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Original Article

Evaluation of Hypolipidemic activity of *Fragaria vesca* Polyphenols in High-Fat Diet-Induced Hyperlipidemia in Wistar Rats

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ABSTRACT:

Background: Dyslipidemia is a major public health issue in developed and developing countries, and it is a major risk factor for ischemic heart disease, atherosclerosis, and cerebrovascular accidents. The current trend is most of the antihyperlipidemic drugs like atorvastatin, fibrates, statins, nicotinic acid, probucol, and other chemical formulations were extensively used to treat hyperlipidemia clinically. The because of their serious adverse effects including diarrhea, nausea, myositis, and altered liver functions with statins and their use is restricted. *Fragaria vesca* is commonly consumed by the population in a routine lifestyle.and it has lipid-lowering properties Hence, the present study is planned to investigate the hypolipidemic activity of *Fragaria vesca* fruit extract on high-fat diet-induced hyperlipidemia in Wistar albino rats was studied**. Material and Methods:** In all groups except Group - I, a high-fat diet was given orally. The study included sixty-six male Wistar albino rats weighing 180-200 gm. After one week of growth, the animals were divided into eleven groups, each group contain six Wistar albino rats, and they were randomly assigned. *Fragaria vesca* fruit extractwas given orally and estimated body weight, lipid profile, and blood sugar levels were in all the groups before and after the induced fat model in Wistar albino rats. **Results:** According to the findings, ellagicacid (500mg/kg per oral for 4 weeks), *Fragaria vesca* (500mg/kg per oral for 4 weeks), tocopherol (500mg/kg per oral for 4 weeks), zinc oxide FV (250mg/kg per oral for 4 weeks), zinc oxide FV (500mg/kg per oral for 4 weeks) were effective into decreases Total Cholesterol, Triglycerides, and LDL and Increasing HDL in the management of hyperlipidemia. **Conclusion:** The study concluded that the Phytochemical compound of *Fragaria vesca* showed a significant decrease in the levels of lipid profile Total Cholesterol, Triglycerides, LDL, and Increased HDL in high fat-induced hyperlipidemic Wistar albino rats.

Keywords: Blood glucose, *Fragaria vesca*, antihyperlipidemic effect, Wistar albino rats.

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INTRODUCTION

In today's lifestyle, changes in lipid levels are a substantial health risk. Dyslipidemia affects between 25-30% of the urban population and 15-20% of the rural population affected in India.[1] Hence if it is not diagnosed early stages, it can cause the development of cardiac problems such as ischemic heart disease and atherosclerosis. As a result, cholesterol-lowering drugs are important to normalize lipid levels in the body. These drugs can be used both prophylactically and therapeutically to treat hyperlipidemia. Hyperlipidemic drugs are effective, but they may cause several side effects.[2–4] Hence long-term administration of these drugs has been restricted.Asthese drugs affect blood glucose levelsleading to hyperglycemia.[5] As a result, there is a need for alternative effective treatment procedures with fewer adverse effects. Plant products were tried because they are natural and produce fewer side effects even after prolonged use. In the present scenario consumption of high-calorie foods, a lack of physical activity, and a stressful lifestyle lead to cause hyperlipidemia and its complications.It is one ofthe most important public health issues globally. It is initially asymptomatic, readily detectable, and often leads to lethal complications if left untreated.

Diabetes mellitus (DM) is a metabolic condition that is caused by a fall in insulin action and/or secretion in the body. With the development of the disease, pathological alternation occurs such as nephritis, retinopathy, cardiovascular problems, Diabetic ketoacidosis, High blood pressure, and stroke. Diabetes Mellitus is generally preventable through lifestyle changes.[6] The current

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hypercholesterolemia drug trend lacks desirable features such as efficacy, long-term safety, adverse effects, expense, ease of administration, and a public health opinion for the simplest therapy for approaching the condition. To reduce hyperlipidemia activity, we found high potency and less adversity. *Fragaria vesca* is one of the plants that has been consumed by humans since the Stone Age. In the traditional system of medicine, the plant is used as a blood purifier. Fruits of this plant are reported to possess many medicinal properties.

