

## Research Article

# Medicinal Herbs of Pakistan Used in Blood Disorders

Murad S<sup>1\*</sup>, Tufail S<sup>2</sup>, Shah S<sup>3</sup>, Sheikh DM<sup>4</sup>, Mastoi AG<sup>5</sup>, Shah J<sup>6</sup> and Niazi MF<sup>7</sup>

<sup>1</sup>Pharmacology at IMDC, Pakistan

<sup>2</sup>Department of Pharmacology at SZMC, Pakistan

<sup>3</sup>Department of Gynecologist at NMC, Pakistan

<sup>4</sup>Department of Microbiology at JSMU, Pakistan

<sup>5</sup>Department of Community Welfare at IMDC, Pakistan

<sup>6</sup>Department of Clinical Psychology at Bahria University, Pakistan

<sup>7</sup>Department of Radiology at BAMC Multan, Pakistan

\*Corresponding author: Murad S, IM&DC, Pharmacology at IMDC, Islamabad, Pakistan

Received: November 22, 2019; Accepted: December 30, 2019; Published: December 31, 2019

## Abstract

High plasma lipids, especially LDL-cholesterol, and low HDL-cholesterol in presence of or frequent formation of free radicals in various metabolic pathways in human body may lead to development of atherogenesis, CAD. Isomer of Vitamin E alpha tocopherol has antioxidant effects like other hypolipidemic drugs used in allopathy. Ziziphus Jujube is medicinal plant having hypolipidemic potential. We conducted study on comparison of hypolipidemic effects of these two agents. Study was placebo-controlled conducted in Jinnah Hospital, Lahore from December 2015 to February 2016. Ninety hyperlipidemic patients were divided in three equal groups including 30 patients in each group. Their base line LDL-cholesterol and HDL-cholesterol was determined and kept in their personal file. Group-1 was on placebo, Group-2 was on Vitamin E 400 mg twice daily for two months. Group-3 was on half Kg Jujube per day for two months. After two months therapy their post treatment LDL and HDL-cholesterol was determined. When analyzed statistically, results showed non-significant effects of herbal fruit/drug Jujube on HDL-cholesterol but significant role on LDL-cholesterol reduction. While vitamin E has highly significant reduction potential in LDL-cholesterol and significant effects on HDL-cholesterol with p-value <0.01. We concluded from the study that Z. Jujube has antioxidant potential by lowering LDL-cholesterol in human plasma. However, this effect is not comparable with hypolipidemic effects of Vitamin E as it also increases good cholesterol i.e. HDL-cholesterol

## Introduction

Elevated levels of total cholesterol and low-density lipoproteins (LDL) in plasma are major risk factors for the development of atherosclerosis [1]. Much evidence provides support for the concept that the oxidized form of LDL causes oxidative stress and increases intracellular Ca in the vessel wall, and represents the pathogenic element in hypercholesterolemia [2,3]. Release of oxidant species from activated leukocytes, such as superoxide radical and hydroxyl radical, in principle, contributes to the oxidation of LDL. Thus, a strategy directed at the use of antioxidants such as vitamin E has been advocated to decrease the susceptibility of LDL to oxidation by interrupting free radical peroxidative chain reactions and to increase the resistance to atherosclerosis by protecting against endothelial dysfunction in hypocholesterolemic patients [4]. VITAMIN E is lipid-soluble, chain-breaking antioxidant. Structural analyses have revealed that molecules having vitamin E antioxidant activity include four tocopherols ( $\alpha$ ,  $\beta$ ,  $\gamma$ ,  $\delta$ ) and four tocotrienols ( $\alpha$ ,  $\beta$ ,  $\gamma$ ,  $\delta$ ) [5]. One form,  $\alpha$ -tocopherol, is the most abundant form in nature [6]. Alpha-Tocopherol is an important lipid-soluble antioxidant. It performs its functions as antioxidant in the glutathione peroxidase pathway and it protects cell membranes from oxidation by reacting with lipid radicals produced in the lipid peroxidation chain reaction. This removes the free radical intermediates and prevents the oxidation reaction from continuing. The oxidized  $\alpha$ -tocopheroxyl radicals produced in this process may be recycled back to the active reduced form through reduction by other antioxidants, such as ascorbate, retinol or ubiquinol [7]. Vitamin E is transported in the blood by the plasma lipoproteins and erythrocytes. Chylomicrons carry tocopherol from the enterocyte to the liver, where they are incorporated into parenchymal cells as chylomicron remnants. The

