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RESEARCH ARTICLE

COMPARATIVE CHARACTERIZATION OF ANTIOXIDANT PROFILE OF VITAMIN-E AND RED DATES IN PLACEBO AND TESTED GROUPS OF HYPERLIPIDEMIC PATIENTS

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ABSTRACT
Antioxidants are nutrients that help minimize free-radical damage to the body. Free radicals are highly reactive compounds that are created in the body during normal metabolic functions or introduced from the environment, such as by exposure to pollution and other toxins. Inherently unstable, free radicals contain "extra" energy which they try to reduce by reacting with certain chemicals in the body, which interferes with the cells' ability to function normally. Current study compared antioxidant characteristics of vitamin-E and red Dates. It was placebo-controlled conducted study conducted at general hospital Lahore Pakistan from January 2018 to march 2018. LDL-cholesterol was calculated as total cholesterol- HDL-cholesterol-VLDL-cholesterol; VLDL-cholesterol was measured directly after ultracentrifugation. After one month therapy their post treatment lipid profile was determined and analyzed statistically by using SPSS version 2.2.01 2013. Paired 't' test was applied for mean values with SD of the parameters before and after treatment. Results showed highly significant change in LDL-cholesterol of group-II patients but HDL-cholesterol was increased 6.6 mg/dl, still it was significant change with p-value of <0.01. In group-III LDL-cholesterol was decreased 10.9 mg/dl which is significant change with p-value <0.01. HDL-cholesterol in this group was increased 4.2 mg/dl which is non significant with p-value of >0.05. Study concluded that red dates have antioxidant potential by lowering LDL-cholesterol in human plasma. But this effect is not comparable with hypolipidemic effects of Vitamin E as it also increases good cholesterol i.e. HDL-cholesterol.
Keywords: CAD, LDL, HDL, mortality, morbidity, prevention.

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INTRODUCTION

When human body uses oxygen, it creates free radicals as a by-product and the damage caused by those free radicals is called "oxidative stress." Superoxide radical and hydroxyl radical may contribute to the oxidation of LDL[1]. These radicals are formed in various metabolic processes in human body[28]. 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[9,10].

Antioxidants combat free radicals in several ways: they may reduce the energy of the free radical, stop the free radical from forming in the first place, or interrupt an oxidizing chain reaction to minimize the damage caused by free radicals. To treat metabolic syndrome by allopathic regimn of allopathic drugs is difficult. Herbal medicines are replacing drug treatment of hyperglycemia, hypertension and hyperlipidemia especially by antioxidant effects of their active ingredients. Vitamin-E 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 ubiquinol[11,12]. Chylomicrons carry vitamin-E from the enterocyte to the liver, where they are incorporated into parenchymal cells as chylomicron remnants[13].

The catabolism of chylomicrons takes place in the systemic circulation through the action of cellular lipoprotein lipase. During this process vitamin-E can be transferred to high-density lipoproteins. This vitamin-E in high density lipoproteins can transfer to other circulating lipoproteins, such as low density lipoproteins and very low-density lipoproteins, causing less oxidative process to occur[14,15]. A full range of plant derived nutritional supplements, phytochemicals, and pro-vitamins which help in sustaining good health and fighting diseases is now being described as functional foods, nutriceuticals, and nutraceuticals[16-20]. Red date is one of them. The hepato-cardio-protective effect is attributed to red date's antioxidant mechanisms and inhibition of oxidative degradation of lipids. Jujube contain higher phenol levels, exhibiting diphenyl picrylhydrazyl antioxidant activity, ferric ion reducing antioxidant power and protective effects against DNA damage. Active ingredients of red date have been found to possess a range of effects: estrogenic and anti-estrogenic activity, anti-proliferative activity, induction of cell cycle arrest and apoptosis, prevention of oxidation, regulation of the host immune system, anti-inflammatory activity, modulation of effect of cytochrome P450 enzymes involved in activation of pro-carcinogens, upregulation of genes producing anti-oxidant enzymes, and the ability to change cellular signaling. The body produces several antioxidant enzymes, including superoxide dismutase, catalase, and glutathione peroxidase, that neutralize many types of free radicals. Supplements of these enzymes are available for oral administration. However, their absorption is probably minimal at best. Supplementing with the "building blocks" the body requires to make superoxide dismutase, catalase, and glutathione peroxidase may be more effective. These building block nutrients include the minerals manganese, zinc, and copper for superoxide dismutase and selenium for glutathione peroxidase[21-23].

