

***Trachyspermum Ammi* and *Linum Usitatissimum* are medicinal herbs used as hypolipidemic agents which protect against coronary artery disease**

***Trachyspermum Ammi* ve *Linum Usitatissimum* hipolipidemik ajan olarak kullanılan bitkilerdir ve koroner arter hastalığından korur**

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ABSTRACT

Abnormal deviations ratio between subgroups of low-density lipoprotein (LDL) cholesterol and high-density lipoprotein cholesterol (HDL) in human body predisposes to the formation of atherogenic plaques which are main etiological factors for the development of Coronary Artery Disease (CAD). Many hypolipidemic herbs have been tested in the literature to prevent the occurrence of CAD. In this study we have used *Trachyspermum Ammi* (Ajwain; corn aniseed) and *Linum Usitatissimum* (Alsi, flaxseed) separately and in combination to investigate their anti-atherogenic and hypolipidemic features. Research was conducted at a Lahore General Hospital of Pakistan from February to June 2016. One hundred patients suffering from hyperlipidemia who were followed up in lipid research clinic of Jinnah Hospital, Lahore-Pakistan were enrolled in and approved written consent was taken from all patients. All patients were assigned to four different groups each, comprising of 25 patients. For three months, Group-I was treated with Ajwain, Group-II with Alsi, and Group-III with Ajwain plus Alsi. After three months therapy it was observed that Ajwain reduced LDL-cholesterol 23.77 mg/dl and increased HDL-cholesterol 3.3 mg/dl. Alsi reduced LDL-cholesterol 7.5 mg/dl and increased HDL-cholesterol 5.3 mg/dl. Whereas combination of both agents decreased LDL-cholesterol 16.1 mg/dl and increased HDL-cholesterol 6.6 mg/dl in three months therapy. It was concluded from this research work that Alsi and Ajwain given separately or in combination, have good enough potential to reduce LDL-cholesterol but are less potent effect on HDL-cholesterol in hyperlipidemic patients.

Keywords: Low density lipoprotein, high density lipoprotein, *trachyspermum ammi*, *linum usitatissimum*

Öz

Düşük dansiteli lipoprotein (LDL) ve yüksek dansiteli lipoprotein (HDL) kolesterol alt gruplarının oranlarındaki anormal sapmalar, insanlarda koroner arter hastalığı (KAH) gelişimi için temel bir etiyolojik faktör olan aterosklerotik plak oluşumuna zemin hazırlar. Literatürde KAH oluşumunun engellenmesine yönelik çeşitli hipolipidemik etkili bitkilerin test edildiği saptanmıştır. Biz de bu çalışmada, *Trachyspermum Ammi* (Ajvain, mısır anasonu) ve *Linum Usitatissimum* (Alsi, keten tohumu) bitkilerinin ayrı ayrı ve beraber kullanımlarının anti-aterojenik ve hipolipidemik etkilerini araştırmayı planladık. Çalışma Pakistan Genel Hastanesi (General Hospital)'inde Şubat-Haziran 2016 tarihleri arasında yürütüldü. Çalışmaya, Pakistan Lahor Jinnah Hastanesi Lipid Araştırma Kliniğinde takip edilen yüz (100) hiperlipidemi hastası alındı. Olgular yazılı onamları alındıktan sonra her biri 25 hastadan oluşan dört farklı gruba atandı. Grup 1 için tek başına Ajvain, Grup 2 için tek başına Alsi, Grup 3 için ise Ajvain ve Alsi kombinasyon tedavisi 3 ay süre ile uygulandı. Üç aylık tedavi süresi sonrasında Ajvain grubunda LDL kolesterol seviyesinde 23.77 mg/dl düşüş ve HDL seviyesinde 3.3 mg/dl artış, Alsi grubunda LDL kolesterol seviyesinde 7,5 mg/dl düşüş ve HDL seviyesinde 5.3 mg/dl artış izlendi. İki ajanın kombine kullanıldığı grupta ise LDL kolesterol seviyesinde 16.1 mg/dl düşüş ile birlikte, HDL kolesterol seviyesinde 6.6 mg/dl artış gözlemlendi. Özetle bu çalışmada, hiperlipidemik hastalarda LDL kolesterolü düşürmede Ajvain ve Alsi'nin ayrı ayrı veya birlikte kullanılması durumunda güçlü bir etki gösterilmişken, HDL kolesterol seviyesini yükseltmede daha az etkili bulunmuştur.