Wild Strawberry is used to treat the liver hyperlipidemic, cardio-vascular, and stomach disorders.[7–11] Leaves and roots are used in the treatment of gum disease. Leaves are used as an astringent in sore throats, cuts, burns, and bruises. Tea made from the leaves is recommended as anti-diarrheal. Fruit is believed to have diuretic and cooling properties. It is usually used in the treatment of arthritis, tuberculosis, gout, and rheumatism. The tincture made from the leaves is useful in the case of gingivitis.The fruit contains ellagic acid, which has therapeutic properties.[12,13] *Fragaria vesca* is commonly consumed by the population in a routine lifestyle and it has lipid-lowering properties. Hence, the present study is planned to investigate the hypolipidemic activity of *Fragaria vesca* fruit extract on high-fat diet-induced hyperlipidemia in Wistar albino rats was studied.

MATERIALS AND METHODS

Plant extract

The pulp of the *Fragaria vesca* fruit extract was employed in this study. The fruits utilized in the experiment were purchased from a local store. The fruits had been cleaned, cut, and the seeds had been removed. It was then dried and pulverized. After that, the fruits were extracted with ethanol in a Soxhlet system. The decoction was used to make the ethanol extract. These extracts were then filtered, and the filtrate was then vaporized to dry the extract.[14]

Chemicals and reagents: Chemical agents such as cholesterol, cholic acid, casein, choline, and sucrose were purchased from Himedia Laboratories Pvt. Ltd., Chennai. Multivitamin multi-mineral capsules Becadexamin and Atorvastatin were obtained from the pharmacy store of the hospital. Elisa kits of Total Cholesterol, triglyceride, and HDL-C were purchased from Coral Ltd., Goa.

Animals

The study included 66 male Wistar albino rats. Rats were kept in clean polypropylene cages with six Wister albino rats in each cage in a controlled environment (26°-28°C) with a 12-hour light/dark cycle. The study protocol was approved by the Institutional animal ethics committee in Basaveshwara Medical College, Chitradurga,Karnataka. The study protocol was approved by the Institutional animal ethics committee in Basaveshwara Medical College, Chitradurga,Karnataka.At all times, standard food and drink were provided. The rats were allowed to acclimatize to controlled room temperatures (26 - 28 Degree Cent) for one week. The animals were randomly separated into eleven groups, each group containing six rats, after one week, using random numbers generated by a randomizer.

Induction of hyperlipidemia

Rats were divided into 6 groups of 6 animals each. The animals of all the groups were given a high-fat diet consisting of cholesterol (1%), cholic acid (0.5%), casein (20%), choline (0.25%), d-l-methionin1(0.4%), coconut oil (25%), multi-vitamin mix (3.5%) and sucrose (48.4%) with standard pellet diet for 30 days.

Antihyperlipidemic effect of *Fragaria vesca* fruit extract:

The animals were divided into eleven groups of six animals each as follows;

Group 1: Control group.

Group 2: Fat model.

Group 3: Fat model + Standard drug atorvastatin (10mg/kg per oral).

Group 4: Fat model + Ellagic acid (250mg/kg per oral).

Group 5: Fat model + Ellagic acid (500mg/kg per oral).

Group 6: Fat model + *Fragaria vesca* (250mg/kg per oral).

Group 7: Fat model + *Fragaria vesca* (500mg/kg per oral).

Group 8: Fat Model + Tocopherol (250mg/kg per oral).

Group 9: Fat model + Tocopherol (500mg/kg per oral).

Group 10: Fat model + Zinc Oxide FV extract (250mg/kg per oral).

Group 11: Fat model + Zinc Oxide FV extract (500mg/kg per oral).

The animals in Group 3 to Group 11 were treated with respective assigned treatment for 4 weeks. Blood sample was collected form the animals before and at the end of the study and used for the biochemical analysis.

Statistical analysis

Data were analyzed using SPSS 20.0 version. Two-way ANOVA was applied to observe the significance of the difference between the groups. Bonferroni post-tests were applied thereafter. A probability value of less than 0.05 was considered significant.

