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Comparing potential of Ficus carica and Allium sativum on triglyceride to HDL ratio in high fat diet fed male Wistar Albino rats

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Abstract

Present study compares the potential of *Ficus carica* and *Allium sativum* on triglyceride to HDL ratio in high fat diet fed male Wistar albino rats. A sample of 36 male Wistar albino rats was randomly divided into 6 groups (A, B, C, D, E and F). Hyperlipidemia was induced by high fat diet (HFD) (banaspati ghee + coconut oil) mixed in normal chow diet. After six weeks, blood was taken through retro – orbital capillary plexus, centrifuged to get sera, stored at -20°C temperature for biochemical analysis of blood lipids. TAG/HDLc ratio (atherogenic index of plasma) was measured as log TAG/HDLc. Statistical package (SPSS ver. 21.0, IBM, incorporation, USA) analyzed the results by 1- ANOVA and post – Hoc Benforinni test ($p \leq 0.05$). Cholesterol, TAGs, LDLc, and HDLc shows significant decrease in F. carica and A. sativum treated experimental groups C – F compared to positive controls (P=0.0001). A. sativum shows more potent hypolipidemic potential and more significant reduction in TAG/HDLc ratio compared to F. carica (P=0.0001). The present study concludes Ficus carica and Allium sativum show hypolipidemic potential with significant decrease in TAG/HDLc ratio and they may be used to prevent atherosclerosis and coronary artery disease as simple home remedy.

Keywords: TAG/HDL ratio, *Ficus carica*, *Allium sativum*, Rats

Introduction

Cardiovascular diseases (CVDs) are the leading cause of mortality. Globally CVDs cause 17.7 million deaths throughout the World that comprise almost 30% of total global deaths [1]. CVD claims 47% of deaths in the Europe [1]. Majority of CVD is caused by the coronary artery disease (CAD), causes highest mortality in the World in particular the Europe and the United States [1]. Hyperlipidemia is characterized by elevated blood lipoproteins and is a cause of CAD. Blood lipoproteins include the cholesterol, triglycerides (TAGs), very low density lipoproteins (VLDL), low density lipoproteins (LDL) and high density lipoproteins (HDL). LDLc is proatherogenic and HDLc is anti – atherogenic naturally [2], [3]. Hyperlipidemia is cause of coronary artery atherosclerosis resulting in myocardial infarction, brain stroke, systemic atherosclerosis, peripheral arterial disease, etc. Hyperlipidemia may either be primary or secondary type. Primary hyperlipidemia is treated by hypolipidemic drugs while secondary hyperlipidemia is caused secondary to diabetes mellitus (DM), hypothyroidism, renal failure, and endocrinopathies [2], [3]. Disordered array of blood lipoprotein is termed as dyslipidemia and is caused by modern life style, dietary habits, high calorie intake and junk food that play role in the atherosclerosis [2]. Triglyceride-to-HDLc ratio (normal value <2) [4] measured as log of TAGs/HDLc, is a predictive marker of CAD and insulin resistance [4].

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In a previous study the TAGs/HDLc ratio was concluded as an independent predictor of CAD [4]**.** This makes the TAGs/HDLc ratio an easy technique to predict the coronary artery disease in primary and secondary hyperlipidemia cases, particularly in the diabetic patients. A study [5] suggested TAGs/HDLc ratio is most useful for identifying the coronary artery disease. A recent study [6] reported TAGs/HDLc ratio is predictive marker of CAD and is well correlated with B-type 'LDL' cholesterol plasma levels. Various drug molecules such as statins and cholesterol resins are marketed but have limited hypolipidemic activity, safety profile and drug reactions and a growing interest is observed in plants and herb remedies.[2,3] More than 200 herbs and plants are analyzed of their hypolipidemic activity. Among hundreds of herbs, the common fig (Ficus carica) and garlic (Allium sativum) are widely studied agents. Both are natural herbs with proved hypolipidemic potential [7], [8] but their effect on the TAGs/HDLc ratio is not studied before. As the coronary artery atherosclerosis disease is rising in Pakistan mostly secondary to rising diabetes mellitus prevalence [9] hence there is need to analyze alternative herbal remedies for hyperlipidemia and dyslipidemia. TAGs/HDLc ratio is already reported[6] as predictive marker of atherosclerosis and coronary artery disease, hence the herbal remedy may add to overcome the health problems. We planned an experimental study of induced hyperlipidemia model to study and compare potential of *Ficus carica* (*F. carica*) and *Allium sativum* (*A. sativum*) on blood lipoproteins in particular the triglyceride to HDL ratio in high fat diet fed male Wistar albino rats.