Anahtar kelimeler: Düşük dansiteli lipoprotein, yüksek dansiteli lipoprotein, *trachyspermum ammi*, *linum usitatissimum*

INTRODUCTION

Dyslipidemia or hyperlipidemia is a scientifically proved independent risk factor for the development of

coronary artery disease (CAD)¹. Physiologically, free radicals are formed in many metabolic reactions occurring in human body which react with body tissues and endogenously synthesized low density lipopro-

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teins, leading to formation of atherosclerotic plaques which are deposited with endothelial linings of blood vessels especially coronary vessels causing CAD². In allopathy, drugs used in primary or secondary hyperlipidemia include HMG-CoA reductase inhibitors (statins), nicotinic acid (niacin), fibric acids (fibrates), and bile acid binding resins. All these allopathy-related hypolipidemic agents have low patient compliance due to their adverse effects. Niacin which is basically a vitamin, causes flushing and urticaria. Statins and fibrates cause rhabdomyolysis. Bile acid binding resins have low compliance due to their metallic taste when used for a prolonged time³. Herbal medications are going to replace allopathy-related hypolipidemic drugs due to good herbal medicine-patient compliance. *Trachyspermum Ammi* (Ajwain) and *Linum Usitatissimum* (Alsi) are herbs having hypolipidemic potential in primary and secondary hyperlipidemia with negligible adverse effects⁴. Major chemical compounds of *T. ammi* include 63.4 % thymol, 19 % p-cymene and 16.9 % γ -terpinene⁵. Ajwain has a potential to reduce LDL-cholesterol, triglycerides and plasma total cholesterol by scavenging free radicals formed in various metabolic processes⁶. Contents of Ajwain scavenge free radicals and so prevent development of atherosclerotic plaques and CAD⁷⁻⁹. Ajwain inhibits enterohepatic circulation by fecal excretion of bile, and causes hepatocytes to synthesize bile acids instead of cholesterol¹⁰⁻¹². Flaxseeds are rich in fibre and contain high amounts of omega-3 and omega-6 fatty acids. They are also rich in antioxidants like lignans, which help in reducing LDL cholesterol and incidence of coronary heart diseases¹³. The oils rich in polyunsaturated fatty acids cause a decrease in "bad" cholesterol i.e; LDL-cholesterol and triglyceride concentrations. Also, omega-3 fatty acids (such as linolenic acid) in oils can increase the level of "good" cholesterol i.e; HDL-cholesterol in circulation¹⁴. Lipid content of flaxseed makes it an important source of omega 3 fatty acids, especially α -linolenic acid which may constitute up to 52% and 59.02% of the total fatty acids^{15,16}. Morris¹⁷ stated that flaxseed oil is a potentially important herbal source of omega-3 as it is relatively stable against oxidation compared to fish oils. Consumption of food products

(such as fat spreads) enriched with flaxseed oil as a source of omega-3 PUFA represents an easy delivery system of such fatty acids into the human body and significantly improves the level and profile of PUFA in the diet and in the tissues of human body¹⁸.

MATERIAL and METHODS

Research study was conducted at Lahore General Hospital in Pakistan from February to June 2016. One hundred hyperlipidemic patients were selected after written, well explained and approved consent obtained from all patients. Male/female patients suffering from primary or secondary hyperlipidemia whose age range was from 17 years to 65 years were included in the research study. We selected already diagnosed hyperlipidemic patients from ward and OPD of the hospital. Diabetic, alcohol additives, cigarette smokers were excluded from the study. As advised by Ethics Committee, to remain on safe side due to adverse effects or low herb compliance we also excluded patients suffering from peptic ulcer, and thyroid disease. Patients with any kidney or liver disease or patients already on medicines due to any disease were excluded. The patients were divided in four groups. For three months in three equally divided doses Group-I was treated with 10 gr Ajwain, Group-II with 10 gr Alsi, and Group-III with 10 gr Ajwain plus 10 gr Alsi, Group-IV was on placebo to take three capsules, containing grinded wheat to be taken three times a day for ninety days. Their baseline lipid profiles before treatment were determined by conventional methods of estimation. The patients were advised to visit lipid research clinic of the hospital fortnightly.

After post-treatment values were obtained, lipid profiles of the patients were estimated and change in LDL-cholesterol and HDL-cholesterol were compared.

Statistical analysis was performed by using IBM SPSS version 2015. Mean values of tested parameters with \pm SD were selected for analysis and paired "t" test was applied for comparison of changes in values ob-

tained before and after treatment. P-value >0.05 was considered as non-significant change in the parameter. P-value <0.01 was considered as significant change and P-value <0.001 was taken as highly significant change in the tested parameter of lipid profile.

RESULTS

When we compiled results, it was proved that pre-, and post-treatment values of three tested groups showed statistically significant (with variation) changes in mean values \pm SD. Statistically significant changes in all parameters including placebo group are shown in Table 1.

