



## **A full range of plant derived nutritional supplements, phytochemicals, and pro-vitamins help in sustaining good health and fighting diseases**

### **Authors**

M. Iqbal, Assoc Prof of Microbiology at QIMS/CMH, Quetta Pakistan  
M. Asif Shahab, Assistant Prof of Forensic Medicine at HITEC-IMS, Taxilla Pakistan  
Sana Dur Muhammad, Research Scholar at SMC/JSMU, Karachi Pakistan  
Shehroz Bashir, Emergency Medicine Resident at Hamad Medical Corporation, Doha, Qatar  
Mohsin Ali Hassni, Lab and Blood Bank Supervisor at IMDC, Islamabad Pakistan  
Shah Murad, Professor of Pharmacology at QIMS/CMH, Quetta Pakistan  
Seema Shah Murad, Research Associate at HSA/NIH, Islamabad, Pakistan

Correspondent Author: PROF DR SHAH MURAD, QIMS, Quetta Pakistan.  
CELL: +923338124611. [shahmurad65@gmail.com](mailto:shahmurad65@gmail.com)

**ABSTRACT:** To treat metabolic syndrome by allopathic drugs cause side effects so Herbal medicines are replacing drug treatment of hyperglycemia, hypertension and hyperlipidemia especially by antioxidant effects of their active ingredients. We have compared antioxidant characteristics of vitamin-E and red Dates. It was placebo-controlled conducted study conducted at General Hospital Lahore Pakistan from January 2022 to march 2022. **Inclusion and exclusion criteria:** 120 male hyperlipidemic patients were included with age range from 18 to 70 years. We excluded patients already suffering from renal, hepatic, pulmonary, or thyroid diseases. We also excluded patients already on cardio and hepato-protective drugs. **Sample size and division of patients:** 120 hyperlipidemic patients were divided in three equal number of patients, 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-III (n=40) was advised to take red dates 20 grams thrice daily for the period of one month. **Method of lipid profile determination:** LDL-cholesterol was calculated as total cholesterol- HDL-cholesterol-VLDL-cholesterol; VLDL-cholesterol was measured directly after ultracentrifugation. **Observations and Results:** 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. **Conclusion:** We concluded from the study that Z. Jujube has 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.

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### **BACKGROUND**

Strategy for 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<sup>1-10</sup>. 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  $\alpha$ -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<sup>11,12</sup>. Chylomicrons carry vitamin-E from the enterocyte to the liver, where they are incorporated into parenchymal cells as chylomicron remnants<sup>13</sup>. 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<sup>14,15</sup>. 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, nutraceuticals, and nutraceuticals<sup>16-20</sup>. Red date is one of them. The hepatocardioprotective effect is attributed to red date's antioxidant mechanisms and inhibition of oxidative degradation of lipids. Jujube contain higher phenol levels, exhibiting diphenylpicrylhydrazyl 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<sup>21-23</sup>.

#### MATERIAL AND METHOD

**Design of Study:** It was placebo-controlled research conducted at general hospital Lahore Pakistan from January 2022 to march 2022. Sample size: 120 male hyperlipidemic patients were included with age range from 18 to 70 years. Exclusion criteria: We excluded patients already suffering from renal, hepatic,

pulmonary, or thyroid diseases. 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-III (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 22.01 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 ie; only 4.2 mg/dl. Changes in mean values with SD and statistical significance is shown in following table.

TABLE showing before and after treatment values, changes and biostatistical significance in lipid profile of placebo group and two tested groups of hyperlipidemic patients

Parameter/Group	BT	AT	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

KEY: 'n' in Parameter/Group column = sample size, BT=before treatment, AT=after treatment, PG in parameter /Group=placebo group, TG-I in parameter/Group=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 are 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.

## DISCUSSION

Free radicals can interact with molecules in the body and damage various cell components such as DNA, protein and lipids, giving rise to various disease states. Reduction or redox potential refers to a substance's ability to gain or lose an electron. A strong reducing agent for an example 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<sup>24</sup>. 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<sup>25</sup>, magliano D et al<sup>26</sup> 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 Lon E et al<sup>27</sup> 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<sup>28</sup> 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<sup>29</sup> who proved almost same changes in LDL and HDL-cholesterol. Abdel-zaher A et al<sup>30</sup> 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<sup>31</sup>. Hala M et al<sup>32</sup> 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. This difference in two study results are guessed to be due to some environmental factors and large sample size in their research work. Abdell LL et al<sup>33</sup> 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<sup>34</sup>.

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