

Original Research Article

Caffeic Acid, Chlorogenic Acid, Garlic Acid, and Protocatechuic Acid as Hypolipidemic Agents

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Abstract: As the pathophysiology of dyslipidemias is clarified, one system is likely to emerge in which the underlying mechanism explains the phenotypic pattern observed on lipoprotein analysis. Every day, millions of vials of blood are drawn to assess patients' risk for the disease. These tests measure three biomarkers, or factors in the blood known to be associated with CAD: low-density lipoproteins (LDL cholesterol), high-density lipoproteins (HDL cholesterol), and triglycerides. All three biomarkers are lipids – water-insoluble molecules that are among the structural and functional building blocks of living cells. Highly altered Body Mass Index (BMI) and hypertension are independent and reversible determinants for coronary artery disease. Hypolipidemia can prevent hyperlipidemic patients to be victim of coronary artery disease. This study was conducted to compare hypolipidemic effects of Niacin and Jujube fruit in primary as well as secondary hyperlipidemic patients. Study was conducted in 2023 at Jinnah Hospital Lahore, Pakistan. Sixty participants were enrolled of both gender male and female hyperlipidemic patients age range from 20 to 70 years. Written and explained consent was taken from all patients. They were divided in two groups. Group-I was advised to take two grams Niacin in divided doses for the period of two months. Group-II was advised to take 500 grams of fruit Jujube daily for the period of two months. Their baseline LDL and HDL cholesterol was determined by conventional method of measuring Lipid Profile. After two months therapy, their post treatment lipid profile was measured and mean values with \pm SEM were analyzed biostatistically. Group-I which was on Niacin their LDL cholesterol decreased significantly and HDL cholesterol was increased significantly. In group-II patients LDL cholesterol was decreased significantly but HDL increase was not significant with p-value of >0.05 . It was concluded from the research work that Niacin is potent in lowering LDL and increasing HDL cholesterol, while Jujube has significant effect as LDL cholesterol lowering agent, but it does not increase HDL cholesterol significantly.

Keywords: LDL cholesterol, HDL cholesterol, Body Mass Index (BMI).

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BACKGROUND

Lipids can enter the walls of arteries and increase risk of developing atherosclerosis, which can lead to stroke, heart attack and the need to amputate. The risk of atherosclerosis is higher if you smoke, or if you have or develop diabetes, high blood pressure and kidney failure. Commonly hypolipidemic agents are used in prevention of ischemia, myocardial infarction, vascular

diseases in periphery, congestive cardiac failure, cardiac arrhythmias [1]. Recommended medications for treatment of dyslipidemia include Statins, Fibrates, Niacin, and Resins. But unfortunately all these agents have potential to cause unwanted effects in human body making low compliance [2]. Vitamin B-3 which is also known as niacin when given in sufficient hypolipidemic doses i.e. more than two grams per day it causes partial inhibition of release of free fatty

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acids from adipose tissue, and increased lipoprotein lipase activity, which may increase the rate of Chylomicrons triglyceride removal from plasma. Niacin decreases the rate of hepatic synthesis of VLDL and LDL by formation of apoproteins (proteins carrying free lipids in plasma) which are integral part of low density lipoprotein and very low density lipoprotein's structure [3]. Many of the herbs have been proved to reduce plasma lipids in human body. Jujubes or *Ziziphus jujube*, commonly called BAIR in urdu, punjabi, pothoharee, hazarvi, siraiiki, and hindi languages in Pakistan and India. These jujubes have hypolipidemic, hypotensive as well as hypoglycemic effects [4]. Jujube fruit is flavorful and contain considerable amount of phenolic compounds like caffeic acid, chlorogenic acid, garlic acid, and protocatechuic acid [5]. These polyphenolic compounds are capable of interacting with free radicals formed in human body in many biotransformatory reactions. This will decrease oxidative stress in human body. Hepatoprotective features of jujubes are proved in many research studies. Many researchers supported presence of biochemical compounds present in this fruit, which protect hepatocytes to be damaged by free radicals [6]. Some studies evaluated the effect of Jujubes fruit in controlling dyslipidemia in obese young hyperlipidemic patients. A placebo-controlled study trial on eighty six obese hyperlipidemic young adults age range from 12 to 18 years proved its effects on plasma lipids, labeling this fruit as hypolipidemic. It was observed by researchers that fruit was well tolerated, tasty for the hyperlipidemic patients which normalized lipid profile parameters in these patients [7]. Jujubes powder was formed by drying and grinding it then used in obese patients with high plasma lipid levels. It reduced all parameters of lipid profile except increase in high density lipoprotein cholesterol. In this research study fruit did not show any harmful effect on liver functions measured by alanine transaminase and aspartate transaminase [8]. Effects of its hydro-alcoholic extract on peripheral blood vessels, monocytes, neutrophils and lymphocytes is proved in many phase-II and phase-III drug's safety trials. Fruit reduced monocytes and neutrophils and increased lymphocytes [9]. Niacin decreases the rate of hepatic synthesis of VLDL and LDL by formation of apoproteins (proteins carrying free lipids in plasma) which are integral part of low density lipoprotein and very low density lipoprotein's structure.

