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## HOW DOES COMMON PAKISTANI FRUIT AFFECT LDL-OXIDATION?

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### ABSTRACT

The effects of dietary fats on the risk of coronary artery disease (CAD) have traditionally been estimated from their effects on LDL cholesterol. Fats, however, also affect HDL cholesterol, and the ratio of total to HDL cholesterol is a more specific marker of CAD than is LDL cholesterol. Hypolipidemic drugs and fruits can play a part to reduce LDL particles decreasing chances of CAD development. This study was conducted to compare hypolipidemic effects of Niacin and Jujube fruit in primary as well as secondary hyperlipidemic patients. Study was conducted from November 2018 to February 2019 at Jinnah Hospital Lahore. Sixty participants were enrolled of both gender male and female patients age range from 20 to 70 years. Consent was taken from all patients. They were divided in two groups. Group-I was advised to take 2 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 potential, but it does not increase HDL cholesterol significantly.

**Key Words:** CAD, hyperlipidemia, Prevention, Fruits, oxidative stress

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## INTRODUCTION

Increased oxidative stress is the consequence of an imbalance between oxidant and antioxidant biological agents and can result in damage to biomolecules, including proteins, nucleic acids, and lipids. Some of these damaged biomolecules have been used as oxidative stress biomarkers, such as oxidized LDL, that can be measured from a regular blood draw. Oxidative stress is suspected to be involved in the pathophysiology of several chronic diseases and has been linked to metabolic syndrome (MS), a cluster of risk factors for cardiovascular disease that includes central obesity, high blood pressure, high fasting glucose, and dyslipidemia. A common hallmark of MS-associated dyslipidemia is the elevation of small and dense LDL particles, which are easily oxidized. High ox-LDL levels are also associated with insulin resistance, which is tightly linked to the pathogenesis of MS<sup>1</sup>. Fats high in lauric, myristic, and palmitic acids, such as dairy fat and tropical oils, were considered the most noxious of fats, and diets low in fat and high in carbohydrates were considered optimal. Such an approach, however, ignores the effects of diet on HDL cholesterol. There is a wealth of observational, mechanistic, and genetic evidence that increasing the concentration of HDL cholesterol through diet will lower the risk of CAD. In addition, a study with gemfibrozil showed that increasing the concentration of HDL cholesterol lowers the risk of CAD. In fact, the ratio of total to HDL cholesterol is considered more important than the total

or lipoprotein cholesterol concentrations in estimating the risk of CAD. There is thus a need for coefficients that estimate the effect of fats on total:HDL cholesterol. This report presents such coefficients, which are based on the outcomes of selected studies published by investigators in 11 countries from 1970 through 1998. The effects of dietary fatty acids on plasma apolipoprotein (apo) B and apo A-I were also evaluated. Four drug groups are used to lower LDL particles and increase HDL in blood; ie statins, fibrates, niacin and bile acid binding resins. These drugs not only decrease the level of fats in blood, but they also decrease risk of atherosclerosis and its complications. Therefore, these drugs may be used in prevention of heart attack, peripheral vascular disease and ischemic stroke<sup>2</sup>. Commonly used medications for treatment of Hyperlipidemia include Statins, Fibrates, Niacin, and Resins. All these medicines have potential for SEs and low compliance due to one reason or another. Niacin when given in hypolipidemic doses i.e. > 2grams per day it causes partial inhibition of release of free fatty acids from adipose tissue, and increased lipoprotein lipase activity, which may increase the rate of chylomicron triglyceride removal from plasma. Niacin decreases the rate of hepatic synthesis of VLDL and LDL by synthesis of apoproteins which are integral part of LDL or VLDL structure<sup>3</sup>. Some herbs have been proved to reduce plasma lipids in human population. Jujubes or Ziziphus