RESULTS

The experiment utilized 66 rats in total. The results showed that ellagicacid (500mg/kg per oral for 4 weeks), *Fragaria vesca* (500mg/kg per oral for 4 weeks), tocopherol (500mg/kg per oral

for 4 weeks), zinc oxide FV (250mg/kg per oral for 4 weeks), and zinc oxide FV (500mg/kg per oral for 4 weeks) were successful in treating hyperlipidemia.

Body weight

Before building the fat model, none of the groups' body weights significantly differed from group 1 in any manner (control group). After inducing the fat model, there was a noticeable increase in body weight when groups 2 to 11 were compared. There was no appreciable variation in body weight between groups 3 to 11 and group 2 before and after the development of the fat model. However, following the same therapy as group 2, there was a significant drop in body weight in groups 3 through 11. Groups 3 (t(10) = 12.19, p 0.001, group 5 (t(10) = 12.19, p 0.001, group 7 (t(10) = 12.36, p 0.001, group 9 (t(10) = 12.11, p 0.001, group 10 (t(10) = 10.27, p 0.001), and group 11 (t(10) = 12.27, p 0.001) were discovered quite helpful, with these individuals who have lost a large amount of weight (Table 1).

Total cholesterol levels

Prior to building the fat model, total cholesterol in each group was similar to group 1 and not significantly different. After inducing the fat model, there was a significant rise in total cholesterol levels when groups 2 to 11 were compared to group 1. There was no detectable variation in total cholesterol between groups 3 to 11 and group 2 before and after the development of the fat model. The total cholesterol levels in groups 3 to 11 showed, however, a significant drop as compared to group 2 following the matching therapy. Extremely significant groups were groups 3(t(10)=5.253, group 5(t(10)=5.298, group 7, group 9(t(10) =5.365, group

Table 1: Data were represented as mean ± SD and analyzed by One-Way ANOVA followed by Bonferroni post-tests.

Parameters		Group 1	Group 2	Group 3	Group 4	Group 5	Group 6	Group 7	Group 8	Group 9	Group 10	Group 11
Body weight (g)	BT	154.66 ± 2.16	208.33 ± 11.48	218.33 ± 9.41	218.00 ± 13.38	219.33 ± 7.86	220.00 ± 6.066	222.00 ± 7.04*	223.66 ± 9.07*	221.33 ± 7.65*	221.33 ± 7.65*	219.66 ± 7.52
	AT	156.5 ± 1.22	219.33 ± 9.43	170.66 ± 4.32***	197.66 ± 7.94**	170.66 ± 9.43 ***	194.00 ± 12.00**	170.00 ± 6.44***	192.33 ± 10.83***	171.00 ± 4.14***	178.33 ± 7.73***	170.33 ± 6.86***
Total cholesterol (TC) (mg/dL)	BT	112.33 ± 12.22	138.33 ± 7.73	142.66 ± 8.91	144.66 ± 7.55	148.66 ± 8.26*	155 ± 12.88*	151.00 ± 16.76	151.00 ± 15.83	150.00 ± 20.31	155 ± 14.79*	153.33 ± 17.46
	AT	110.66 ± 13.24	143.5 ± 6.50	104.66 ± 7.11***	120.66 ± 8.16***	104.33 ± 12.98***	123.5 ± 5.57***	104.33 ± 12.98***	103.16 ± 13.27***	103.83 ± 12.43***	103.66 ± 19.72***	97.33 ± 20.73***
Triglycerides (TG) (mg/dL)	BT	107 ± 15.63	130.66 ± 9.00	128.00 ± 10.80	124.33 ± 9.58	125.66 ± 7.08	128 ± 9.79	123.66 ± 13.23	125.33 ± 13.48	125.33 ± 13.48	126.00 ± 13.79	122.33 ± 15.30
	AT	107 ± 16.62	130.33 ± 7.94	82.00 ± 11.17***	101.33 ± 7.65***	84.00 ± 8.76***	102.33 ± 9.91***	79.66 ± 10.07***	101.33 ± 15.31**	84.66 ± 6.15***	80.66 ± 13.06***	86.33 ± 5.27***
LDL (mg/dL)	BT	72.66 ± 9.68	95.00 ± 7.09	95.66 ± 6.21	95.66 ± 6.21	97.33 ± 5.12	96.5 ± 5.99	96.83 ± 6.27	96.00 ± 5.51	97.33 ± 5.88	99.83 ± 5.60	98.16 ± 4.30
	AT	73.83 ± 8.35	95.00 ± 7.09	54.66 ± 6.53***	74.33 ± 8.33***	58.00 ± 5.65***	77.33 ± 8.26**	57.33 ± 6.02***	72.66 ± 6.77***	51.16 ± 6.70***	47.00 ± 4.73***	51.16 ± 6.70***
HDL (mg/dL)	BT	13.766 ± 0.98	14.66 ± 1.03	15.33 ± 5.22	13.9 ± 1.59	15.10 ± 1.65	14.75 ± 1.28	15.58 ± 0.49	15.76 ± 1.09	15.7 ± 0.54	16.2 ± 1.35	14.23 ± 2.13
	AT	13.91 ± 0.80	15.00 ± 0.98	20.33 ± 1.75***	17.33 ± 2.42	20.73 ± 1.55***	16.7 ± 1.66	21.83 ± 1.94***	16.33 ± 0.81*	20.16 ± 1.32***	20.33 ± 1.63***	19.33 ± 1.86***
Blood glucose (mg/dL)	BT	75.66 ± 2.94	102.66 ± 5.98	102.83 ± 2.56	103.83 ± 5.74	101.5 ± 4.086	102.5 ± 3.33	102.5 ± 3.33	102.00 ± 4.89	105.33 ± 7.00	99.66 ± 5.85	99.66 ± 5.85
	AT	77 .00 ± 3.28	104.33 ± 3.44	82.33 ± 4.96***	92.3 3± 5.85**	75.66 ± 2.94***	84.5 ± 5.71***	74.33 ± 4.63***	82.5 ± 2.16***	77.66 ± 6.50***	77.33 ± 6.40***	76.66 ± 4.32***