Materials and Methods

The present experimental rat study of high fat diet induced hyperlipidemia/dyslipidemia was planned at the Department of Biochemistry, Liaquat University of Medical and Health Sciences, Jamshoro & Animal house of Sindh Agriculture University was used for animal experimentation.

Animal Selection and Housing

Animals were housed at the animal house of Sindh Agriculture University Tando Jam. A sample of 36 male Wistar albino rats was purchased from the animal house according to the inclusion criteria. Male rats, age 4-6 weeks, Wistar strain, body weight 180 – 200 grams, moving actively in the cages, and feeding well was included. Housing of rats strictly obeyed the Guidelines of Animal Experimentation Institute. Animal cages were equipped for feeders and water containers with nozzle clips. Six rats were put in each stainless steel cage under optimal environmental conditions. Temperature was kept at 21 ± 2°C. 12 – 12 hours light/dark cycle was ensured. Ventilation of room was kept at 12 rpm and humidity at 50 ± 5%. Water and animal feed were made available ad – libitum.

Induction of Hyperlipidemia

Hyperlipidemia was induced by high fat diet (HFD) mixed in normal chow diet. HFD was as banaspati ghee + coconut oil in a ratio of 3:1 at a dose of 3ml/kg per day. It was fed for 6 weeks given orally [10].

Animal Groups

36 male Wistar albino rats were randomly divided into 6 equal groups (A, B, C, D, E and F) [11] Group A – kept as negative control, given normal diet, (no hyperlipidemia induction), Group B – kept as positive control, given normal diet + hyperlipidemia induction (HFD) (no treatment), Group C - normal diet + hyperlipidemia induction (HFD) + concomitant *Ficus carica* (400mg/kg bwt.) – preventive group for 6 weeks, Group D – normal diet + hyperlipidemia induction (HFD) for 3 weeks followed by Ficus carica (400mg/kg bwt) – curative group for 3 weeks, Group E - normal diet + hyperlipidemia induction (HFD) + concomitant *Allium sativum* (400mg/kg bwt) [12] for 6 weeks – preventive group, and Group F – normal diet + hyperlipidemia induction (HFD) – curative group for 3 weeks followed by Allium sativum (400mg/kg bwt) for 3 weeks.

Anesthesia and Blood sampling

After six week experimental period, the animals were anesthetized by I/M injection of xylocaine at gluteal region. Blood was taken from retro – orbital capillary plexus as cited [13]. Centrifugation of blood samples carried for 15 minutes at 2000 rpm to get sera separated. Sera were stored at -20°C temperature till biochemical analysis conducted.

Biochemical Analysis

Sera were analyzed for the blood cholesterol, triglycerides, low and high density lipoproteins (LDLc and HDLc). Variables were estimated on Cobas chemistry analyzer (Roche, USA, 2019). TAG/HDLc ratio (atherogenic index of plasma) was measured as log TAG/HDLc. Value TAG/HDLc ratio of 0.3 – 0.1 was defined as low risk of atherogenesis, of 0.1 – 0.24 as medium risk of atherogenesis and value >0.24

defined as high risk of atherogenesis /atherogenic tendency [14].