catabolism of chylomicrons takes place in the systemic circulation through the action of cellular lipoprotein lipase. During this process tocopherol can be transferred to high-density lipoproteins (HDLs). The tocopherol in HDLs can transfer to other circulating lipoproteins, such as LDLs and very low-density lipoproteins (VLDLs). During the conversion of VLDL to LDL in the circulation, some  $\alpha$ -tocopherol remains within the core lipids and thus is incorporated in LDL. Most  $\alpha$ -tocopherol then enters the cells of peripheral tissues within the intact lipoprotein through the LDL receptor pathway, although some may be taken up by membrane binding sites recognising apolipoprotein A-I and A-II present on HDL [8-11]. Jujube fruit is known to contain considerable amount of phenolic compounds, including chlorogenic acid, gallic acid, protocatechuic acid and caffeic acid [12]. It has been proved by researchers that level at which LDL oxidizes, decreases linearly with increasing phenolic concentration in plasma. Phenolic compounds are able to bind to LDL and this may account for the increase in LDL resistance to oxidation [13]. It is also possible that increases in HDL-cholesterol concentrations may contribute to the suppression of LDL oxidation and that polyphenolic compounds present in Jujube may contribute to an elevation in HDL cholesterol [14].

## Material and Method

It was placebo controlled research study conducted in Jinnah Hospital, Lahore-Pakistan from December 2015 to February 2016. Ninety hyperlipidemic patients were enrolled in the study. Both gender male and female patients age range from 20 to 65 years were included. Written consent was taken from all participants. Their base line LDL and HDL cholesterol was measured in Biochemistry Lab. of the Hospital. Separate Proforma/file was made for every person.

**Table 1:** Showing pre and post-treatment values with their statistical significance in two months therapy.

	LDL-c	HDL-c
At day-0	G1 n=30 189.9±1.22 G2 n= 29 199.9±1.70 G3 n= 29 190.1±1.77	G1= 38.8±1.11 G2= 38.9±1.78 G3= 40.6±1.20
At day-60	G1= 188.0±1.91 G2= 187.7±1.17 G3= 183.6±2.10	G1= 38.6±1.71 G2= 45.7±1.11 G3= 44.9±1.29
Change	G1= 1.9 mg/dl G2= 12.2 mg/dl G3= 6.5 mg/dl	G1= 0.2 mg/dl G2= 6.8 mg/dl G3= 1.1 mg/dl
p-value	G1= >0.05 G2= <0.001 G3= <0.01	G1= >0.05 G2= <0.01 G3= >0.05

G1: placebo group; G2: Vitamin E group; and G3: Jujuba group. 'n' stands for sample size. P-value >0.05 was considered as non-significant change, p-value <0.01 was considered as significant and p-value <0.001 was considered as highly significant change in the parameter.

Patients suffering from any hepatic, renal or thyroid impaired disease were excluded from the study. They were divided in three groups, 30 individuals in each group. Group-1 was on placebo therapy i.e. advised to take one capsule (containing grinded wheat) thrice daily with each meal. Group-2 was on Capsule Evion 400 mg (containing Vitamin E). They were advised to take one capsule twice daily with their lunch and dinner. Group-3 was advised to take half kilograms Jujuba in three divided times per day. All were advised to take their advised medicine for two months. Fortnightly clinic visit was advised to all participants. At the end of study, we determined their lipid profile in the same Hospital Lab. SPSS version 26 was selected to determine and analyze change in the parameters. Mean values with  $\pm$  SEM were analyzed applying paired 't' test for determination of significance changes in parameters. P-value >0.05 was considered as non-significant change, p-value <0.01 was considered as significant and p-value <0.001 was considered as highly significant change in the parameter.