*p< 0.05, **p< 0.01, ***p< 0.001 when compared high-fat diet-induced hyperlipidemia group (group 2) with *Fragaria vesca* polyphenols treated groups. Bodyweight, Total cholesterol, Triglycerides, LDL, HDL, and Blood glucose levels in the control and intervention groups before and after treatment. BT- Before treatment, AT- After Treatment.

10(t(10)=5.388, group 11, and group 12(t(10) = 6.245, resulting in a substantial decrease in total cholesterol (Table 1).

Triglycerides

Triglycerides were not noticeably changed in any of the groups compared to group 1 prior to creating the fat model (control group). In groups 2 through 11, the fat model was induced and compared to group 1, there was an increase in triglycerides. When compared to group 2 both before and after the fabrication of the fat model, there was no noticeable variation in the triglyceride levels across groups 3 to 11. But after receiving the same therapy as group 2, groups 3 through 11 had a significant decrease in triglycerides. Significant decreases in triglycerides were seen in groups 3 (t(7.114, p=0.001), group 5 (t(10)= 6.820, p=0.001, group 7 (t(10)= 7.458, p=0.001, group 9 (t(10)= 6.722, p=0.001, group 10 (t(10)=7.311, p=0.001, and group 11 (t(10)= 6.477, p=0.001 (Table 1).

LDL levels

There were no significant variations in LDL in any of the groups compared to group 1 prior to the preparation of the fat model (control group). After generating the fat model in groups 2 through 11, there was an increase in LDL relative to group 1. There was no discernible change in LDL when comparing groups 3 to 11 to group 2 before and after the creation of the fat model. However, following the same therapy as group 2, there was a substantial decrease in LDL in groups 3-11. Extremely substantial LDL cholesterol decreases were seen in groups 3 (t(10)=9.973, p=0.001), group 5 (t(10)=9.148, p=0.001), group 7 (t(10)=9.313, p=0.001), group 9 (t(10)=10.840, p=0.001), group 10 (t(10)=11.870, p=0.001), and group 11 (t(10)=10.840, p=0.001) (Table 1).

HDL levels

There was no noticeable variation in HDL between groups 3 to 11 and group 2 before and after the creation of the fat model. However, following the same therapy as group 2, groups 3-11 saw a significant increase in HDL levels. A substantial rise in HDL was seen in those in groups 3(t(10)=6.690, p=0.001, group 5(t(10)=7.192, p=0.001, group 7(t(8.571, p=0.001), group 9(t(10)=6.481, p=0.001, group 10(t(10)=6.69, p=0.001, and group 11(t(10)=5.435, p=0.001 (Table 1).

