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RESEARCH ARTICLE

Core approaches in therapeutics: Lipid profile

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ABSTRACT

Fenugreek dried seed is known for their valuable antibacterial, anticancer, and anti-inflammatory properties in India, Egypt, and some European countries. These seeds are also known to work as antioxidants having reviving properties. Inflammation likely acts to increase cardiovascular disease risk through the dyslipidemic atherogenic triad of elevated triglycerides (TGs), low high-density lipoprotein (HDL) cholesterol, and an increase in small, cholesterol-poor low-density lipoprotein (LDL) particles. High plasma lipids interact with free radicals in the human body leading to develop coronary artery disease. We in this study have compared hypolipidemic effects of fenugreek, *Curcuma longa*, and lemon. Study was conducted at Jinnah Hospital Lahore-Pakistan from January 2018 to May 2018. Ninety hyperlipidemic patients of age group 19–70 were included in the study. Exclusion criteria were diabetic, alcoholic additives, hypertensive patients, and those whose kidney or liver functions were impaired. Consent was taken from all participants. Their baseline lipid profile was taken in biochemistry laboratory of the hospital. They were divided in three groups, i.e., 30 patients in each group. Group-I was advised to take 500 mg of *C. longa* (haldi) mixed in fresh milk without cream, thrice daily for 2 months. Group-II patients were advised to take 100 g of fenugreek leaves mixed with salad in each meal (thrice daily) for the period of 2 months. Group-III patients were advised to take 40 mL of fresh lemon juice mixed with 40 mL mineral water thrice daily for 2 months. They all were advised not to take heavy meal rich with any type of fat such as junk food. One hour daily brisk walk was advised to all participants. 15-day follow-up visit was scheduled for them. After 2 months, their lipid profile was re-determined. When results were compiled and statistically analyzed by applying paired "*t*" test, it revealed that *C. longa* decreased total cholesterol (TC), TG, LDL cholesterol 16.10, 20.01, and 17.59 mg/dL, respectively. Fenugreek decreased TC, TGs, and LDL cholesterol 14.70, 17.33, and 17.06 mg/dL, respectively. Lemon in 2-month therapy decreased TC, TGs, and LDL cholesterol 15.45, 10.13, and 11.97 mg/dL, respectively. None of the above-mentioned herbs raised HDL cholesterol significantly. It was concluded from this research work that *C. longa*, Fenugreek leaves, and lemon are mild to moderately effective hypolipidemic herbs to lower total plasma cholesterol, TGs, and LDL cholesterol but have no potential to raise HDL cholesterol when analyzed biostatistically.

Keywords: Antibacterial agent, Fenugreek, Hypolipidemic agent, Anticancer, Anti-inflammatory

INTRODUCTION

Previous studies examined the antimicrobial effects of fenugreek. In a study by Fezea *et al*.,[1] ethanolic extract of fenugreek seed showed an inhibition zone of 70.3 mm on *Escherichia coli*. The inhibition zone of methanolic extract was 44.1 mm. Many vegetables are being used as antibacterial agents in India, Pakistan, Bangladesh, Sri Lanka, and Afghanistan.[2]

As arteriosclerosis, can begin in youth, generally exacerbated by exposure to factors associated