## Results

After two months therapy when pre and post-treatment results were compared, it was observed that Vitamin E reduced LDL-cholesterol 12.2 mg/dl and increase in HDL-cholesterol was 6.8 mg/dl. In Group-3 who was on Z. Jujuba their LDL-cholesterol reduced 6.5 mg/dl and HDL-cholesterol increase was 1.1 mg/dl, as shown in following Table 1.

## Discussion

Vitamin E molecules can interrupt free radical chain reactions by capturing the free radical. This imparts to them their antioxidant properties. The free hydroxyl group on the aromatic ring of vitamin E is responsible for the antioxidant properties. The hydrogen from this group is donated to the free radical; resulting in a relatively stable free radical form of vitamin E. Vitamin E also reduces LDL-cholesterol. As in our results it decreased LDL-cholesterol 12.2 mg/dl in two months therapy for hyperlipidemic patients. JW chen et al [15] proved almost same results. BN Wang et al [16] stated mechanism of alpha tocopherol that it prevents oxidation of LDL particles and scavenges free radicals already formed in various tissues of human body. H Wang et al [17] explained that when produced synthetically, it is composed of eight stereoisomers in which RRR- $\alpha$ -tocopherol is the most biologically active form, which takes up and reacts with

free radicals and may lead to form less toxic metabolites. J W Li et al [18] proved that HDL cholesterol increase 8.15 mg/dl when 400 mg Evion (vitamin E) was used in 20 hyperlipidemic patients twice daily for three months. We proved 6.8 mg/dl increase in HDL cholesterol when 400 mg vitamin E was used in 29 hyperlipidemic patients. This contrast in results are due to their small sample size in their study. When half Kg Jujuba was used by 29 hyperlipidemic patients in our research work it was we proved that LDL cholesterol reduction was 6.5 mg/dl in two months therapy. HDL cholesterol increase in our result is non significant biostatistically in these patients i. e. 1.1 mg/dl. Results match with results of study conducted by Xu et al [19] who proved 1.18 mg/dl increase in HDL cholesterol and 5.55 mg/dl decrease in LDL cholesterol. Same results proved studies conducted by GH Jagannadha Rao et al [20] and SH Abd-Alrahman et al [21] by using 600 grams Jujuba per day in 20 hyperlipidemic patients. AM Sabzghabae et al [22] explained presence of various phytochemical compounds which act as antioxidant in human body preventing development of atherogenesis in human body. JW Li et al [23] supported viewpoints of AM Sabzghabae et al regarding presence of phytochemicals in various herbal plants and their hypolipidemic potential with lesser SEs.

## Conclusion

It was concluded from this research study that Vitamin E is very potent antioxidant agent when used alone or in combination with herbal medications like Ziziphus Jujuba. Ziziphus Jujuba when used alone have more hypolipidemic effects on 'Bad' cholesterol i.e. LDL cholesterol but non-significant effects on Good cholesterol i.e. HDL cholesterol.

## References

- Maruyama K, Iso H. Overview of the Role of antioxidant vitamins as Protection against Cardiovascular Disease: Implications of aging. Available from: Aging: Oxidative stress and dietary antioxidants (1 ed.). New York: Elsevier Inc. 2014; 21.
- Lu Z, Nie G, Belton PS, Tang H, Zhao B. Structure–activity relationship analysis of antioxidant ability and neuroprotective effect of gallic acid derivatives. *Neurochem Int.* 2015; 48: 263-274.
- Simon E, Gariepy J, Cogny A, Moatti A, Simon A. "Erythrocyte, but not plasma, vitamin E concentration is associated with carotid intima–media thickening in asymptomatic men at risk for cardiovascular disease". *Atherosclerosis.* 2011; 159: 193-200.
- Subcommittee on Vitamin Tolerance, Committee on Animal Nutrition, National Research Council. "Vitamin E, in Vitamin Tolerance of Animals". National Academy of Sciences. 2013; 9: 313-318.
- Shute WE, Shute EV, et al. Alpha Tocopherol (Vitamin E) in Cardiovascular Disease. *Cardiol.* 2013; 23: 119-123.
- Vogelsang A, Shute EV, Shute. "Effect of vitamin E in coronary heart disease". *Nature.* 2012; 157: 772.
- Shute EV, Vogelsang AB, Skelton FB, Shute WE, Vogelsang. "The influence of vitamin E on vascular disease". *Surg Gynecol Obstet.* 2012; 86: 1-8.
- Skelton F, Shute E, Skinner HG, Waud RA, Shute; Skinner; Waud. "Antipurpuric Action of A-Tocopherol (Vitamin E)". *Science.* 2012; 103: 762.
- György P, Rose CS, Rose. "Effect of dietary factors on early mortality and hemoglobinuria in rats following administration of alloxan". *Science.* 2012; 108: 12.
- Singh N, Rajini PS. Antioxidant-mediated protective effect of potato peels extract in erythrocytes against oxidative damage. *Chem Biol Interact.* 2008; 173: 97-104.