Statistical Analysis

Results were saved in a pre – structure proforma and copied to Microsoft Excel Sheet. Statistical package (SPSS ver. 21.0, IBM, incorporation, USA) analyzed the results using one – way analysis of variance (1-ANOVA), descriptive statistics, and differences among groups were calculated by post – Hoc Benforinni test. Data level of statistical significance was taken at Cl 95% ($p \leq 0.05$).

Results

Cholesterol, TAGs, LDLc, and HDLc shows significant reduction in F. carica and A. sativum treated experimental groups C – F compared to positive controls (P=0.0001). A. sativum shows more potent hypolipidemic potential compared to F. carica (Table – 1). We noted serum cholesterol in F. carica treated groups – C and D as 224.61±7.9 and 241.1± 8.5 mg/dl and 194.0±10.5 and 206.7±3.5 mg/dl in *A. sativum* treated groups E and F respectively. Comparison was made with the positive control 303.1±6.1 mg/dl (P=0.0001). TAGs in *F. carica* groups C and D was found 273.5±16.1and 298.5±5.0 mg/dl and 239.0±8.9 and 260.5±7.6mg/dl in *A. sativum* groups E and F respectively (P=0.0001). Serum LDLc in *F. carica* C and D was found as 177.0±13.9 and 187.1±9.7 mg/dl compared to 152.8±15.1 and 162.3± 9.1 mg/dl in *A. sativum* groups E and F (P=0.0001). We found significant increase in serum HDL in both F. carica and A. sativum groups; however, the later proved having more potent lipid lowering effect. TAG/HDLc ratio was decreased significantly in F. carica and A. sativum groups however; the later produced more significant reduction (P=0.0001) (Table – 2). Bar graph – 1 shows the significant decline in the TAG/HDLc ratio, found most significant in *A. sativum* treated groups E and F.

Table -1. Blood Lipids in control and experimental rats

Parameters	Animal Groups					
	A	B	C	D	E	F
Cholesterol	113.6±6.4	303.1±6.1	224.5±7.9	241.1±8.5	194.0±10.5	206.7±3.5
TAGs	153.5±8.4	389.0±9.7	273.5±16.1	298.5±5.0	239.0±8.9	260.5±7.6
LDLc	96.3±11.8	201.3±6.5	177.0±13.9	187.1±9.7	152.8±15.1	162.3±9.1
HDLc	37.3±2.3	23.0±2.3	34.5±3.4	27.9±2.9	39.7±1.0	37.4±1.05

Table -2. TAG/HDLc ratio in control and experimental rats

Groups	Mean	SD	SEM	95% CI		P-value
				LB	UB	
Group A. Negative control	0.130	0.088	0.036	0.038	0.223	0.0001
Group B. Positive control	1.366	0.276	0.112	1.076	1.655	
Group C. HFD + Fc (400mg/kg)	1.322	0.241	0.098	1.069	1.574	
Group D. Hyper+ Fc (400mg/kg	1.277	0.200	0.082	1.067	1.487	
Group E. HFD + As (400mg/kg)	1.117	0.120	0.049	0.991	1.243	
Group F. Hyper + As (400mg/kg)	0.680	0.281	0.115	0.385	0.976	

