

## A Prospective Study on Hypolipidaemic Effects in Fresh and Dried Ginger Varieties

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### ABSTRACT

**Background:** The secretion of VLDL is influenced by the availability of apolipoprotein (apo) B in the liver and the activities of regulatory enzymes involved in the assembly and transport of VLDL, including microsomal transfer protein and acyl-coenzyme A (CoA):cholesterol acyltransferase. Dyslipidemia is well known factor to increase incidence of heart diseases. This may lead to development of atherosclerotic plaques which is major etiological factor for establishing coronary artery disease (CAD). Hypolipidemic drugs used in allopathy include Statins, Fibric acids, Niacin, and Resins but all have their low compliance due to frequent side effects. Medicinal herbs like Onion and Ginger are hypolipidemic agents commonly used as flavoring agents and making foods spicy and tasty. We have compared hypolipidemic potential between these two medicinal herbs.

**Methods:** The study was conducted at Ghurki Trust teaching hospital, Lahore from January to June 2017. Eighty secondary hyperlipidemic patients were enrolled after getting written consent which was approved by Ethics committee of the hospital. They were divided in two equal groups comprising 40 patients in each group. Group-I was treated by Ginger 10 grams daily in three divided doses for 2 months. Group-II was advised to take Onion 200 grams daily in divided amount with each meal i.e.; breakfast, lunch, and dinner for two months.

**Results:** After two months therapy it was observed by statistical analysis that 10 grams ginger reduced TC (total cholesterol) of 38 hyperlipidemic patients 12.4 gm/dl and LDL-C (low density lipoprotein cholesterol) 27.3 mg/dl. In group-II, onion reduced TC in 35 patients 17.9 mg/dl and LDL-C 14.8 mg/dl. Changes in tested parameters are significant biostatistically with p-values <0.01 to <0.001.

**Conclusion:** We concluded from this research work that Onion and Ginger reduces risk of CAD by decreasing plasma total cholesterol and LDL cholesterol.

**Keywords:** Hypolipidemic effects, Ginger, VLDL

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### INTRODUCTION

The effects of fatty acids in regulating gene expression may also contribute to the mechanisms that determine plasma LDL-C. Fatty acids regulate at least 4 families of transcription factors: the peroxisome proliferator activated receptors (PPARs), liver X receptors (LXRs), hepatic nuclear factor-4 (HNF-4), and sterol regulatory element binding proteins (SREBPs). A brief review of the postulated effects of fatty acids in regulating plasma cholesterol

follows. Metabolic syndrome is not a single disease, rather complication of three diseases ie; hyperlipidemia, hypertension, and diabetes mellitus. Increased amount of blood lipids cause atherosclerotic phenomenon, which cause hypertension. This process do not stop here, it leads to metabolic alterations of lipids, proteins and carbohydrates naming metabolic syndrome<sup>1-5</sup>.

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Metabolic syndrome is complicated to treat by medicines combination therapy including hypoglycemic, hypolipidemic, and hypotensive agents<sup>6</sup>. Allopathic drug regimens used in metabolic syndrome have low patients compliance due to their life long utilization and from mild to severe side effects<sup>7</sup>. Look at only hypolipidemic allopathic agent's side effects. Statins and Fibrates causes rhabdomyolysis (muscular dystrophy) causing muscular pain, Niacin causes flushing resembling to allergic reactions and Resins which are difficult to use for prolonged period due to their metallic taste, and stomach bloating<sup>8</sup>. Medicinal herbs are alternative therapeutic agents with no or very less frequency, and intensity of side effects. For example onion and ginger are used in various food recipes. These two agents have been proved scientifically as hypolipidemic characteristics<sup>9,10</sup>. Onion byproduct contains factors with the ability to modulate plasma lipids and lipoprotein levels. High in vitamin C, onions are a good source of dietary fiber, and folic acid. They also contain calcium, iron, and have a high protein quality. Onions are low in sodium and contain no fat. Onions contain quercetin, a flavonoids; one category of antioxidant compounds<sup>11-13</sup>. Antioxidants are compounds that help delay or slow the oxidative damage to cells and tissue of the body<sup>14</sup>. Studies have indicated that quercetin helps to eliminate free radicals in the body, to inhibit low-density lipoprotein oxidation which is an important reaction in the atherosclerosis and coronary heart disease. It also protect and regenerate vitamin E, which is a powerful antioxidant. It also inactivates the harmful effects of chelate metal ions<sup>15-17</sup>. At least 115 constituents in fresh and dried ginger varieties have been identified by a variety of analytical processes<sup>18</sup>. Ginger roots contain carbohydrates, sugars, dietary fibers, fat, protein, vitamin B1,2,3,5,6,9, vitamin C and vitamin E. It also contains calcium, iron, magnesium, manganese, phosphorous, potassium, sodium, and zinc<sup>19</sup>. It contains antioxidant compounds like gingerols, shogaol, and paradols. Gingerol inhibits nitric oxide synthesis in activated macrophages and prevents peroxynitrite-induced oxidation and nitration reactions. Peroxynitrite induces DNA base damage predominantly at guanine (G) and 8-oxoguanine (8-oxoG) nucleobases via oxidation reactions<sup>20</sup>. Generation of free radicals or reactive oxygen species (ROS) during metabolism beyond the antioxidant capacity of a biological system results in oxidative stress, which plays an essential role in heart diseases, neurodegenerative diseases, cancer, and in the aging process<sup>21</sup>. The bioactive molecules of ginger like gingerols have shown antioxidant activity in various modules<sup>22</sup>.

