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ANALYSIS OF ANTI HYPERLIPIDEMIC ACTIVITY OF *FAGONIA ARABICA* WHOLE PLANT EXTRACT

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ABSTRACT

One of the most prevalent medical conditions is obesity, which is linked to abnormal blood lipid and lipoprotein levels is hyperlipidemia. But toxicological issues continue to be the main concern with anti hyperlipedemic medication. In this situation nature has potential to treat diseases without exhibiting any side effects. Thus, this study aims at assessing anti-hyperlipedemic activity of *F. arabica.* The plant material was collected subjected to extraction and qualitative, quantitative analysis was carried out. Further In vivo study was also conduceted. Results revealed that the % yield for pet ether & ethanolic extract was observed to be 5.7%& 10.5% respectively. The phytochemical test revealed the presence of flavonoid, phenol, protein, carbohydrate, saponin & tannin respectively. The total phenolic & flavonoid content was found to be 1.02& 0.56 mg/100mg respectively. Further effects of different treatments on food intake of diet-induced hyperlipidimic rats were analyzed. On the day 7th it was seen that for rats treated with EEFA 200mg/kg & 300mg/kg daily food intake was reduced to 22.47±0.15 g & 20.65±0.22 g respectively. The TC content was reduced to 203.56±6.54 mg/dL for rats treated with treated with EEFA 300mg/kg. Further the triglyceride content was also found to be reduced to 130.51±4.11 mg/dL. While in case of atorvastatin treated rats the triglyceride content was found to be 161.99±0.24 mg/dL. The HDL & LDL was estimated to be 61.99±3.33 & 116.46±6.11 respectively in EEFA 300mg/kg. The VLDL was found to be 27.10±1.04 mg/dL. The rats treated with EEFA 300mg/kg observed to have 8.51±0.12 mg/g fecal cholesterol excreted while fecal bile bile acid was seen to excrete in amount 3.94±0.10 mg/g. From results it can be concluded that *F. arabica* can be used as an adjuvant in current therapy for the treatment of hyperlipidemia or as a medicinal agent with antihyperlipidemic properties.

Keywords: Hyperlipedemia, Medicinal plants, Phytochemicals, *F.arabica*, HDL, LDL, VLDL, TG.

INTRODUCTION

One of the most prevalent medical conditions is obesity, which is linked to abnormal blood lipid and lipoprotein levels (hyperlipidemia and hyperlipoproteinemia, respectively). Elevated blood levels of lipids and cholesterol are indicative of many illnesses related to lipoprotein metabolism and are known as hyperlipidemic conditions. Hyperlipidemia is a medical disorder characterized by elevated levels of

lipids, primarily cholesterol and triglycerides, in the bloodstream. Hyperlipoptoteinemia is the name given to this disorder, in which there is an excess of lipid in the blood that is linked to protein. It is the fats that stay dissolved throughout circulation. Elevation in plasma concentrations of different lipid and lipoprotein fractions is the primary risk factor for cardiovascular disease (CVD) and causes this impairment of lipid metabolism. Triglycerides, phospholipids, and cholesterol esters are also increased by it. The most frequent cause of death in both industrialized and developing countries is a predisposition to peripheral, cerebral, and coronary artery disorders, which are mostly brought on by irregularities in plasma lipid levels [1,2].

Patients with hyperlipidemia who do not receive treatment or control run the risk of developing extra-coronary atherosclerosis and coronary heart disease (CHD). Adopting healthy eating and lifestyle practices, such as abstaining from alcohol and tobacco, limiting simple carbs, and consuming too much table salt, can reduce the risk of coronary heart disease (CHD). These are the initial steps in treating hyperlipidemia [3,4].

The preferred pharmacological treatments for treating hyperlipidemia are vertebrates and statins. Even though these treatments have been used for more than 40 years, it was impossible to ignore the various side effects, which include diabetes, myalgia brought on by statins, and possible hepatotoxicity, nephrotoxicity, and neurotoxicity. Furthermore, different people may react differently to the treatments used, and many patients find statins intolerable. Toxicological issues continue to be the main concern with statin medication, nevertheless. Patients with hyperlipidemia frequently introduce herbal medicines as an alternative or extra therapy, keeping in mind the potential complications of the condition as well as the adverse effects of the conventional medication [5-6].

The huge treasure trove of diverse plant products is found in nature. The use of medicines in daily life is vital. Since ancient times, nature has provided medicinal substances, and numerous contemporary medications have been derived from these diverse natural sources. Medicine has been derived from plants and their derivatives since the dawn of human civilization. The value of therapeutic plants and their therapeutic benefits have been understood from the beginning of scientific inquiry. The application of herbal medicine was taught to humanity by old empirical experiences [7].