Blood glucose levels

All the groups' blood glucose levels before creating the fat model were comparable to group 1 and did not differ substantially from it. Blood glucose levels significantly rose following the induction of the fat model when groups 2 to 11 were compared. Blood glucose levels did not differ significantly between groups 3 through 11 and group 2 before and after the development of the fat model. But in groups 3-11, the same therapy resulted in a significant decrease in blood glucose compared to group 2 after the same procedure. Significant drops in blood glucose levels were seen in groups 3(t(10)=8.147, group 5(t(10)=10.620, group 7(t(10)=11.110, group 9(t(10)=9.875, group 10(t(10)=9.998, and group 11(t(10)=10.250, respectively (Table 1).

DISCUSSION

Increased lipid levels in the body can cause atherosclerosis and are harmful to health. In the next 10 years, hyperlipidemia will impact around 2.3 million individuals globally, according to the World Health Organization. There are effective therapies for hyperlipidemia, but they come with a number of side effects. Alternative, efficient, and affordable hyperlipidemia treatment modalities are so required. It is necessary to demonstrate the benefits of *Fragaria vesca* in lowering cholesterol.

The purpose of the current study was to assess the antihyperlipidemic activity of *Fragaria vesca*. The animals' body weight, total cholesterol, triglycerides, LDL, and blood glucose levels all dramatically rose after being fed a high-fat diet. With notable drops in body weight, total cholesterol, triglycerides, LDL, and blood glucose, groups 3, 5, 7, 9, 10, and 11 were shown to be particularly effective. There was a significant rise in HDL levels in these groups. Berries are little fruits that can be eaten on their own or as an ingredient in processed food like juice. They include a lot of ligands, tannins, and flavonoids. Fruits containing a lot of sugar, like strawberries and blueberries, are very nutritious.

The most commonly consumed fruit is the strawberry (*Fragaria vesca*), which is also considered to offer a variety of medicinal and preventative benefits. The anthocyanin pigments are what provide the color red. It has been demonstrated that it can reduce cholesterol levels[10]. One of the most popular fruits in the world, according to reports, is the strawberry[14,15]. The fruit has several chemicals that can aid in reversing hypolipidemia and dysregulated lipids. Additionally, as this is a natural substance, there have been no negative effects observed[16,17]. Consuming fruit has been associated with better blood glucose regulation[18]. Vitamin C content for these fruits is considerable. Seven weeks of eating fruit or fruit-related items have been shown to significantly decrease cholesterol levels in obese people[19].

In another study, persons with diabetes or excess body weight who ate fruit had reductions in their triglycerides, cholesterol, and diastolic blood pressure. All of these qualities make it possible to utilize it as a hyperlipidemia treatment method. The results of the current investigation agree with earlier studies. One more study[20] found that consuming strawberries did not affect the blood glucose levels of obese individuals. In the present investigation, a significant decrease in blood glucose was observed. The prior study, though, was conducted on humans, so the outcomes are not similar. After consuming strawberries, another study indicated that the lipid profile of women with metabolic syndrome significantly improved[21]. Earlier studies[22–26]

discovered that strawberries had anti-hyperlipidemic properties. The findings of this study agree with those of earlier ones.

CONCLUSION

According to the research results, ellagic acid (500mg/kg per oral for 4 weeks), ethanolic extract *Fragaria vesca* acid (500mg/kg per oral for 4 weeks), Tocopherol (500mg/kg per oral for 4 weeks), zinc oxide FV (250mg/kg per oral for 4 weeks), zinc oxide FV (500mg/kg per oral for 4 weeks), zinc oxide FV (500mg/kg), Further research is needed to recommend the use of *Fragaria vesca* in the treatment of hyperlipidemia, and its associated disorders.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

LDL: Low-density lipoprotein; **HDL:** High-density lipoprotein; **DM:** Diabetes mellitus, **HDL CHDL:** Cholesterol, **FV;** *Fragaria vesca*

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