## METHODS

This study was conducted at Ghurki Trust Teaching Hospital Lahore, Pakistan from January 2017 to June 2017. Eighty newly diagnosed secondary hyperlipidemic patients were selected with age range from 20 to 60 years. Exclusion criteria were peptic ulcer, any gastrointestinal upset, hypothyroidism, diabetes mellitus, renal impairment, and patients suffering from any liver or heart disease. All patients were divided in three equal numerical groups i.e.; 25 in each group. Their baseline vital organ function's data were taken at start of research work i.e.; lipid profile, blood pressure and pulse rate. The study period was sixty days. Forty patients of group-I were advised to take Ginger 10 grams daily in divided amount with each meal for two months. Forty patients of group-II were advised to take 200 grams Onion daily as salad with breakfast, lunch and dinner for 2 months. Fortnightly follow-up visit was advised to all patients. They were also advised not to take fast or junk food for two months of research study duration. Drug compliance to the regimen was monitored by interview and counseling at each

follow-up visits. Serum LDL-cholesterol was calculated by Friedwald formula ( $\text{LDL-Cholesterol} = \text{Total Cholesterol} - (\text{Triglycerides}/5 + \text{HDL-Cholesterol})$ ). Data were expressed as the mean  $\pm$  SD and "t" test was applied to determine statistical significance as the difference. A probability value of  $<0.01$  was considered as significant and  $P < 0.001$  was considered as highly significant change in the parameter tested in study.

## RESULTS

Results of study are shown in following table. After two months treatment of eighty hyperlipidemic patients lipid profile's changes before and after treatment were analyzed biostatistically. In group-I two patients discontinued drugs, and in Group-II five patients withdrew from the study due to low compliance of herbs or due to their personal problems. Mean values with  $\pm$  SD before and after treatment are shown in following table with their p-values in Statistical significance column.

**Table 1: Distribution of side effects among study population**

Group and parameters	At day-0	At day-60	Overall change	Change in %	p-value
<b>GROUP-I n=38</b>					
TC	269.13 $\pm$ 3.10	256.77 $\pm$ 1.87	12.4 mg/dl	4.6	p<0.01
LDL-C	177.64 $\pm$ 2.02	150.32 $\pm$ 1.98	27.3 mg/dl	15.4	p<0.001
<b>GROUP-II n=35</b>					
TC	287.33 $\pm$ 2.00	269.44 $\pm$ 3.01	17.9 mg/dl	6.2	p<0.01
LDL-C	203.17 $\pm$ 2.22	188.42 $\pm$ 1.85	14.8 mg/dl	7.3	p<0.01

cholesterol, n= sample size.  $\pm$  indicates SEM. P-values  $<0.01$  = significant change in the parameter. P-value  $<0.001$  = highly significant changes in the tested parameters.

## DISCUSSION

Modulation of cholesterol synthesis is not a major mechanism by which PUFAs lower plasma LDL cholesterol. This has been confirmed using deuterium incorporation into newly synthesized cholesterol as a sensitive method, with results that closely resemble those obtained from traditional methods such as sterol balance. Cardiovascular problems in human population are mainly related with acquired facts like sedentary life style, smoking, alcohol use, utilization of drugs without prescription, and high intake of junk foods<sup>23</sup>. Elevated oxidant stress linked to pro-inflammatory conditions contributes to the development of alterations in the bioavailability of vascular nitric oxide and some endothelial cell dysfunctions that can culminate in profound impairments to vascular reactivity<sup>24</sup>. Low density lipoproteins in plasma will be oxidized, if there is burden of reactive oxygen species (ROS) in human body<sup>25</sup>. Atherosclerotic plaques leading to cause coronary artery disease is key factor for morbidity/mortality all over the world. To reduce hyperlipidemic state is essential step to decrease risk of CAD<sup>26</sup>. Allopathic hypolipidemic medicines are being replaced by herbal hypolipidemic agents due to wide range of pharmacological actions produced by allopathic drug regimens<sup>27</sup>. Ginger have had been used since long to treat gastrointestinal, respirac toy, skin, pulmonary, brain, heart diseases. Ginger root contains a very high level (3.85 mmol/100 g) of total antioxidants, surpassed only by pomegranate and some types of berries<sup>28</sup>. Ginger was reported to suppress TPA-induced oxidative stress in human promyelocytic leukemia<sup>29</sup>. In some research works it have been proved that ginger compounds effectively inhibit superoxide production<sup>30</sup>. Several reports indicate that ginger suppresses lipid peroxidation and protects the levels of reduced glutathione<sup>31</sup>. Ginger was reported to decrease age-related oxidative stress markers and was suggested to guard against ethanol-induced hepatotoxicity by suppressing oxidative consequences in rats treated with ethanol<sup>32</sup>. When we used 10 grams of ginger root in 38