The pharmacological characteristics of the secondary metabolites derived from plants include anti-oxidative, antiallergic, hypoglycemic, and anti-carcinogenic effects. Since synthetic drugs have numerous negative impacts on human health, plant-based medications are traditionally thought to be the

safest in the healthcare system. It is thought that lipid abnormalities linked to hyperlipidemia result in cardiovascular problems [8,9].

The development of novel medications from medicinal plants has benefited greatly from the simplification of chemical principles derived from natural sources. Many compounds, including saponins, tannins, alkaloids, alkenyl phenols, glycol-alkaloids, flavonoids, sesquiterpenes, lactones, terpenoids, and phorbol esters, provide certain plants their beneficial therapeutic qualities. Some of them work in concert with one another to increase the bioactivity of other substances [10,11].

Tropical herbs like *F. arabica*, also called Dhamasa, Suchi boti, dhamanian kunda, Damoo, Shaukat-e-Albeefa, and Shokat-e-albaiza, are widespread throughout the Indian subcontinent. This green plant, which grows to a height of one to three feet, is typically found growing on calcareous rocks in Africa, Afghanistan, India, and Pakistan. The anticancer, antioxidant, analgesic, astringent, febrifuge, and prophactic properties of fagonia species have led to much research on them. Additionally, they have a long history of use in the treatment of kidney, bladder, stomach, and cancer illnesses, fever, asthma, toothaches, and toothaches. It is also regarded as a powerful family of antifungal and antibacterial agents[12,13]. Thus this study aims at assessing antihyperlipedemic activity of *F. arabica.*

MATERIALS AND METHODS

Collection of plant material

The whole plant materials of *Fagonia arabica* were collected from local area of Bhopal in the month of March, 2023.

Defatting of plant material

52 gram shade dried whole plant materials was coarsely powdered and subjected to extraction with petroleum ether by maceration.

Extraction by maceration process

Defatted powdered of *Fagonia arabica* has been extracted with ethanol solvent using maceration process for 48 hrs, filtered and dried using vacuum evaporator at 40ºC.

Determination of percentage yield

It is calculated by dividing weight of extract by by weight of powdered drug multiplied by 100.

Phytochemical screening

The phytochemical screening was performed according to standard protocol.

Estimation of total flavonoids content

Determination of total flavonoids content was based on aluminium chloride method. 10 mg quercetin was dissolved in 10 ml methanol, and various aliquots of 5- 25µg/ml were prepared in methanol. 10mg of dried extracts of were dissolved in 10 ml methanol and filtered. 3 ml (1mg/ml) of this solution was used for the estimation of flavonoid. 1 ml of 2% $AlCl_3$ methanolic solution was added to 3 ml of extract or standard and allowed to stand for 15 min at room temperature; absorbance was measured at 420 nm[14].

Estimation of total phenolic content

The total phenolic content of the extract was determined by the modified Folin-Ciocalteu method. 10 mg Gallic acid was dissolved in 10 ml methanol, various aliquots of 10- 50µg/ml was prepared in methanol. 10 mg of dried extract was dissolved in 10 ml methanol and filter. Two ml (1mg/ml) of this extract was for the estimation of phenol. 2 ml of extract and each standard was mixed with 1 ml of Folin-Ciocalteu reagent (previously diluted with distilled water 1:10 v/v) and 1 ml (7.5g/l) of sodium carbonate. The mixture was vortexed for 15s and allowed to stand for 10min for colour development. The absorbance was measured at 765 nm using a spectrophotometer [15].

Animals

The study involved the use of albino rats (SD strain) with weights ranging from 150 to 200 grams, regardless of their sex. These rats were provided with a regular diet and tap water without any restrictions. They were exposed to a 12-hour cycle of light and dark, which mimicked a natural day-night pattern. Before the actual experiments took place, the rats were given time to adapt to the laboratory conditions. The care of the animals adhered to the standards set by the Committee for The Purpose of Control and Supervision of Experiments on Animals (CPCSEA).

Drugs and extract

extract was suspended in distilled water using 1% w/v gum acacia. The reference drugs Atorvastatin suspended in distilled water using 1% carboxymethyl cellulose (CMC).

Acute oral toxicity study

The first control group mice received 0.5% carboxymethyl cellulose (CMC) suspension in distilled water while the other groups received ethanolic extract of *Fagonia arabica* in 0.5% CMC at doses of 200, 600, and 2000 mg/kg. Animals were observed closely for first 4 hours, for any toxicity manifestation, like increased motor activity, salivation, convulsion, coma, and death. Subsequently observations were made

at regular intervals for 24 h. The animals were under further investigation up to a period of 14 days and no mortality was reported within the study period.

