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EFFECTS OF *FICUS CARICA* AGAINST HIGH FAT DIET INDUCED HYPERLIPIDEMIA IN WISTAR ALBINO RATS.

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ABSTRACT

INTRODUCTION Ficus carica (*F. carica*) is a native plant of Asia that is widely spread in the Mediterranean region too since ancient times. Fruits (figs) and leaves of *F. carica* are rich in sugars, amino acid, minerals, vitamins, phenols, coumarins, flavonoids, sterols, and volatile compounds, etc. **OBJECTIVE:** To study and analyze the preventive and curative lipid lowering effects of *F. carica* in high fat diet induced hyperlipidemia model of Male Albino Wistar Rat. **STUDY DESIGN:** Experimental study. **PLACE & DURATION:** Animal House of the Sindh Agriculture University, Tando Jam from April 2021 to September 2021. **METHODS:** A sample of 60 male albino rats (Wistar strain) was selected by criteria. Hyperlipidemia was induced with high fat diet (HFD) (60% fats, 20% proteins and 20% carbohydrates). Rats were equally divided into 4 groups (n=15); A to D. F.carica was given in dose of 400 mg/Kg bwt daily for six weeks. 3 – 5 ml blood was collected and stored at -20^{0}C and blood lipid levels detected. Data was put in SPSS 21.0 ver. (IBM, Incorporation, USA). 1 –way ANOVA and post – Hoc Fischer`s LSD analyzed the continuous variables at 95% CI ($P<0.05$). **RESULTS:** Preventive and curative efficacy of *F. carica* was positively proved in the hyperlipidemia induced rat model. Lipid lowering potential of Ficus carica was observed. Significant decrease in TC, TG, LDLc was found and HDLc was found increased concomitantly ($P=0.0001$). **CONCLUSION:** The present study observes significant lipid lowering effect of *Ficus carica* in high fat fed rats hence it may be consumed as a dry fruit for improving the hyperlipidemia and dyslipidemia.

KEY WORDS: *Ficus carica*, Cholesterol, Triglycerides, LDLc, HDLc Rats

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How to cite this article: Bhutto A[1] Siddiqui M[2] Hingoro MA[3] Siddiqui SS[4] Sodhar JM[5] Abbasi P[6] Kashif M[7] Shaikh KR[8]. **EFFECTS OF *FICUS CARICA* AGAINST HIGH FAT DIET INDUCED HYPERLIPIDEMIA IN WISTAR ALBINO RATS.** *JPUMHS; 2021:11:04,03-07.* http://doi.org/10.46536/jpumhs/2021/11.04.328

Received July 4 2021, Accepted On 15 august 2021, Published On 31 December 2021

INTRODUCTION

Ficus carica (*F. carica*) is a native plant of Asia that is widely spread in the Mediterranean region too since ancient times. Fruits (figs) and leaves of *F. carica* are rich in sugars, amino acid, minerals, vitamins, phenols, coumarins, flavonoids, sterols, and volatile compounds, etc. Much health related effects are attributed to its phytochemicals present in it. It has been used in the preparation of alcoholic drinks such as the spirit, liqueur, wine, etc. Its medicinal and therapeutic effects are known

