

Research Article

Fruits are as Effective as Allopathic Medications

Qudoos A¹, Murad S^{2*}, Iftikhar S³, Murad JS⁴, Ghaffar A⁵ and Mahar MR⁶

¹Department of Pharmacology, HBS Medical College, Pakistan

²Department of Pharmacology, IMDC/DANTH, Pakistan

³Department of Pharmacology, RLMC, Pakistan

⁴Clinical Psychologist at Bahria University, Pakistan

⁵CWO at DANTH and IMDC, Pakistan

⁶Dentist at IDH, Pakistan

*Corresponding author: Shah Murad, Department of Pharmacology, IMDC/DANTH, Islamabad, Pakistan

Received: August 08, 2019; Accepted: September 09, 2019; Published: September 16, 2019

Abstract

Coronary artery disease occurs when excess cholesterol in the bloodstream is deposited in the walls of blood vessels, particularly in the arteries that supply blood to the heart (coronary arteries). Inherited forms of hypercholesterolemia can also cause health problems related to the buildup of excess cholesterol in other tissues. According to the Low-Density-Lipoprotein (LDL) receptor hypothesis, development of atherosclerosis is caused by a high concentration of LDL-cholesterol in the blood, and lowering LDL-cholesterol reverses, or at least retards, atherosclerosis, thus preventing cardiovascular disease. Isomer of alpha tocopherol has antioxidant effects like other hypolipidemic drugs used in allopathy. Ziziphus Jujuba is medicinal plant having hypolipidemic potential. We conducted study on comparison of hypolipidemic effects of these two agents. Study was placebo-controlled conducted in General Hospital, Lahore from December 2018 to February 2018. 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 400mg twice daily for two months. Group-3 was on half Kg Jujuba 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. Jujuba 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.

Conclusion: It was concluded from this research work that Vitamin E is much more effective as hypolipidemic fruit Jujuba with p-value <0.001 and <0.01 respectively.

Keywords: Herbs; Fruits; CAD; Heart attack; Hyperlipidemia

Introduction

High LDL cholesterol makes you more likely to have narrowing of the arteries from atherosclerosis at an early age. The condition is typically passed down through families in an autosomal dominant manner. That means you only need to get the abnormal gene from one parent in order to inherit the disease [1]. 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 [2]. Vitamin E is lipid-soluble, chain-breaking antioxidant. Structural analyses have revealed that molecules having vitamin E antioxidant activity include four tocopherols and four tocotrienols [3]. One form, -tocopherol, is the most abundant form in nature [4]. 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 α -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 ubiquinol5. 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) [6]. During the conversion of VLDL to LDL in the circulation, some α -tocopherol remains within the core lipids and thus is incorporated in LDL. Most α -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 recognizing apolipoprotein A-I and A-II present on HDL [7]. Jujube fruit is known to contain considerable amount of phenolic compounds, including chlorogenic acid, gallic acid, and protocatechuic acid and caffeic acid [8]. It has been proved by researchers that level at which LDL oxidizes, decreases linearly with increasing phenolic concentration in plasma [8,9]. Phenolic

compounds are able to bind to LDL and this may account for the increase in LDL resistance to oxidation [10]. 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 [11]. The body exerts a certain effort to regulate its tissue levels with specific tocopherol transport proteins and membrane receptors. Antiproliferative and protein kinase C-suppressing effects of alpha-tocopherol have been previously demonstrated, which have not been mimicked by beta-tocopherol or probucol. Protein kinase C promises to be an important area of interest in the means of glaucoma and cataractogenesis [12]. Phenolic profiles and antioxidant activity of jujube made this fruit meaningful in therapeutics discipline of medicine. In response to different fertilizers [13]. Application of organic fertilizer appeared to enhance the phenolics and antioxidant activity accumulation of jujubes, compared to conventional fertilized jujubes [14].