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with increased cardiovascular risk. Atherosclerotic problems are encountered with enhancement of low-density lipoprotein (LDL) uptake by monocytes and macrophages.[3] In the liver, uptake of plasma LDL is mediated through specific LDL receptors, but a scavenger receptor system is employed by macrophages. Plasma LDL must be modified before uptake by macrophages. Analysis of the lipid content in the oxidatively modified LDL from hyperlipidemic patients revealed that the level of lysophosphatidylcholine was greatly elevated, and the high level of the lysolipid was shown to impair the endothelium-dependent relaxation of the blood vessels.[4-8] In allopathy, blood lipid levels are normalized by statins, fibrates, niacin, and bile acid binding resins (BABRs). All of these allopathy-related drugs have low compliance ranges from mild compliance due to metallic taste of BABRs to severe side effects such as rhabdomyolysis by fibrates and statins[9] Due to low compliance and adverse effects of conventionally used hypolipidemic agents, herbal medicines are going to be famous among physicians and cardiologists.[10] Medicinal herbs such as *Curcuma longa*, fenugreek, and lemon contents are being used as mild to moderate hypolipidemic agents. *C. longa* commonly known as haldi in India and Pakistan is used to lower plasma lipids in view of their contents. It contains curcuminoids (curcumin, demethoxycurcumin, and bisdemethoxycurcumin), turmerone, atlantone, zingiberene, proteins, and resins.[11] Curcumin reduces both the oxidation and circulation of oxidized levels of LDL cholesterol which leads to reduction in the occurrence or treatment of already present atherosclerosis in the subjects.[12] Research has revealed that curcumin from turmeric is an extremely efficient agent in increasing cholesterol uptake by the liver cells.[13] Several independent studies have shown that curcumin increases the expression of cholesterol and lipoprotein receptors in the liver cells.[14] Curcumin also increases cholesterol and bile acid excretion in feces.[15] Additionally, curcumin also increases the amount of ATP-binding cassette (ABC) transporters. These transporters are basically involved in flushing out excess cholesterol from the inside of the macrophages. When the numbers of ABC transporters are increased on the surface of a macrophage, the deposited cholesterol is effluxes out through these channels again into the blood. Through the blood, it reaches liver where it is metabolized efficiently.[16] The composition of fenugreek includes a large number of chemical components. They include proteins and amino acids, flavonoids, saponins and steroidal saponins, coumarin, lipids, vitamins, minerals, galactomannan fiber, and alkaloids, such as trigonelline. Extracts are available standardized to contain 50% saponins or 20% of the amino acid 4-hydroxyisoleucine.[17] Treatment with fenugreek seed powder normalized the enhanced lipid peroxidation and increased susceptibility to oxidative stress associated with the depletion of antioxidants.[18] The steroidal saponins (diosgenin, yamogenin, tigogenin, and neotigogenin) are thought to inhibit cholesterol absorption and synthesis and hence its potential role in arteriosclerosis.[19] Phenolics in *C. longa* have potential health benefits mainly due to their antioxidant properties such as reactive oxygen species scavenging and inhibition, electrophile scavenging, and metal chelation.[20] Epidemiological studies support a relationship between the consumption of phenolic-rich food products and a low incidence of coronary heart disease, atherosclerosis, certain forms of cancer, and stroke.[21] Lipid peroxidation is inhibited by flavonoids and flavanones present in lemon.[22] Fenugreek (*Trigonella foenum-graecum*) is a common herb, used for its anti-diabetic, anti-hyperlipidemic, breast milk increasing properties.[7] In previous studies, fenugreek was shown to have anti-bacterial and antiplasmodial effect.[23-28]

PATIENTS AND METHODS

Place and period of research work

The research work was conducted at Jinnah Hospital, Lahore, from January 2018 to May 2018 with approval of the Research Ethics Committee of the Hospital.

Sample size

Ninety hyperlipidemic patients were selected for research work.

Consent

Written consent was taken from all patients. Specific performa was designed for the research work. Hyperlipidemic patients were selected with age range from 19 to 70 years.

Exclusion criteria

Exclusion criteria were hypertension, hypothyroidism, diabetes mellitus, alcohol addictive patients, peptic ulcer, any gastrointestinal upset, renal impairment, and any hepatic or cardiac problem.

Grouping

All patients were divided in three groups (group-I, group-II, and group-III), 30 patients in each group. Their baseline lipid profile data were taken and filed in specifically designed performa, at start of taking medicine, such as lipid profile, blood pressure, and pulse rate.

Lipid profile

Serum lipid profile (total cholesterol [TC], high-density lipoprotein [HDL]-cholesterol, and triglyceride [TG]) parameters were determined after a 12 h overnight fast by standard methods. LDL-cholesterol level was calculated according to the Friedewald's formula. Thirty patients of group-I were advised to take 500 mg of *C. longa* (haldi) mixed in fresh milk without cream, thrice daily for 2 months. Group-II patients were advised to take 100 g of fenugreek leaves mixed with salad in each meal (thrice daily) for the period of 2 months. Group-III patients were advised to take 40 mL of fresh lemon juice mixed with 40 mL mineral water thrice daily for 2 months. They all were advised not to take heavy meal rich with any type of fat such as junk food. One hour daily brisk walk was advised to all participants. 15-day follow-up visit was scheduled for them. After 2 months, their lipid profile was re-determined.

Statistical analysis

Mean values of the day-0 and day-60 of tested parameters (TC, LDL cholesterol, TGs, and HDL cholesterol) ± standard deviation were taken to be analyzed statistically. The Statistical Package for the Social Sciences (SPSS) 10 version 2.00.01.10 was used to analyze pre-treatment and post-treatment values of all parameters. Paired *t*-test was applied to determine changes in pre and post-treatment values. $P > 0.05$ was considered a non-significant change in tested parameters, and $P < 0.01$ were considered a significant change.