DISCUSSION

Coronary artery disease is major cause of morbidity and mortality all over the world. The disease starts from just a minor personal negligence ie; being lethargic or adapting sedentary life-style. Taking highly fatty-riched junk food, smoking, alcohol consumption in large amounts may cause dyslipidemia along with genetic LDL receptors which lead to high oxidative stress in human body and formation of atherosclerotic plaques causing CAD. There are already established drug regimens for treating dyslipidemia

for example statins, fibrates, niacin and bile acid binding resins including psyllium husk. But all these medicines have low patient compliance due to their scientifically proven adverse effects as mentioned in the introduction section of this article. Objective of this research work was to compare of hypolipidemic and antioxidant potential of herbal medicines Ajwain and Alsi separately or in combination. When ten grams of Ajwain were used daily for three months, LDL-C in 24 hyperlipidemic patients was reduced from 231.67 ± 2.11 to 207.96 ± 1.98 mg/dl which is 10.3% reduction in this parameter. Besides, HDL-C increased from 43.65 ± 1.09 to 46.99 ± 1.08 mg/dl. These results are matched with results of Shakyar R et al.¹⁹ and Lokerra F et al.²⁰ who proved that Ajwain has more hypolipidemic potential than Alsi. Alsi in our results reduced LDL-C from 207.50 ± 1.11 to 200.02 ± 1.11 mg/dl which is approximately 3.6% reduction in the parameter, while HDL-C increased about 3.6 percent. These results match with the study results of Duaare G et al.²¹ who observed same changes in HDL-cholesterol, but they proved lesser reduction in LDL-cholesterol i.e. only 2 percent. This contrast may be due to ethnicity-related genetic variations in hyperlipidemias in different populations of the world, which needs more elaborative research work. When Ajwain and Alsi were administered in 23

Table 1. Table showing before and after treatment values of lipid profile, change in pre and post-treatment values, percentage change in values and statistical significance when *Trachyspermum Ammi* and *Linum Usitatissimum* were used alone and in combination.

Medicine/groups	Parameter	Before treatment	After treatment	change	% change	p-values and SS
Gp-1	LDL-C	231.67 \pm 2.11	207.96 \pm 1.98	-23.77	-10.3	p-value < 0.001
	HDL-C	43.65 \pm 1.09	46.99 \pm 1.08	+7.6	+3.3	p-value < 0.01
Gp-2	LDL-C	207.50 \pm 1.11	200.02 \pm 1.11	-7.5	-3.6	p-value > 0.05
	HDL-C	33.33 \pm 1.61	38.60 \pm 2.10	+15.9	+5.3	p-value < 0.01
Gp-3	LDL-C	204.11 \pm 1.04	188.01 \pm 2.05	-16.1	-7.9	p-value < 0.01
	HDL-C	33.10 \pm 2.22	39.71 \pm 1.11	+19.9	+6.6	p-value < 0.01
Gp-4	LDL-C	201.97 \pm 2.10	198.82 \pm 1.91	-3.2	-1.6	p-value > 0.05
	HDL-C	33.98 \pm 1.99	33.99 \pm 1.76	+0.0	+0.0	p-value > 0.05

KEY: HDL-c and LDL-c values are measured in milligrams per milliliter. HDL-C means high density lipoprotein cholesterol, LDL-C means low density lipoprotein cholesterol, 'n' written along with drug group of patients indicates number of patients in tested and placebo group. P-value <0.01 means significant, p-value >0.05 means non-significant change in tested parameter. Gp-1 = *Trachyspermum Ammi* (n=24), Gp-2 = *Linum Usitatissimum* (n=22), Gp-3 = combination of two herbs (n=23). Gp-4 was on placebo (n=25). SS stands for statistical significance.

hyperlipidemic patients, LDL-cholesterol levels decreased 7.9% and HDL-cholesterol levels increased 19.9% and these changes match with results of study conducted by Urtave M et al.²². They proved and explained about that much increase in HDL-cholesterol realized by using Ajwain and Alsi in combination, and demonstrated synergistic effects of two herbal medicines on two different parameters of lipid profile. Teruve Q et al.²³ have described change in inter-drug response may be observed by combination of two herbal drugs having the same hypolipidemic potential due to same active ingredients. Samaseta T et al.²⁴ proved too much reduction in LDL-cholesterol when 30 grams of Ajwain and 15 grams of Alsi was used in 111 male hyperlipidemic patients. They proved 20.91% reduction in LDL-cholesterol and 33.12% increase in HDL-cholesterol. These contrasts in two results are/or may be due to environmental factors, individual patient's compliance, individual and ethics concerned with research work, follow-up and differences in the concentrations of both drugs, and sample size. Parwakave R et al.²⁵ have described that oxidative stress is naturally occurring in human body due to various metabolic processes, and free radicals produced via these mechanisms are naturally be used as body's own antioxidants. Yutare E et al.²⁶ is in favour of using herbs instead of allopathic hypolipidemic agents due to their side effects and they focused on requirement of the era of research on herbal medications.

CONCLUSION

It was concluded from this research effort that *Trachyspermum Ammi* and *Linum Usitatissimum* are herbal medicines which have admirable hypolipidemic potential with lesser adverse effects as compared to allopathic drug regimens used as hypolipidemic drugs alone. We suggest prescribing these herbs to use along with low doses of statins to get good patient-drug compliance.

RECOMMENDATIONS: It is recommended that further research work must be kept on to disclose hypolipidemic, hypoglycemic and hypotensive effects of

these herbs so that we can treat metabolic syndrome with low doses of allopathic drugs used in combination with these herbs.

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