HFD- high fat diet, Hyper- hyperlipidemia, Fc- Ficus carica, As- Allium sativum

Discussion

The present experimental study suggests the *F. carica and A. sativum* shows preventive and curative effects in high fat diet (HFD) and hyperlipidemia induced rat model. In present study, the TAG/HDLc ratio was decreased significantly in F. carica and A. sativum groups however; the later produced more significant reduction (P=0.0001). The finding is of clinical importance as the TAGs/HDLc ratio is an independent predictor of coronary artery disease [4], [6]. We found reduction in the serum cholesterol, LDLc and increase in serum HDLc, the findings are in agreement with previous studies [15], [16]. Our findings of significant improvement of hyperlipidemia and dyslipidemia of *F. carica* are in line previous reports [15], [16] and similarly *A. sativum* was reported lowering blood lipids [17], [18]. The present study is of clinical importance as the TAG/HDL-c ratio has predictive value that is already proved in clinical studies in patients suffering from systemic hypertension, DM, obesity, etc [1]. A previous study [1] concluded the TAG/HDLc ratio as early predictor of coronary artery disease. Although, our present study is an experimental study but the findings of herbal agents *F.carica and A. savitum* on TAG/HDLc ratio are new in particular their comparisons with each. The *A. sativum* shows more potent to *F. carica*. Findings of present study may be used for clinical purpose as the dyslipidemia and hyperlipidemia are inclining urban adult population of Pakistan [19], [20]. Presently, the country is showing rising trends of dyslipidemia in 34% male and 49% female and hypercholesterolemia in 17.3%. The data shows lipid metabolic disorders will incline seriously in near future in Pakistan [19], [20] and we must be ready to research herbal remedies that may be easily available, cost effective and public may be informed of taking herbs to attenuate the lipid metabolic disorders. Currently, prevalence of obesity in Pakistan is 21% and DM is 10%, and the disorders are strongly associated with hyper – and dyslipidemia. Hence the national strategy be launched seriously and alternative therapy may prove easier to combat the lipid metabolic disorders in indigenous population of country. In present study, the TAG/HDLc ratio was decreased significantly in *F. carica* and *A. sativum* groups indicating the herbal therapy may be used for the clinical purpose as it is non – toxic free from adverse drug effects.

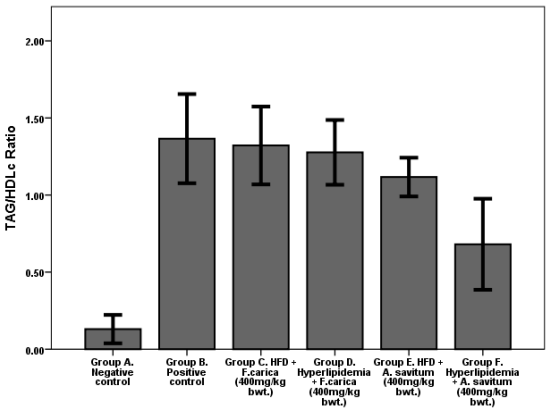

Fig 1. TAG/HDLc ratio in control and experimental rats.

A previous research [21] suggested the *F. carica* was effective in correcting HFD induced hyperlipidemia in Sprague – Dawley rat model. Similar hypolipidemic effect of *F. carica* is reported by another previous study in HepG2 cells [22]. The *A. sativum* is also proved attenuating the hyperlipidemia, dyslipidemia, atherosclerosis, systemic hypertension and thrombosis [23]. A previous animal research [24] concluded the *A. sativum* retarded atheroma formation through protecting the tunica intima against lipid deposition in carotid artery in rabbits given HFD. Previous studies [24], [25] reported *A. sativum* ameliorated dyslipidemia with improvement of blood lipoproteins. The findings of above studies support our findings. As the TAG/HDLc ratio is already proved [1], [6] hence the findings of present study are of clinical significance. Scientifically proved and evidence based findings of *F. carica* and *A. sativum* of present study merit clinical significance as their lipid lowering potential and anti – atherogenic effects (TAG/HDLc ratio) may prove useful for treating grave consequence of hyperlipidemia and dyslipidemia. Both herbs are freely available and they may be used as simple home remedy for the prevention and cure of atherosclerosis and related disorders.

Conclusions

The present study concludes *Ficus carica* and *Allium sativum* show hypolipidemic potential with significant decrease in TAG/HDLc ratio that may be used to prevent hyperlipidemia, dyslipidemia, atherosclerosis and coronary artery disease. Herbal agents may be used to treat hyperlipidemic conditions that are prevailing in urban population as they are home

available, safe, non – toxic and free from adverse effects.

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