RESULTS

When results were compiled and statistically analyzed using SPSS 10 version 02.00.01.10, it revealed that *C. longa* decreased TG, TC, and LDL cholesterol of 29 hyperlipidemic patients 20.01, 16.10, and 17.59 mg/dL, respectively. Raise in HDL cholesterol in this group was 03.70 mg/dL. Fenugreek leaves reduced TG, TC, and LDL cholesterol of 28 hyperlipidemic patients 17.33, 14.70, and 17.06 mg/dL, respectively. Lemon juice reduced TC, TG, and LDL cholesterol 15.45, 10.13, and 11.97 mg/dL, respectively. HDL raised 03.55 mg/dL in this group. Changes in all tested parameters and their statistical significance are shown in Tables 1-3.

DISCUSSION

Antibiotics have been widely used as standard antibacterial treatment for long but exploited use of these drugs and have led microorganisms to develop resistance against many antibiotics. While 33% of the population are dependent on therapeutic plant

Table 1: Parameters values before and after treatment with their statistical significance in group-1 (n=29) (*Curcuma longa* or haldi)

TC at day-0	TC at day-60	Difference in mg/dL	*P* - value
TC at day-0 271.87±1.04	TC at day-60 255.77±2.77	Difference in mg/dL 16.10	*P*<0.001
TG at day-0 216.09±2.43	TG at day-60 196.08±2.45	20.01	*P*<0.001
LDL-C at day-0 179.65±2.87	LDL-C at day-60 162.06±2.51	17.59	*P*<0.001
HDL-C at day-0 37.95±1.45	HDL-C at day-60 41.65±1.91	3.70	*P*<0.001

All values are written in mean±standard error of mean. T-C: Serum total cholesterol, TG: Serum triglycerides, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol. All parameters pre and post-treatment are measured in mg/d. *n*=sample size. *P*<0.01 stands for significant change

Table 2: Parameters values before and after treatment with their statistical significance in group-2 (*n*=28) (fenugreek or methi)

TC at day-0	TC at day-60	Difference in mg/dL	*P* - value
TC at day-0 280.56±1.06	TC at day-60 265.86±2.65	Difference in mg/dL 14.70	*P*<0.001
TG at day-0 224.87±1.55	TG at day-60 207.54±1.98	17.33	*P*<0.001
LDL-C at day-0 213.13±2.78	LDL-C at day-60 196.07±1.56	17.06	*P*<0.001
HDL-C at day-0 35.19±2.32	HDL-C at day-60 38.08±1.67	2.89	*P*<0.001

All values are written in mean±standard error of mean. T-C: Serum total cholesterol, TG: Serum triglycerides, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol. All parameters pre and post-treatment are measured in mg/d. *n*=sample size. *P*<0.01 stands for significant change

Table 3: Parameter values before and after treatment with their statistical significance in group-3 (*n*=29) (lemon water)

TC at day-0	TC at day-60	Difference in mg/dL	*P* - value
TC at day-0 258.21±2.12	TC at day-60 242.76±1.89	Difference 15.45	*P*>0.05
TG at day-0 246.56±2.11	TG at day-60 236.43±2.43	10.13	*P*>0.05
LDL-C at day-0 179.08±2.87	LDL-c at day-60 167.11±1.77	11.97	*P*>0.05
HDL-C at day-0 36.22±1.77	HDL-C at day-60 39.77±1.55	3.55	*P*>0.05

All values are written in mean±standard error of mean. T-C: Serum total cholesterol, TG: Serum triglycerides, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol. All parameters pre and post-treatment are measured in mg/d. *n*=sample size. *P*>0.05 stands for non-significant change