hyperlipidemic patients, it reduced total cholesterol in plasma 12.4 mg/dl and LDL cholesterol reduction was 27.3 mg/dl in two months. Same results were observed in study conducted by Makroue S et al<sup>33</sup> who used ginger roots 12 grams daily in 49 hyperlipidemic patients for three months. Palisa V et al<sup>34</sup> explained mechanism of action of ginger as antioxidant that it scavenge free radicals in plasma due to its content ie; gingerol. Palisa V et al<sup>34</sup> proved 13% decrease in TC, and 17 % decrease in LDL cholesterol when they used 8 grams of ginger roots in 103 hyperlipidemic patients for six months. This mismatch in two studies may be due to large sample size and ingestion of drug used for long period. Recently, great attention has been focused on the role of the antioxidative defense system in oxidative stress. Endogenous antioxidants in medicinal herbs may play an important role in antioxidative defense against oxidative damage, possibly protecting the biological functions of cells. There is increasing interest in the protective biological function of natural antioxidants contained<sup>35</sup>. Onion when we used in 35 hyperlipidemic patients it reduced plasma total cholesterol 17.9 mg/dl, and LDL cholesterol 14.8 mg/dl in two months therapy. These results match with research study conducted by Mustavay J et al<sup>36</sup> who proved almost same changes in these two parameters of lipid profile in 55 hyperlipidemic patients when they used 100 grams of onion for two weeks only. These results are in contrast with our results. May be the environmental factors change research study results. We restricted junk food to our patients and keep continue brisk walk for half an hour daily for the duration of study period. The antioxidant action of ginger has been proposed as one of the major possible mechanisms for the protective actions of the plant against a number of toxic agents such as carbon tetrachloride and cisplatin. Recently, it has been shown that 6-gingerol is endowed with strong anti-oxidant action both in vivo and in vitro, in addition to strong anti-inflammatory and anti-apoptotic actions<sup>37</sup>. Floreie C et al<sup>38</sup> mentioned that numerous enzymatic and nonenzymatic mechanisms take place to protect the cell against oxidative damage. The radical chain reaction of lipid peroxidation appears to be a continuous physiological process. This process, if out of control, can alter essential cell functions and lead to cell death<sup>39</sup>. Reactive oxygen species (ROS) can be detoxified by an enzyme defense system, comprising superoxide dismutase (SOD), catalase (CAT), and selenium-dependent glutathione peroxidase, or non-enzymatic systems by the scavenging action of GSH, while organic peroxides can be detoxified by the activity of glutathione S-transferase (GST)<sup>40</sup>. Onion contains phytochemicals that can increase detoxifying enzymes for ROS, but exact mechanism is not known yet<sup>41</sup>. A group of volunteers fed a high fat diet plus 100 g onion once a day and those fed fat diet only showed a significant decrease in serum triglycerides, but not cholesterol, as compared to those only fed with fat diet only. Another study reported that oral administration of a butanol onion extract to patients with elementary lipemia prevented an increase in total serum cholesterol, lipoprotein cholesterol, and J-lipoprotein and serum triglycerides. Gyvesta YF et al<sup>42</sup> described that quercetin (one of the content of onion) has been shown to have antioxidant activity related to a strong scavenging capacity. Various studies have had proved fundamental use of phytochemical to reduce risk for coronary artery diseases as mentioned by Noor M et al<sup>43</sup>.

Jan MM et al<sup>44</sup> proved same effects of onion extracts used in rats and found this phytochemical quercetin (present in onion) as potent as statins as hypolipidemic agent.

Fovuca M et al<sup>45</sup> explained that onion is natural antioxidant plant and it works as modulator of detoxification in human population.

## CONCLUSION

It was concluded from this work that medicinal plants can be used with good compliance to reduce high plasma lipids leading to reduce incidence of coronary artery diseases (CAD).

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