Diet-induced hyperlipidemia in rats

Table 1: Diet-induced hyperlipidemia model

S. No.	Groups	Treatments	No. of Animals
1.	Normal	Vehicles (1 mL of 1% gum acacia and 1% CMC)	6
2.	Hyperlipidimic control	High cholesterol diet	6
3.	Treated with Standard (Atorvastatin)	High cholesterol diet + Atorvastatin (50mg/kg, p.o.)	6
4.	Treated with EEFA 200mg/kg	High cholesterol diet + EEFA (200mg/kg, p.o.)	6
5.	Treated with EEFA 300mg/kg	High cholesterol diet + EEFA (300mg/kg, p.o.)	6

Lipid profile

The serum lipid profile was determined on day 8 in the case of diet-induced hyperlipidemia. The total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C) levels were estimated using commercially available kits. Very low-density lipoprotein cholesterol (VLDL-C) was calculated as TG/5. LDL-cholesterol (LDL-C) levels were calculated using Friedewald's formula. The atherogenic index was also calculated.

Estimation of cholesterol

Ferric chloride-acetic acid (9.9 ml) reagent was added to 0.1 ml of serum for deproteinization. The contents were centrifuged at 3000 rpm for 15 min. 5 ml of the supernatant was taken and to this added 3 ml of concentrated Sulphuric acid and kept for 20 min at room temperature. The pink colour formed was read at 540 nm against a blank containing 5 ml of ferric chloride-acetic acid reagent. A set of standards were also performed in the similar manner [16].

Estimation of triglyceride

Plasma (0.1 ml) was taken in a glass stoppered centrifuge tube and to this added 4 ml of isopropanol and 400 mg of alumina. The tubes were tightly capped and shaken vigorously for 10 min. The tubes were centrifuged at 3000 rpm for 15 min and 2 ml of the supernatant was pipette into clean, dry test tubes. To these added 0.6 ml of alcoholic KOH and kept at 70°C for 15 min. The tubes were cooled to room temperature. To this added 0.5 ml of acetyl acetone reagent, 1.0 ml of meta periodate reagent and incubated at 50oC for min. Standard was also run in the same fashion with triolein instead of plasma. The colour developed was read at 405 nm against the reagent blank [17].

Estimation of HDL-Cholesterol (HDL-C)

Plasma (0.5 ml) was taken in a centrifuge tube and to this added 0.25 ml of Phosphotungstic acid reagent and 0.25 ml of MgCl2 and was centrifuged at 1500 x g for 30 min in a refrigerated centrifuge and the amount of cholesterol was determined in the supernatant by the method of Zlatkis et al., (1953) [18].

Estimation of VLDL and LDL cholesterol (VLDL-C and LDL-C)

By using Freidwald formula the concentration of VLDL and LDL cholesterol in serum were calculated.

$$LDL\text{-}C = (TC) - (HDL\text{-}C) - (TG/5)$$

RESULTS AND DISCUSSION

The % yield for pet ether & ethanolic extract was observed to be 5.7%& 10.5% respectively. The phytochemical test revealed the presence of flavonoid, phenol, protein, carbohydrate, saponin & tannin respectively. The total phenolic & flavonoid content was found to be 1.02& 0.56 mg/100mg respectively. Further effects of different treatments on food intake of diet-induced hyperlipidimic rats were analyzed.

On the day 7^{th} it was seen that for rats treated with EEFA 200mg/kg & 300mg/kg daily food intake was reduced to 22.47±0.15 g & 20.65±0.22 g respectively. The TC content was reduced to 203.56±6.54 mg/dL for rats treated with Treated with EEFA 300mg/kg. Further the triglyceride content was also found to be reduced to 130.51±4.11 mg/dL. While in case of atorvastatin treated rats the triglyceride content was found to be 161.99±0.24 mg/dL. Triglyceride levels can drop because of two possible causes: either lipoproteinlipase releases fatty acids from chylomicrons and very low-density lipoproteins (VLDL) in the bloodstream (of which half are taken up for storage) or lipolysis is inhibited so that fatty acids are not converted to triglycerides. Catecholamines can also suppress lipolysis by acting on 2-adrenoceptors, but

they primarily have the opposite effect of insulin and by acting on 3-adrenoreceptors, they increase cyclic AMP and the phosphorylation of hormone-sensitive lipase, stimulating lipolysis and the release of fatty acids into the bloodstream.

The HDL & LDL was estimated to be 61.99±3.33 & 116.46±6.11 respectively. The VLDL was found to be 27.10±1.04 mg/dL.

Thus it can be caoncluded that There was a significant increase in the serum levels of TC, TG, LDL-C, VLDL-C, and HDL-C in the hyperlipidimic control group as compared with the normal control group. All the treatment groups produced a significant decrease in serum TC, TG, HDL-C, and VLDL-C levels. In addition to the above, the serum LDL-C levels were significantly decreased by the ethanolic extract of *Fagonia arabica*.