since time immemorial.[1] Recently, it has been rigorously researched of its hypolipidemic efficacy in experimental studies.[1,2] It is stated that >200 herbs and shrubs are researched of their potential lipid lowering effect.[3] *F. carica* contains phytochemical and phytosterols of medicinal value. Phytosterols of *F. carica* increase the excretion of cholesterol in bile in human beings. Many ingredients of *F. carica* are found as inhibitors of cholesterol synthesis and esterification. *F. carica* intake decreases serum cholesterol and low density lipoprotein cholesterol with concomitant rise in high density lipoprotein cholesterol. Phenolic compounds of therapeutic potential have proved of decreasing blood lipoproteins by increasing lipid metabolism.[4,5] Lowering of blood pressure has been reported due to hypolipidemic effectiveness.[6] *F. carica* has shown anti – oxidant, anti – hypertensive, anti – inflammatory, and anti – bacterial activity, etc.[7] Hyperlipidemia is a dilemma of modern urban community and is a major risk factor of atherosclerosis, coronary artery disease (CAD), etc. CAD is leading cause of mortality in developed and developing countries. Primary lesion of atherosclerosis is the atheroma formation within the wall of an artery that later on enlarges in size and may occlude the lumen completely causing ischemic heart disease. Hyperlipidemia and dyslipidemia are the declared risk factors for the atherosclerosis and vascular ischemic diseases. Phenolic compounds of fruits such as in *F. carica* have been positively linked with reduction in vascular ischemic disorders and are beneficial in preventing the coronary artery diseases.[4,7] Various classes of drugs are being used for treating hyperlipidemia and dyslipidemia but the side effects are worrisome. With the economic growth in the Pakistan and urbanization, the hyperlipidemia and dyslipidemia have emerged secondary to eating habits and obesity. Hence there is need to identify new herbs such *F. carica* of their possible potential of decreasing blood lipid levels. The present study induced hyperlipidemia in rat model to evaluate the preventive and curative lipid lowering effects of *F. carica* in scientific way to make it a simple, inexpensive and easily available remedy for an increasing health problem.

METHODOLOGY

An experimental study was planned by the Departments of Basic Medical Sciences, Suleman Roshan Medical College, Tando Adam, Sindh. Ethical approval was applied for conducting research and work begun once it was approved by the ethics committee of institute in writing. Rats were purchased from the Animal house of the Sindh Agriculture University, Tando Jam (SAUT). Rats and experiments were completed at the Animal house (SAUT). Research was completed from April to September 2021 (six months duration). A sample of 60 male rats (Wistar strain) was selected by criteria. Albino male rats (Wistar strain) eating and moving normally, having body weight (120 – 180 grams) that developed hyperlipidemia successfully with high fat diet (HFD) were included. Inactive, lazy rats, not feeding and feeling well without hyperlipidemia were excluded. Control and experimental rats were kept in standard conditions as per instructions of NIH, USA guidelines. Rats were harbored in stainless steel cages feeding normal diet to controls and high fat diet to experimental rats.[4,5] Access to feed and water was easy and available all time (*ad libitum).* 60 rats were equally divided into 4 groups; each group comprised of fifteen (15) rats. Group – A (negative control) were fed normal diet composed as 70% carbohydrates, 20% proteins and 10% fats.[4] Group – B (positive control) were fed high fat diet that was prepared as 60% fats, 20% proteins and 20% carbohydrates.[5] Experimental group C (preventive group) was given F.carica 400 mg/Kg bwt with high fat diet concomitantly. Hyperlipidemia was induced by feeding HFD (60% fats, 20% proteins and 20% carbohydrates) for 6 weeks.[4,5] While experimental group D (curative group) was induced with successful hyperlipidemia with high fat diet then treated with F.carica 400 mg/Kg bwt for six weeks.[4,5] Branded *F. carica* was purchased from market and verified by the botanist. Rats were examined daily for six weeks of their feed, water, room environment till end of experiment. Each rat of separate groups was isolated for blood sampling that was taken from the "retro – orbital venous plexus (ROVP)". A sharp capillary tube was put behind eye – ball to collect blood into a tube. 3 – 5 ml blood was collected and stored at -20^0C. Blood was analyzed for the lipid levels using standard methods. Data was put in SPSS 21.0 ver. (IBM, Incorporation, USA). 1 – way ANOVA and post – Hoc Fischer`s LSD analyzed the continuous variables. Descriptive option was highlighted in program to get variable values. Continuous variables of lipids were tabulated as mean+/- SD with P – value. Data was analyzed at 95% CI ($P<0.05$) taken statistically significant.

RESULTS

Preventive and curative efficacy of *F. carica* was positively proved in the hyperlipidemia induced rat model. Body weight of different rat groups was found increased at the end experiment period compared to baseline body weight (P=0.0001).Ficus carica treated rat groups reveal significantly less increase in body weight. Lipid lowering potential of Ficus carica is depicted in table – 2 and graphs 1 – 4. Significant decrease in TC, TG, LDLc was found and HDLc was found increased concomitantly (P=0.0001).