MATERIALS AND METHOD

It was placebo-controlled research conducted at general hospital Lahore Pakistan from January 2018 to march 2018. Sample size: 120 male hyperlipidemic patients were included with age range from 18 to 70 years.

Exclusion criteria: Patients already suffering from renal, hepatic, pulmonary, or thyroid diseases were excluded. Patients already taking medicines for any cardiac problem were also excluded.

Consent: Written and already explained consent was taken from all participants. Patients were divided in three equal numbers, ie; 40 patients in each group. Group-I (n=40) was on placebo. They were provided capsules which were filled with grounded brown rice taking 8 hourly daily for one month. Group-II (n=40) was on capsules of vitamin E 400 mg taking eight hourly daily for one month. Group-II (n=40) was advised to take red dates 20 grams thrice daily for the period of one month. Their separate folder was made to keep their medical record regarding their progress to drug treatment, follow-up and drug compliance. They were advised to visit clinic (research centre) fortnightly for checkup and follow-up or any other miscellaneous advice/query.

Method: Their lipid profile was determined in biochemistry laboratory of the hospital. LDL-cholesterol was calculated as total cholesterol − HDL-cholesterol− VLDL-cholesterol; VLDL-cholesterol was measured directly after ultracentrifugation.

Statistical Significance: Biostatistical analysis was determined by applying paired't' test using SPSS version 2.2.01 2013. P-value >0.05 was considered as non-significant change, p-value <0.01 was significant change in the parameters and p-value <0.001 was considered as highly significant change in the parameter. We emphasized on changes in LDL-cholesterol and HDL-cholesterol because these two parameters are core factors for development of atherosclerosis leading to development of coronary artery disease which is again core cause of hypertension or even metabolic syndrome.

RESULTS

After one month therapy by vitamin-E and red dates when pre and post-treatment results were compared, it was observed that Vitamin E reduced TC 19.3, TG 14.2, LDL-c 20.2 mg/dl. HDL increased in this group 6.6 mg/dl. Red dates decreased TC 8.2, TG 4.0, LDL-c 10.9 mg/dl. HDL-c in this group increased non-significantly i.e.; only 4.2 mg/dl. Changes in mean values with SD and statistical significance are shown in Table 1.

DISCUSSION

In the last three decades, the search for natural bioactive compounds that can serve as antioxidant and antimicrobial agents had increased tremendously. The reasons for these are increasing understanding of the harmful nature of reactive oxygen species (ROS) produced during oxidation processes, harmful nature of synthetic antioxidant such as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) and the increasing resistance posed by microorganisms to synthetic antibiotics. A strong reducing agent will have a high-electron transfer potential. When the presence of free radicals causes only a small change in the redox potential of a cell, the cell's antioxidant system is stimulated and protects the body from the damage caused by free radicals. In more severe cases, however, a cell can become necrotic and die. Many studies have proved that vitamin E significantly lowers C-reactive protein, and also reduces urinary F2-isoprostanes ie; a