11. Chaudhuri S, Banerjee A, Basu K, Sengupta B, Sengupta PK. Interaction of flavonoids with red blood cell membrane lipids and proteins: antioxidant and antihemolytic effects. *Int J Biol Macromol.* 2007; 41: 42-48.
12. Panseeta P, Lomchoey K, Prabpai S, Kongsaree P, Suksamram A, Ruchirawat S, et al. Antiplasmodial and antimycobacterial cyclopeptide alkaloids from the root of *Ziziphus Jujuba*. *Phytochemistry.* 2011; 72: 909-915.
13. Schmidt U, Lieberknecht A, Bokens H, Griesser H. Phenols in *Ziziphus Jujuba*. *J Org Chem.* 2012; 48: 2680-2685.
14. Suksamram S, Suwannapoch N, Aunchai N, Kuno M, Ratananukul P, Haritakun R, et al. LDL oxidation and polyphenolic compounds. *Tetrahedron.* 2015; 61: 1175-1180.
15. Chen JW, Zhu ZQ, Hu TX, Zhu DY. Vitamin E affects LDL cholesterol. *Acta Pharmacol Sin.* 2012; 23: 667-672.
16. Wang BN, Cao W, Gao H, Fan MT. Alpha tocopherol and CAD. *Circulation.* 2010; 71: 703-707.
17. Wang H, Gao XD, Zhou GC, Cai L, Yao WB. Effects of Vitamin E on oxidative stress. *Food Chem.* 2011; 106: 888-895.
18. Wang J, Li LT, Dan Y. The correlation between hyperlipidemia and alpha tocopherol. *J Food Eng.* 2013; 60: 481-484.
19. Xuedan Huang, Akiko Kojima-Yuasa, Toshio Norikura, David Opere Kennedy, Tadayoshi Hasuma, Isao Matsui-Yuasa. *Ziziphus* and free radicals in body. *Am J Chin Med.* 2007; 35: 517.
20. G. Hari Jagannadha Rao, P. Lakshmi, G. Hari Jagannadha Rao. Anti-diabetic activity of *Jujuba* plant. *International Journal of Pharma and Bio Sciences.* 2012; 3: 90-95.
21. Sherif H Abd-Alrahman, Mounir M Salem-Bekhit, Manal EA Elhalwagy. Chemical Composition and Antioxidant Activity of *Ziziphus jujuba* Seeds Extract. *Journal of Pure and Applied Microbiology.* 2013; 7: 379-385.
22. Ali Mohammad Sabzghabae, Iman Khayam, Roya Kelishadi, Alireza Ghannadi, Rasool Soltani, Shirinsadat Badri, et al. Effect of *Zizyphus Jujuba* Fruits on Dyslipidemia in Obese Adolescents: a Triple-masked Randomized Controlled Clinical Trial. *Med Arh.* 2013; 67: 156-159.
23. JW Li, SD Ding, XL Ding. Comparison of antioxidant capacities of extracts from five cultivars of Chinese jujube. *Process Biochem.* 2012; 40: 3607-3613.