Materials and Methods

It was placebo controlled research study conducted in General Hospital, Lahore-Pakistan from December 2018 to February 2018. 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 and the study work on patients was approved by ethics committee vide reference letter no: JHL/RW-102 dated 29th November 2018. Their total cholesterol, HDL and triglycerides were all measured directly and the LDL was calculated using the formula: $TC = LDL + HDL + (Triglycerides/5)$ [10]. Separate Performa/file was made for every person. 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 400mg (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 dried, small size pulp of 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 with Z Jujuba and vitamin E, it was observed that one patient withdrew from each group due to their personal reasons. When pre and post-treatment results were compared, it was observed that Vitamin E reduced LDL-cholesterol from 199.9mg/dl to 187.7mg/dl which is 12.2mg/dl change in the parameter in 29 hyperlipidemic patients. When statistically analyzed this change was highly significant. HDL-cholesterol raised from 38.9mg/dl to 45.7mg/dl in this group which is 6.8mg/dl increase in this parameter. It is significant change with p-value <0.01 . In group-3,

LDL-cholesterol decreased from 190.1mg/dl to 183.6mg/dl. This decrease in tested parameter is significant with p-value <0.01 . HDL cholesterol in this group increased from 40.6mg/dl to 44.9mg/dl in two months therapy by Z. Jujuba. Change in this parameter is 1.1mg/dl, which is statistically non-significant with p-value >0.05 . In placebo group both parameters showed non-significant changes with p-values >0.05 .

Discussion

α -Tocopherol accounts for 90% of the vitamin E in human tissues and acts as an antioxidant (i.e., stops the chain reaction of free radicals producing more free radicals). Vitamin E protects cell membranes, proteins, and DNA from oxidation and thereby contributes to cellular health. The Recommended Daily Allowance (RDA) for vitamin E is 8mg (12IU) for females and 10mg (15IU) for males, Packer recommends up to 1,000-1,200 IU intake of vitamin E in some pathologies including cataract. The principal reserve of natural vitamin E is vegetable oil where its function is to protect tissue from oxidative damage. It is a liposoluble molecule, and, therefore, after dietary intake, vitamin E is not only absorbed easily from the intestinal lumen but is also dispersed between lipids and proteins in cell membranes [15]. 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 [16]. As in our results, it decreased LDL-cholesterol 12.2mg/dl in two months therapy for hyperlipidemic patients. JW chen et al., [17] in 2012 proved almost same results. BN Wang et al., [18] in 2010 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., [19] in explained that when produced synthetically, it is composed of eight stereoisomers in which RRR- α -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., [20] in 2013 proved that HDL cholesterol increase 8.15mg/dl when 400mg Evion (vitamin E) was used in 20 hyperlipidemic patients twice daily for three months. We proved 6.8mg/dl increase in HDL cholesterol when 400mg 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 proved that LDL cholesterol reduction was 6.5mg/dl in two months therapy. HDL cholesterol increase in our result is non-significant biostatistically in these patients i. e. 1.1mg/dl. Results match with results of study conducted by Xuddan huang et al., [21] in 2007 who proved 1.18mg/dl increase in HDL cholesterol and 5.55mg/dl decrease in LDL cholesterol. Same results proved studies conducted by GH Jagannadha Rao et al., [22] in 2012 and SH Abd-Alrahman et al., [23] in 2013 by using 600grams Jujuba per day in 20 hyperlipidemic patients. AM Sabzghabae et al., [24] in 2013 explained presence of various phytochemical compounds, which act as antioxidant in human body, preventing development of atherogenesis in human body. Iloakov Li et al., [25] in 2012 supported viewpoints of AM Sabzghabae et al regarding presence of phytochemicals in various herbal plants and their hypolipidemic potential with lesser SEs.

With calcium, potassium, saponins, flavonoids, betulinic acid, and vitamins A and C filled to the brim of this fruit, jujube is pretty much a powerhouse of health benefits. It provides a line of defense from small aches and pains to something as major as cancer and heart attack [26]. Amongst inorganic fertilizers, supplemental potassium as an individual nutrient improved the accumulation of phenolics in jujubes [27]. This fruit is not only flavorful, but also commonly used in Traditional Chinese Medicine for detoxification, preventing anemia, analeptic, palliative and immunity improvements [28].