measure of oxidative stress[24]. Remarkable number of research works had have mentioned about reduced release by monocytes of superoxide and tumor necrosis factor ie; inflammatory cytokine. In our research study 1200 mg per day consumption of vitamin E for one month reduced LDL-cholesterol 20.2 mg/dl in 38 hyperlipidemic patients. Our results match with results of Meydani SN *et al.*[25], Magliano D *et al.*[26] who proved same highly significant results from small sample size to meta analysis that high doses of vitamin E can lower LDL-cholesterol and enhance plasma HDL-cholesterol even used for short period of time in moderately to severe hyperlipidemic patients. In our results HDL-cholesterol increased only 6.6 mg/dl when vitamin E was used in 35 hyperlipidemic patients. But it is biostatistically significant change in the parameter. Same results were proved in study conducted by Lonn E *et al.*[27] when they used 1200 mg vitamin E in fifty six hyperlipidemic patients for three months. Our results are in contrast with results achieved by Salonen RM *et al.*[28] who proved lesser amount of reduction in LDL-cholesterol and less increase in HDL-cholesterol in 10 hyperlipidemic patients. Even they used 1500 mg vitamin E for the period of three months. This contrast in two studies is self explanatory ie; due to lesser sample size in the study work. Red dates in our results reduced LDL-cholesterol of 35 hyperlipidemic patients 10.9 mg/dl which is significant change in the parameter causing atherosclerosis, and increased HDL-cholesterol 4.2 mg/dl which is non-significant change in this parameter. These results match with study of Ghedira K *et al.*[29] who proved almost same changes in LDL and HDL-cholesterol. Abddel-zaher A *et al.*[30] have mentioned that mucous secretion and content of red dates may inhibit enterohepatic circulation of bile acids leading to induction of hepatocytes to synthesize bile acids instead of cholesterol. Same mechanism of action of red dates is mentioned by Abdul Rahim Al-J *et al.*[31]. Hala M *et al.*[32] proved very high level of reduction in 40 hyperlipidemic patients ie; 31 mg/dl reduction in LDL-cholesterol when they used half kilograms of red dates in eighty one hyperlipidemic patients for the period of two months. These differences in two study results were guessed to be due to some environmental factors and large sample size in their research work. Abdell LL *et al.*[33] observed high increase in HDL-cholesterol in twenty three hyperlipidemic patients ie; 13.28 mg/dl when they used 250 grams of red dates for the period of only three weeks. It is believed that red dates help prevent anemia and give a natural flush to one's cheeks due to its iron content. With substantial amounts of Vitamin E, red dates offer a sturdy source of antioxidants, and are highly recommended for people at high risk of coronary artery disease. The calcium in red dates also boosts bone health and forestalls osteoporosis. Red dates contain many vitamins. B vitamins are well represented in dates and this means that you get a lot of vitamin B if you regularly eat dates. In particular, vitamin B6, also called pyridoxin, is common in dates. If you eat 100 grams of dates, you get nearly 20% of the Recommended Daily Intake (RDI) of Vitamin B6; and 16% of the vitamin B5 RDI. Other vitamins in dates are the Vitamin A, Vitamin B2, B3, and B11[34].

CONFLICT OF INTEREST

"No conflict of interest associated with this work".

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Table 1: Before and after treatment values, changes and biostatistical significance in lipid profile of placebo group and two tested groups of hyperlipidemic patients

Parameter/Group	Before treatment	After treatment	Change	p-value
Placebo group (n=40)				
TC	270.11±1.98	265.11±2.00	5.0	>0.05
TG	210.33±2.10	200.98±1.54	9.4	<0.01
LDL-c	180.54±2.19	178.29±1.63	2.3	>0.05
HDL-c	34.76±2.65	35.11±1.56	0.4	>0.05
Tested Group-I(n=38)				
TC	289.14±1.93	269.88±1.94	19.3	<0.001
TG	270.27±2.11	256.12±2.66	14.2	<0.001
LDL-c	241.61±1.46	221.38±2.22	20.2	<0.001
HDL-c	33.51±1.19	40.15±1.90	6.6	<0.01
Tested Group-II(n=35)				
TC	243.61±1.88	235.44±3.11	8.2	>0.05
TG	231.86±2.16	227.91±2.11	4.0	>0.05
LDL-c	203.28±3.11	192.39±2.97	10.9	<0.01
HDL-c	37.83±2.04	41.99±1.96	4.2	>0.05

'n'= sample size, PG =placebo group, TG- =tested group-I (vitamin-E), TG-II in parameter/group=tested group-II (red dates), TC=total-cholesterol, TG=triglycerides, LDL-c=low density lipoprotein cholesterol, HDL-c=high density lipoprotein cholesterol.
All parameters were measured in mg/dl. 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.