Table - 1. Body weight (grams) in different rat groups

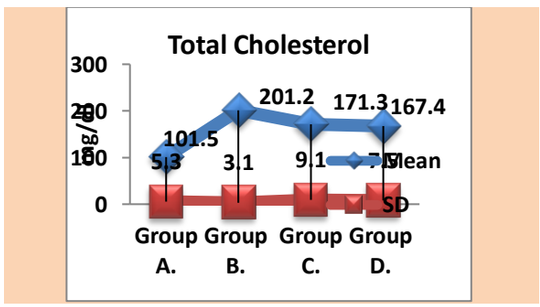
Rat groups	Bwt. (grams)			
	Baseline		End – Experiment	
	Mean	SD	Mean	SD
Group A. Control (-ve)	151.3	8.7	217.0	3.5
Group B. Control (+ve)	155.3	7.2	257.3	9.1
Group C. HFD + F. carica	141.1	5.1	211.1	7.3
Group D. Hyperlipidemia + F. carica	140.1	7.3	210.3	5.3
P-value	0.0001		0.0001	

Bwt. – body weight

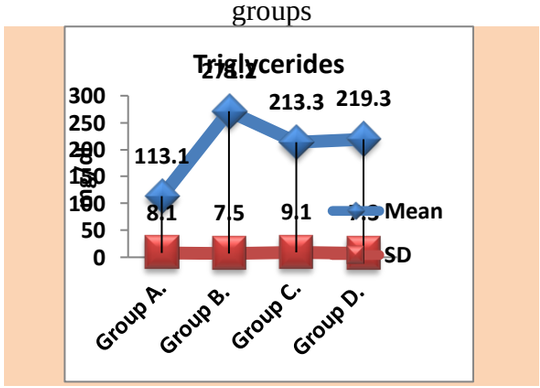
Table - 2. Total cholesterol, triglycerides, low and high density lipoproteins

Groups	TC	TG	LDLc	HDLc
Group A. Control (-ve)	101.5±5.3	113.1±8.1	100.1±3.5	42.3±3.1
Group B. Control (+ve)	201.2±3.1	271.2±7.5	179.1±6.7	23.4±3.3
Group C. HFD + F. carica	171.3±9.1	213.3±9.1	161.3±5.2	33.1±9.3
Group D. Hyperlipidemia + F. carica	167.4±7.5	219.3±7.3	160.5±4.1	39.1±5.1
P-value	0.0001	0.0003	0.0001	0.0002

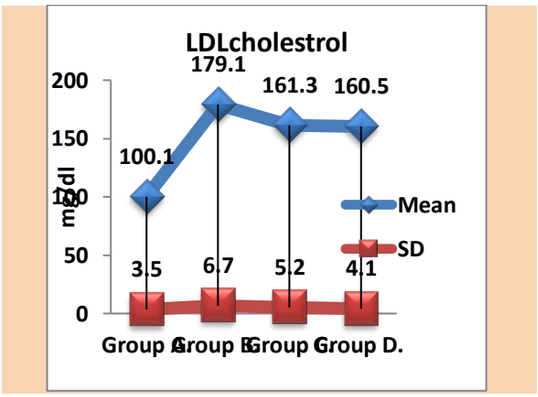
TC – total cholesterol, TG – triglycerides, LDLc – low density lipoprotein cholesterol, HDLc – high density lipoprotein cholesterol



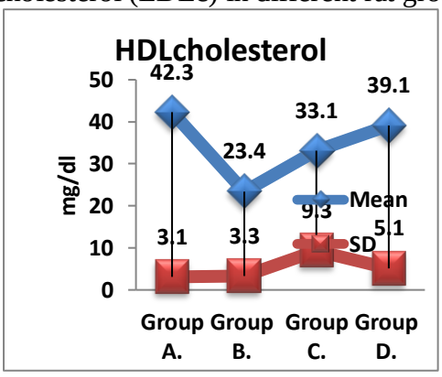
Graph –1. Total Cholesterol in different rat groups