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

- Iso H. Overview of the role of antioxidant vitamins as protection against cardiovascular disease. *IJMSR* 2012; 88: 88-90.
- Tang H, Zhao B. Structure activity relationship analysis of antioxidant ability and neuroprotective effect of gallic acid derivatives. *J Med Plants*. 2017; 22: 166-170.
- Olui B, Simon E, Garipey J, Cogny A, Moatti N, Simon A, et al. Erythrocyte, but not plasma, vitamin E concentration is associated with carotid intima-media thickening in asymptomatic men at risk for cardiovascular disease. *Med Sc J*. 2016; 10: 55-59.
- Werger T. Subcommittee on Vitamin Tolerance, Committee on Animal Nutrition, National Research Council. "Vitamin E, in Vitamin Tolerance of Animals". *JMSP*. 2016; 12: 88-90.
- Ertvyte ER, Shute WE, Shute EV. Alpha Tocopherol (Vitamin E) in Cardiovascular Disease. *Cardiol*. 2013; 23: 119-123.
- Vogelsang A, Shute EV. Effect of vitamin E in coronary heart disease. *Nature*. 1946; 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, Waud SS. Antipurpuric action of α -tocopherol (Vitamin E). *Science*. 2012; 103: 762.
- György P, Rose CS. Effect of dietary factors on early mortality and hemoglobinuria in rats following administration of alloxan. *Sci*. 1948; 108: 716-768.
- Yang L, Fan B, Yang K, Zhu H. A simple and sensitive method for lipoprotein and lipids profiles analysis of individual micro-liter scale serum samples. *Chem Phys Lipids*. 2012; 165: 133-141.
- 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.
- Panseeta P, Lomchoey K, Prabpai S, Kongsaree P, Suksamrarn A, Ruchirawat S, et al. Antiplasmodial and antimycobacterial cyclopeptide alkaloids from the root of *Ziziphus Jujuba*. *Phytochemistry*. 2011; 72: 909-915.
- Schmidt U, Lieberknecht A, Bokens H, Griesser H. Phenols in *Ziziphus Jujuba*. *J Org Chem*. 2012; 48: 2680-2685.
- Suksamrarn S, Suwannapoch N, Aunchai N, Kuno M, Ratananukul P, Haritakun R, et al. LDL oxidation and polyphenolic compounds. *Tetrahedron*. 2015; 61: 1175-1180.
- Chen JW, Zhu ZQ, Hu TX, Zhu DY. Vitamin E affects LDL cholesterol. 2002; 23: 667-672.
- Wang BN, Cao W, Gao H, Fan MT. Alpha tocopherol and CAD. *Circulation*. 2010; 71: 703-707.
- JW Chen, Wang H, Gao XD, Zhou GC, Cai L, Yao WB. Effects of Vitamin E on oxidative stress. *Food Chem*. 2011; 106: 888-895.
- BN Wang, Wang J, Li LT, Dan Y. The correlation between hyperlipidemia and alpha tocopherol. *J Food Eng*. 2013; 60: 481-484.
- H Wang, Huang X, Akiko Kojima-Yuasa, Norikura T, Kennedy DO, Hasuma T, et al. *Ziziphus* and free radicals in body. *Am J Chin Med*. 2007; 35: 517.
- JW Li, Hari JR, Lakshmi P. Anti diabetic activity of jujuba plant. *Int J Pharm Bio Sci*. 2012; 3: 90-95.
- Xuddan, Abd-Alrahman SH, Salem-Bekhit MM, Elhalwagy ME. Chemical composition and antimicrobial activity of *Ziziphus jujuba* seeds extract. *J Pure and Applied Microbiol*. 2013; 7: 379-385.
- Jagazen GH, Sabzghabae AM, Khayam I, Kelishadi R, Ghannadi A, Soltani R, et al. Effect of *Ziziphus jujuba* fruits on dyslipidemia in obese adolescents: A triple-masked randomized controlled clinical trial. *Med Arh* 2013; 67: 156.
- Abd-Alrahman SH, Li JW, Ding SD, Ding XL. Comparison of antioxidant capacities of extracts from five cultivars of Chinese jujube. *Process Biochem*. 2015; 40: 3607-3613.
- AM Sabzghabae, 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. *UJMS*. 2013; 41: 42-48.
- Iloakov Li, Panseeta P, Lomchoey K, Prabpai S, Kongsaree P, Suksamrarn A, et al. Antiplasmodial and antimycobacterial cyclopeptide alkaloids from the root of *Ziziphus Jujuba*. *IJMP* 2012; 72: 909-915.
- Erthy M, Schmidt U, Lieberknecht A, Bokens H, Griesser H. Phenols in *Ziziphus Jujuba*. *J Org Chem*. 2012; 48: 2680-2685.
- Julia GT, Shute EV, Vogelsang AB, Skelton FB, Shute WE. The influence of vitamin E on vascular disease. *SJP*. 2016; 12: 145-148.
- Oliya T, Herbou F, Skelton F, Shute E, Skinner HG, Waud RA. Antipurpuric action of α -tocopherol (Vitamin E). *UJMP*. 2012; 11: 44-49.