The ethanolic extract of *Fagonia arabica* significantly increased fecal cholesterol excretion. The fecal bile acid excretion was significantly increased by all the treatment groups except Atorvastatin. The rats treated with EEFA 300mg/kg observed to have 8.51±0.12 mg/g fecal cholesterol excreted while fecal bile bile acid was seen to excrete in amount 3.94±0.10 mg/g.

These pharmacological characteristics could be attributed to *Fagonia arabica* lipid-lowering action.The impact of *Fagonia arabica* on the fecal excretion of bile acids, which may affect cholesterol homeostasis, may contribute to its hypocholesterolemic effect. To demonstrate that the aqueous and ethanolic extract of *Fagonia arabica* lowers cholesterol and TG levels, further thorough research is needed in the clinical and molecular levels. Additionally, there is a need for clinical prevention of cardiovascular and cerebrovascular illnesses.

Table 2: % Yield of ethanolic extract of *Fagonia arabica*

S. No.	Extracts	% Yield (w/w)
1.	Pet. Ether	5.7%
2.	Ethanolic	10.5%

Table 3: Phytochemical screening of extract of *Fagonia arabica*

S. No.	Constituents	Ethanolic extract

1.	**Alkaloids**	
	Mayer's Test	-ve
	Wagner's Test	-ve
	Dragendroff's Test	-ve
	Hager's Test	-ve
2.	**Glycosides**	
	Legal's Test	-ve
3.	**Flavonoids**	
	Lead acetate	+ve
	Alkaline test	+ve
4.	**Phenol**	
	Ferric chloride test	+ve
5.	**Proteins**	
	Xanthoproteic test	+ve
6.	**Carbohydrates**	
	Molisch's Test	-ve
	Benedict's Test	+ve
	Fehling's Test	+ve
7.	**Saponins**	
	Froth Test	+ve
8.	**Diterpenes**	
	Copper acetate test	-ve
9.	**Tannins**	
	Gelatin Test	+ve

Table 4: Estimation of total flavonoids and phenol content of extract of *Fagonia arabica*

S. No.	Extract	Total flavonoids content (mg/ 100 mg of dried extract)	Total phenol content (mg/ 100 mg of dried extract)
1.	Ethanolic	1.02	0.56

Table 5: Diet-induced hyperlipidemia model

Group (n = 6)	Daily food intake (g)

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Normal	20.25±0.12	22.32±0.16	20.14±0.36	20.32±0.15	21.15±0.12	20.65±0.32	20.98±0.36
Hyperlipidimic control	20.35±0.25	20.36±0.14	20.45±0.25	20.95±0.32	21.85±0.25	21.74±0.15	21.22±0.25
Atorvastatin	19.45±0.32	20.36±0.25	21.15±0.14	21.45±0.15	22.85±0.32	20.65±0.12	22.85±0.32
Treated with EEFA 200mg/kg	20.45±0.14	20.45±0.32	21.45±0.25	20.36±0.36	22.45±0.15	22.65±0.33	22.47±0.15
Treated with EEFA 300mg/kg	21.74±0.16	22.32±0.17	20.65±0.30	22.14±0.25	22.15±0.22	21.14±0.14	20.65±0.22

Table 6: Effect of ethanolic extract of *Fagonia arabica* on serum lipid profile of diet-induced hyperlipidemia in rats

Group (n = 6)	TC (mg/dL)	TG (mg/dL)	HDL-C (mg/dL)	LDL-C (mg/dL)	VLDL-C (mg/dL)
Normal	131.64±3.12	100.46±2.14	63.12±2.47	51.43±2.54	21.09±0.48
Hyperlipidemic control	324.23±3.45*	301.80±9.57*	101.56±5.66*	162.91±6.32	61.76±1.58*
Atorvastatin	160.00±5.51**	161.99±0.24**	65.87±1.71†	61.53±5.44**	33.60±0.27**
Treated with EEFA 200mg/kg	241.26±2.14**	107.42±3.21**	65.50±4.14†	154.08±2.11	22.68±0.62**
Treated with EEFA 300mg/kg	203.56±6.54**	130.51±4.11**	61.99±3.33†	116.46±6.11**	27.10±1.04**

CONCLUSION

The findings of this study provide insights into the in vivo anti-hyperlipidemic potential of the ethanolic extract of *Fagonia arabica*. The absence of acute toxicity at the administered doses indicates that the extract has a reasonable safety margin. However, further investigations are warranted to comprehensively assess the anti-hyperlipidemic effects of the EEFA, including its impact on lipid levels and related metabolic parameters. Long-term studies involving different animal models and possibly clinical trials in humans could shed more light on its potential as a therapeutic agent for managing hyperlipidemia. In conclusion, the present study lays the foundation for future research endeavors aimed at elucidating the full range of antihyperlipidemic effects and mechanisms of action of the ethanolic extract of *Fagonia arabica*.

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