Jujube have some what hypolipidemic as well as hypoglycemic effects<sup>4</sup>. Jujube fruit is known to contain considerable amount of phenolic compounds, including chlorogenic acid, gallic acid, protocatechuic acid and caffeic acid<sup>5</sup>. High polyphenolic content of Z Jujube suggests its potent capacity in clearing of oxidants. Many studies proved the hepatoprotective effect of methanolic extract of *Zizyphus jujuba* fruits. Histopathological studies supported the biochemical findings. Study concludes a hepatoprotective activity probably due to its antioxidant effect<sup>6</sup>. Some studies evaluated the effect of Z Jujube fruit in controlling dyslipidemia in obese adolescents. A triple-blind randomized placebo-controlled trial of 86 obese adolescents aged 12--18 with dyslipidemia. Proved its hypolipidemic features. Results showed the fruits to be generally well tolerated, with potential favorable effects on serum lipid profile<sup>7</sup>. Study evaluated the effect of a hydroalcoholic extract of the fruit of Z. Jujube on peripheral blood cells in male and female hyperlipidemic actions. Results showed a significant reduction in percentage of monocytes and neutrophils and an increase in the percentage of lymphocytes. Remarkable number of researches have proved jujuba fruit as free radicals scavenger so reduces risk of developing cardiac problems like CAD. This fruit is also helpful as hepatoprotective agent<sup>8</sup>. Saturated fat has been demonised as a dietary culprit in heart disease due to its ability to raise low-density lipoprotein cholesterol (LDL-C), whereas

omega-6 polyunsaturated fatty acid (PUFA) has been regarded as heart healthy due to its ability to lower total and LDL-C. And replacing saturated fat with omega-6 has consistently been found to lower total cholesterol and LDL-C levels<sup>9</sup>.

## PATIENTS AND METHOD

This research work was conducted from November 2018 to February 2019. Sixty hyperlipidemic patients were selected from National Hospital Lahore-Pakistan to compare hypolipidemic effects of Niacin and commonly used fruit in winter season in Pakistan i.e. Jujube (Bair in urdu). 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 were alcoholics, cigarette smokers, habitual to enjoy sedentary life, with impaired liver or renal functions. Consent was taken from all participants. Baseline Lipid Profile was determined in Biochemistry lab of the Hospital. 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 drugs 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 parameter.

cholesterol and HDL-cholesterol were changed, which are shown in following table:

## RESULTS

With two months therapy by Niacin and Jujube, plasma total cholesterol, LDL-

TABLE SHOWING PRE AND POST TREATMENT MEAN VALUES WITH  $\pm$  SEM AND THEIR SIGNIFICANCE CHANGE IN PARAMETERS

	<b>LDL-c</b>	<b>HDL-c</b>
Before treatment	G1= 210.1 $\pm$ 2.11 G2= 198.8 $\pm$ 2.17	37.9 $\pm$ 1.91 38.6 $\pm$ 2.19
After treatment	G1= 180.9 $\pm$ 2.22 G2= 190.9 $\pm$ 1.73	45.2 $\pm$ 2.19 41.9 $\pm$ 2.97
Change in mg/dl	G1= 29.2 G2= 7.9	7.3 3.3
Change in %	G1= 13.9 % G2= 4.0 %	16.2 % 7.9 %
p-value	G1= <0.001 G2= >0.05	<0.001 <0.01

KEY: G1 is group on Niacin, G2 is group on drug-2 ie Jujube,  $\pm$  stands for SEM, p-value >0.05 is non-significant change, p-value <0.01 is used for significant change in parameter, and p-value <0.001 is highly significant change in tested parameter.

## DISCUSSION

The use of total:HDL cholesterol implies that diet-induced decreases in HDL cholesterol increase CAD risk. Such a causal role for diet-induced changes in HDL cholesterol has not been proven in controlled clinical trials. However, results of prospective observational studies, controlled clinical trials with drugs, mechanistic studies, and genetic "experiments of nature" all strongly suggest that high concentrations of HDL cholesterol in the circulation help to prevent CAD and other cardiovascular

diseases. 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<sup>10</sup>



and W Cao et al<sup>11</sup> proved same results when they used 2 grams of Niacin in 66 hyperlipidemic patients, but WB Yao et al<sup>12</sup> observed lesser effects of Niacin on HDL cholesterol, i.e. only 4.4 % increase in HDL cholesterol. Hung PG et al<sup>13</sup> 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<sup>14</sup> and Tripathi M et al<sup>15</sup> observed same reason of Jujube on LDL and HDL-cholesterol, which augment our results. Tschesche R et al<sup>16</sup> observed more effects of Jujube as we observed in low density lipoprotein cholesterol. Um S et al<sup>17</sup> proved that LDL cholesterol is much decreased as compared to our results. KB Kang et al<sup>18</sup> 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. Johanson M et al<sup>19</sup>, Jogiyal M et al<sup>20</sup>, Lufersa T et al<sup>21</sup> explained and advised to use medicinal plants with caution as these agents interact with other allopathic medications and enhance or reduce their metabolism causing toxicity or failure in other therapeutic considerations.

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