PATIENTS AND METHOD

STUDY TYPE/DURATION/PLACE: This research work was parallel comparison of two medicinal agents conducted in 2023. **SAMPLE SIZE:** Sixty hyperlipidemic patients were selected from Jinnah Hospital Lahore-Pakistan to compare hypolipidemic

effects of Niacin and commonly used fruit in winter season in Pakistan i.e. Jujube (Bair in urdu). **INCLUSION CRITERIA:** Both male and female patients suffering from primary or secondary hyperlipidemia were selected. The age limit for patients was 20 to 70 years. **EXCLUSION CRITERIA:** Alcoholic addictive patients, cigarette smokers, habitual to enjoy sedentary life, with impaired liver or renal functions were excluded from the research study. **CONSENT:** Written/approved/well explained consent was taken from all participants. **METHOD:** Baseline Lipid Profile was determined in Biochemistry lab of the Hospital. Serum cholesterol was estimated by enzymatic method using kit Cat. No: 303113050 by Eli Tech Diagnostic, France. Serum HDL-cholesterol was determined by using kit Cat No: 303210040 by Elli Tech Diagnostic, France. Chylomicrons, low density lipoprotein and very low density lipoprotein are specially precipitated with phosphotungstic acid and magnesium ions can then be removed by centrifugation, while high density lipoproteins remain in the supernatant. Cholesterol included in this phase is measured by an enzymatic method. LDL-cholesterol was calculated according to Friedwald formula [3], i.e; $LDL = TC - (TG/5 + HDL-C)$. **PATIENTS GROUPING:** Patients were divided in two groups, 30 patients in each group. Group-I was on Tab. Niacin 2 grams daily in three divided doses. Group-II was on Jujube 500 grams daily in three divided times to eat. They were advised to take this fruit for two months. **STATISTICAL ANALYSIS:** Mean values \pm SEM were taken for statistical analysis using SPSS version 26 (2015). Paired 't' test was applied to get significance changes in parameters before and after treatment. 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 tested parameter.

RESULTS

With two months therapy by Niacin LDL-cholesterol in 27 hyperlipidemic patients reduced 29.2 mg/dl and HDL increase in this group was mg/dl. Three patients withdrew from the study work in this group due to non-compliance of Niacin i.e. it produced flushing, urticaria and heat perception. All these effects produced by Niacin were not its adverse effects but it was production of prostaglandin D-2 which caused vasodilatation leading to these effects. In group-2 (n = 30) two months therapy by Jujubes reduced LDL-cholesterol from 198.82 ± 2.17 mg/dl to 190.91 ± 1.73 mg/dl, which is 7.9 mg/dl change in the parameter. HDL-cholesterol in this group increased from 38.6 ± 2.19 mg/dl to 41.9 ± 2.97 mg/dl, which is 3.3 mg/dl change in the parameter. Biostatistically it is non-significant change in the tested parameter of lipid profile.

Table 1: Showing Pre and Post Treatment Mean Values With \pm Sem and their Statistical Significance Changes in two Lipid Profile Parameters. Biostatistical Significance in Mean Values \pm Sem Shown By P-Values

	LDL-cholesterol	HDL-cholesterol
At day-0	G1= 210.16 \pm 2.11 G2= 198.82 \pm 2.17	G1 = 37.9 \pm 1.91 G2 = 38.6 \pm 2.19
At day-60	G1= 180.97 \pm 2.22 G2= 190.91 \pm 1.73	G1 = 45.2 \pm 2.19 G2 = 41.9 \pm 2.97
Change in mg/dl	G1= 29.2 G2= 7.9	G1= 7.3 G2 = 3.3
Change in %	G1= 13.9 % G2= 4.0 %	G1 = 16.2 % G2 = 7.9 %
p-value	G1= p-value <0.001 G2= p-value <0.01	G1 = p-value <0.001 G2 = p-value >0.05

Key: G1 (n= 27) is group on Niacin, G2 (n= 30) is group on Jujubes, \pm stands for Standard Error of Mean values, p-value >0.05 is non-significant change, p-value <0.01 is significant change in parameter, and p-value <0.001 is highly significant change in tested parameter. n = sample size.

DISCUSSION

Niacin is commonly used drug which inhibit lipoprotein lipase activity, so lesser formation of free fatty acids will be available which are main sources of TG-rich lipoproteins (VLDL) formation. Lesser amount of VLDL lead to lesser synthesis of LDL particles which are rich in cholesterol. In our results Niacin 2 grams daily intake for two months decreased LDL-cholesterol about 13.9 % which is highly significant changes. HDL-cholesterol in this group increased about 16.2 % which is again highly significant change. ZQ Zhu *et al.*, [10], and W Cao *et al.*, [11], proved same results when they used 2 grams of Niacin in 66 hyperlipidemic patients, but WB Yao *et al.*, [12], observed lesser effects of Niacin on HDL cholesterol, i.e. only 4.4 % increase in HDL cholesterol. Hung PG *et al.*, [13], explained different mechanisms of hypolipidemic response of Nicotinic acid on persons with different genetic code. One of the favorable mechanism for patients with CAD they described is fibrinolytic activity of Niacin. In our results Jujube fruit decreased LDL cholesterol is 7.9 mg/dl, which is significant change in the parameter. HDL cholesterol is not increased significantly in our results with p-value of >0.05. Tan H *et al.*, [14], and Tripathi M *et al.*, [15], observed same reason of Jujube on LDL and HDL-cholesterol, which augment our results. Tschesche R *et al.*, [16], observed more effects of Jujube as we observed in low density lipoprotein cholesterol. Um S *et al.*, [17], proved that LDL cholesterol is much decreased as compared to our results. KB Kang *et al.*, [18], observed too less effects of Jujube fruit in 5 hyperlipidemic patients. This difference in two studies are obviously due to their small sample size, i.e. they tried herb only on five hyperlipidemic patients, while we tried in 30 hyperlipidemic patients. As per a research study conducted by the National Cancer Institute, it was observed that smokers who took beta-carotene supplements on a regular basis for a long period of time were at a higher risk of developing lung cancer in comparison to those who didn't take beta-carotene supplement [19-22].

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Conflict Of Interest: N/A

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