ried, K., Frank, O.R., Stocks, N.P., Fakler, P. and Sullivan, T., 2008. Effect of garlic on blood pressure: a systematic review and meta-analysis. *BMC cardiovascular disorders*, 8(1), p.13.
7. Lee, Y.M., Gweon, O.C., Seo, Y.J., Im, J., Kang, M.J., Kim, M.J. and Kim, J.I., 2009. Antioxidant effect of garlic and aged black garlic in animal model of type 2 diabetes mellitus. *Nutrition research and practice*, 3(2), pp.156-161.
8. Dada, N., Kim, N.W. and Wolfert, R.L., 2002. Lp-PLA2: an emerging biomarker of coronary heart disease. *Expert review of molecular diagnostics*, 2(1), pp.17-22.
9. Mannheim, D., Herrmann, J., Versari, D., Gössl, M., Meyer, F.B., McConnell, J.P., Lerman, L.O. and Lerman, A., 2008. Enhanced expression of Lp-PLA2 and lysophosphatidylcholine in symptomatic carotid atherosclerotic plaques. *Stroke*, 39(5), pp.1448-1455.
10. Rashid, A. and Khan, H.H., 1985. The mechanism of hypotensive effect of garlic extract. *J Pak Med Assoc*, 35(12), pp.357-62.
11. Sendl, A., Elbl, G., Steinke, B., Redl, K., Breu, W. and Wagner, H., 1992. Comparative pharmacological investigations of *Allium ursinum* and *Allium sativum*. *Planta medica*, 58(01), pp.1-7.

12. Kim-Park, S. and Ku, D.D., 2000. Garlic elicits a nitric oxide-dependent relaxation and inhibits hypoxic pulmonary vasoconstriction in rats. *Clinical and Experimental Pharmacology and Physiology*, 27(10), pp.780-786.
13. Fallon, M.B., Abrams, G.A., Abdel-Razek, T.T., Dai, J., Chen, S.J., Chen, Y.F., Luo, B., Oparil, S. and Ku, D.D., 1998. Garlic prevents hypoxic pulmonary hypertension in rats. *American Journal of Physiology-Lung Cellular and Molecular Physiology*, 275(2), pp.L283-L287.
14. Kaye, A.D., De Witt, B.J., Anwar, M., Smith, D.E., Feng, C.J., Kadowitz, P.J. and Nossaman, B.D., 2000. Analysis of responses of garlic derivatives in the pulmonary vascular bed of the rat. *Journal of Applied Physiology*, 89(1),pp.353-358.
15. Gonçalves, I., Edsfeldt, A., Ko, N.Y., Grufman, H., Berg, K., Björkbacka, H., Nitulescu, M., Persson, A., Nilsson, M., Prehn, C. and Adamski, J., 2012. Evidence supporting a key role of Lp-PLA2-generated lysophosphatidylcholine in human atherosclerotic plaque inflammation. *Arteriosclerosis, thrombosis, and vascular biology*, 32(6),pp.1505-1512.
16. Ross, R., 1999. Atherosclerosis—an inflammatory disease. *New England journal of medicine*, 340(2), pp.115-126.
17. Cojocaru, M., Cojocaru, I.M. and Silosi, I., 2010. Lipoprotein-associated phospholipase A2 as a predictive biomarker of sub-clinical inflammation in cardiovascular diseases. *Maedica*, 5(1), p.51.