extract to meet their essential need, the awareness toward these phytochemical extracts has gained wide acceptability and is being prescribed by physicians as a treatment option for antibacterial medications. The activity of cholesterol ester transfer protein, which supports the transfer of cholesterol esters from HDL to triglyceride-rich lipoproteins, is increased. Furthermore, patients with chronic kidney disease have reduced activity of the HDL-associated enzymes, such as paraoxonase, which might be responsible for impaired antioxidative and anti-inflammatory function of HDL. All these factors can contribute to accelerated atherogenesis in this specific population. For childhood cancer survivors, the mechanism for accelerated atherosclerosis is not clear and likely multifactorial. Insulin resistance and the dyslipidemic atherogenic triad clearly play a role, with the process likely exacerbated by mechanisms such as growth hormone deficiency. Engagement of the sympathetic nervous system in this stress response contributes to hypertension. In our results, lemon, *C. longa*, and fenugreek proved that significant reduction occurs in TC, TG, LDL cholesterol using these herbal preparation/mixture. However, all of these three herbs have no significant influence on HDL cholesterol. The same results were proven in the study conducted by Wiseman *et al*.[23] who described that pectin present in these three herbs inhibit enterohepatic circulation of bile acids and excrete cholesterol in feces. Flavonoids present in fenugreek are responsible for the inhibition of cholesterol synthesis.[24] Gidez *et al*.[25] stated that herbal medications have more than one or two mechanisms to balance plasma lipids in hyperlipidemic patients. Bingham *et al*.[26] stated that the major reasons for hypercholesterolemia in today's world are obesity, consuming high-fat food, diabetes, and having a family history of high cholesterol. This disorder is reported to affect a large number of people all across the world and is one of the leading causes of death as well. Cholesterol is reduced in the body by managing weight and diet. Regular exercise, lesser consumption of fatty foods, and more consumption of fruits and vegetables help in ameliorating the symptoms of hypercholesterolemia. However, in most cases, medications also known as anti-hypertensive and anticholesterol drugs are also required, especially in chronic cases. There are several problems associated with medications though and people are now switching toward newer and less toxic therapies to control and reduce cholesterol levels in the body. Several natural herbs, supplements, and food products are known to maintain healthy cholesterol levels and reduce cholesterol in mild hypercholesterolemia. These therapies, if opted for, help in preventing the disorder but are less helpful in chronic cases of this disease. In an experiment,[27] controlled dosing of turmeric was used to feed hypercholesterolemic rabbits and the effects on LDL oxidation were analyzed. It was found that turmeric extracts efficiently and quickly reduced the levels of cholesterol in the blood along with the incidences of atherosclerosis with time. The reason for these therapeutic effects, when analyzed, was

found to be the preventive action of turmeric on the oxidation of LDL cholesterol. Mattern *et al*.[28] have also explained the same important mechanism of action of turmeric that oil of these seeds inhibits enterohepatic circulation causing biosynthesis of bile acids instead of cholesterol by hepatocytes. The results obtained from research work conducted by Geleijnse *et al*.[29] revealed that all extracts of the fenugreek exhibit antioxidant activity. These findings suggest that the fenugreek extracts could act as potent source of antioxidants. Magee *et al*.[30] mentioned that many herbs and their constituents have potential to reduce total plasma cholesterol LDL cholesterol and triglycerides but they do not raise HDL cholesterol because it needs special plasma proteins as lipoproteins responsible for structural and functional integrity of HDL particles. Jhumarr *et al*.,[2] Loversa *et al*.,[31] Hundahg *et al*.,[3] and Sueawath *et al*.[4] described about citrus fruit lemon that its citric acid is antioxidant which leads to decrease oxidative stress in the human body. Determining minimum inhibitory concentration, for this purpose, first 100 μL of Mueller-Hinton broth medium was inoculated in each well of 96-well (12 × 8) plates, and then, 100 mg/mL of fenugreek extracts to the 1st well and up to 10th well were serially diluted. The 11th well was considered as the negative control (Mueller-Hinton broth only) and the 12th well containing the culture medium and a bacterium was considered as the positive control.[32-34]

CONCLUSION

We in this study have compared hypolipidemic effects of fenugreek, Curcuma longa, and lemon. Study was conducted at Jinnah Hospital Lahore-Pakistan from January 2018 to May 2018. Ninety hyperlipidemic patients of age group 19–70 were included in the study. Exclusion criteria were diabetic, alcoholic additives, hypertensive patients, and those whose kidney or liver functions were impaired. Consent was taken from all participants. Their baseline lipid profile was taken in biochemistry laboratory of the hospital. They were divided in three groups, i.e., 30 patients in each group. Group-I was advised to take 500 mg of C. longa (haldi) mixed in fresh milk without cream, thrice daily for 2 months. Group-II patients were advised to take 100 g of fenugreek leaves mixed with salad in each meal (thrice daily) for the period of 2 months. Group-III patients were advised to take 40 mL of fresh lemon juice mixed with 40 mL mineral water thrice daily for 2 months. They all were advised not to take heavy meal rich with any type of fat such as junk food. One hour daily brisk walk was advised to all participants. 15-day follow-up visit was scheduled for them. After 2 months, their lipid profile was re-determined. When results were compiled and statistically analyzed by applying paired "t" test, it revealed that C. longa decreased total cholesterol (TC), TG, LDL cholesterol 16.10, 20.01, and 17.59 mg/dL, respectively. Fenugreek decreased TC, TGs, and LDL cholesterol 14.70, 17.33, and 17.06 mg/dL, respectively. Lemon in 2-month therapy decreased TC, TGs, and LDL cholesterol 15.45, 10.13, and 11.97 mg/dL, respectively. None of the above-mentioned herbs raised HDL cholesterol significantly. It was concluded from this research work that C. longa, Fenugreek leaves, and lemon are mild to moderately effective hypolipidemic herbs to lower total plasma cholesterol, TGs, and LDL cholesterol but have no potential to raise HDL cholesterol when analyzed biostatistically.

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