Graph –2. Serum triglycerides in different rat groups



Graph –3. Low Density Lipoproteins cholesterol (LDLc) in different rat groups



Graph: 4. High Density Lipoproteins cholesterol (HDLc) in different rat groups

DISCUSSION

The obesity is increasing throughout the World and in urban community of Pakistan due to economic prosperity. Obesity has emerged a public health challenge. Obesity is a risk factor for hyperlipidemia, dyslipidemia, diabetes mellitus, and atherosclerosis and associated disorders such as the systemic hypertension, coronary artery disease, peripheral arterial disease, etc.[8-10] The increasing prevalence of obesity and associated metabolic disorders demands newer effective therapy in particular herbs. As the herbs are inexpensive, cost effective,

and easily available and effective hence the interest is growing for analyzing the herbs.[11,12] The present experimental study was conducted with control and randomization. Hyperlipidemia – preventive and curative groups C and D rats were treated with *F. carica* fulfilling the experimental protocol. High fat diet (HFD) was prepared for induction of hyperlipidemia. *F. carica* therapy was begun with HFD or after induction of hyperlipemia. We found statistically significant hypolipidemic (lipid lowering) effects of *F. carica*. Both preventive and curative hypolipidemic effects of *F. carica* were observed in our present study. TC, TG and LDLc show decreased levels in experimental rats (groups C and D) compared to negative and positive controls (groups A and B). HDLc levels were elevated in experimental rats. Hypolipidemic effect of *F. carica* is concordant to previous studies.[13-16] Hypolipidemic and dyslipidemic effects of *F. carica* have also been observed in above studies.[13-15] A previous study[16] of Sprague – Dawley rats studied the lipid lowering effects of *F. carica* in HFD induced hyperlipidemia. That previous study reported significant rise in HDLc with concomitant reduction in TC, TG and LDLc. Findigns of above study is consistent with the present *F. carica* study. A previous study[17] of HepG2 cells treated with leaves of *F. carica* significantly decreased the cholesterol secretion the findigns are consistent with the present study. Hypolipidemic findigns of present study are of clinical importance for treating the increasing prevalence of obesity, dyslipidemia and hyperlipidemia in the urban population of country.[8,10] Currently, the country is facing rising trends of 21% obesity and hyperlipidemias. Hypercholesterolemia is rated as 17.3%, dyslipidemia 34% in male and 49% in female while hypertension in 41%, the figures point towards the gravity of metabolic disorders that will be agonizing the public health of country in near future.[9,10] DM prevalence is rated as 10% that is strongly associated with obesity. Obesity is associated with hyperlipidemia and dyslipidemia. Previous reports[9,10] suggest the modifiable risk factors of coronary artery disease and myocardial infarction may be minimized by overcoming the dietary habits, stress, smoking, sedentary life, hyperlipidemia, dyslipidemia, etc. Hypolipidemic effects – both preventive and curative potential of *F. carica* was observed positively in rats of present study.[18,19] A previous study[20] treated the hyperlipidemic rat models with *F. carica* and observed hypolipidemic effects with reduction in oxidative markers the malondialdehyde (MDA) and tumor necrosis factor (TNF-α) in Sprague Dawley Rats. The findigns are consistent to present study. Hypolipidemic effects of *F. carica* of a previous study[21] are in line with present study that concluded that this effect may be exploited clinically for treating hyperlipidemia. Findings of present study in light of literature review prove and support the lipid lowering potential of *F. carica* hence it may be used as alternative herbal remedy.

CONCLUSION

The present study observes significant lipid lowering effect of *Ficus carica* in high fat fed rats in an experimental study. Hypolipidemic effect of *Ficus carica* is attributed to its rich content of phenolic compounds, sterols, phytosterols, flavonoids, vitamins and minerals. Phenolic compound and flavonoids play vital role against oxidative stress found in metabolic disorders such as the hyperlipidemia and dyslipidemia. Ficus carica may be consumed as a dried fruit for overcoming the hyperlipidemia and dyslipidemia. Present study recommends further large scale studies to validate the finding to use it as *add – on* therapy.

ETHICS APPROVAL: The ERC gave ethical review approval

FUNDING: The work was not financially supported by any organization. The entire expense was taken by the authors

ACKNOWLEDGEMENTS: We would like to thank the all contributors and staff and other persons for providing useful information.

AUTHORS' CONTRIBUTIONS: All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST: No competing interest declared.

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