ORIGINAL ARTICLE

Phytochemical and *in vivo* pharmacological evaluation of various extracts of *Ficus racemosa* L.

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Abstract

Background: *Ficus racemosa* Linn. (FR) is commonly known as gula fig/cluster fig. It is moderate sized avenue tree found throughout India either wild or cultivated for its fruits eaten by villagers. **Objective:** The main aim of the study was to evaluate the antidiabetic potential of various polar and non-polar extracts of leaves and bark of FR in animals. **Materials and Methods:** The crude drugs were extracted using various polar and non-polar solvents and preliminary phytochemical screening was performed for the presence of various phytocompounds. Diabetes was induced by a single I.P. injection of streptozotocin in normal control animals and treatment of different polar and non-polar extracts of leaves and bark of FR in diabetic animals. Blood glucose levels and various lipid parameters were evaluated in normal, diabetic, and various drug-treated animals. **Results:** In 21-day, glibenclamide as standard drug restored the blood glucose level and it is highly significantly($P < 0.001$) in 14 days, where as methanolic extracts of FR (200 and 400 mg/kg) reduced the glucose level moderately and highly significant ($P < 0.001$). Petroleum ether, chloroform, ethyl acetate, and ethanolic extracts of FR had moderately significant effects ($P < 0.01$) on 14th and 21st days. **Conclusion:** This study reveals that methanolic extract of the plant is more effective in both cause of potential evaluation. In future, this plant can be used as antidiabetic and hypolipidemic drug for developing new pharmaceuticals and treatment of several diseases.

Key words: Antidiabetic activity, cholesterol, *Ficus racemosa*, high-density lipoprotein, lipids

INTRODUCTION

Ficus racemosa Linn. (FR) (family - Moraceae) plant is a large deciduous tree distributed all over India, from outer Himalayan ranges, Punjab, Chota Nagpur, Bihar, Orissa, West Bengal, Rajasthan, Deccan, and common in South India.[1] The tree is up to 18 m high, leaves ovate, ovate-lanceolate or elliptic, sub-acute, entire, and petiolate. Leaves are shed by December and replenished on January.[2] Leaves and bark are widely used as an antibacterial, demulcent, bitter tonic, laxative, carminative, refrigerant, and febrifuge, diuretic, useful in chronic cystitis, gonorrhea and cardiotonic, acute-chronic inflammatory conditions and in a treatment of diabetes mellitus, liver diseases, and as an antiulcer.[3] It was reported that FR contain various classes of bioactive principles such as cycloartenol, euphorbol, campesterol, hentriacontane, hentriacontanol, kaempferol, stigmasterol, methyl ellagic acid, tetra triterpene, glauanol acetate, racemosic acid, a-amyrin, β-sitosterol, cycloartenol, cycloeuphordenol, and 4-deoxyphorbol, and its esters, euphol, euphorbinol, isoeuphorbol, palmitic acid, taraxerol, tinyatoxin, and tirucallol.[4,5]

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Diabetes has been recognized as a major health problem worldwide for the 21st century. Diabetes mellitus was known to ancient Indian physicians as "Madumeha." Developing countries Asia and Africa are the most viable areas where the disease is feared to raise 2–3 folds.[2,6] It is well-established fact that microvascular diseases such as retinopathy, nephropathy, and neuropathy are closely associated with chronic diabetes. Postprandial blood glucose levels may be elevated in the presence of normal levels of fasting blood glucose level, constituting an early stage in type 2 diabetes. This state not only initiates the development of early microvascular and macrovascular complications, but it can contribute to more rapid progression to symptomatic diabetes by causing glucose toxicity in muscle and pancreatic β-cells. Chronic exposure to elevated levels of glucose and fasting blood glucose causes β-cell dysfunction and may induce β-cell apoptosis in type 2 diabetes. The deficit of β-cell mass seems to be caused mainly by increased β-cell apoptosis.[3] Hyperlipidemia is a collective term used to describe human conditions when a plasma level of one or more classes of lipids, namely, cholesterol, triacylglycerides, phospholipids, and fatty acids increases above normal levels. It is one of the major causes of the development of cardiovascular disorders. Hyperlipidemias are divided into primary and secondary subtypes. Primary hyperlipidemia is usually due to genetic causes (such as a mutation in a receptor protein), while secondary hyperlipidemia arises due to other underlying causes such as diabetes. Lipid and lipoprotein abnormalities are common in the general population and are regarded as modifiable risk factors for cardiovascular disease due to their influence on atherosclerosis.[7,8]

Hence, the present study was undertaken specifically to investigate the *in vivo* antidiabetic and hypolipidemic potential of various extracts of FR. The consequences of this investigation suggest that the extracts of FR can be used as antidiabetic and hypolipidemic agent for developing new pharmaceuticals and treatment of several illnesses.

EXPERIMENTAL

Chemicals

All solvents were of Qualigens and chemicals used of Merck Pvt. Ltd.

Drugs

Free sample of glibenclamide was procured from Nicholas Piramal, Mumbai.

Animals

Wistar Albino rats of either sex (150–200 g) were purchased from the CPCSEA approved vendors for *in vivo* antidiabetic and hyperlipidemic activity.

Collection and authentication of the plant

The leaves and barks of FR were collected from village Surapur, Sultanpur district, in July that shows the green color with rough surface. The plant leaves and barks were washed, shade dried, and coarsely powdered with domestic mixer. Plant was identified (LWG-64) by Herbarium, CSIR-National Botanical Research Institute, Lucknow, UP.

Successive solvent extraction methods

Coarsely powdered drug of leaves and bark (40 g each) were extracted by Soxhlet using non-polar to polar solvents (300 ml). Then, after extraction, solvents were removed by Rotavapor (Buchi, England) and solid mass of extracts was procured.

Phytochemical screening

Preliminary screening was done for the presence of different phytoconstituents, i.e. fatty acids, terpenoids, steroids, alkaloids, flavonoids, carbohydrates etc.[9,10]

In vivo pharmacological evaluation

Experimental animals

Wistar Albino rats of either sex (150–200 g) were purchased from the CPCSEA approved vendor New Delhi. They were maintained under standard laboratory conditions at 25 ± 2°C, relative humidity (50 ± 15%) and normal photoperiod (12-h light-dark cycle) were used for the experiment. Commercial pellet diet (MFD, by Nav Maharashtra Chakan Oil Mills Ltd., New Delhi, India) and water were provided *ad libitum* throughout the course of study.

Selection and preparation of dose

Acute oral toxicity test was carried out according to the OECD guideline No. 423. Wistar Albino rats were kept for overnight fasting before drug administration. A total of three animals were used, which received a single oral dose in 2000 mg/kg, body weight of different extracts. The animals were observed for 24 h for the changes in behavior, hypersensitivity reactions, etc. Mortality, if any, was determined over a period of 2 weeks. Hence, in our studies, we selected 1/10 and 1/5th dose, i.e. 200 and 400 mg/kg dose. Doses equivalent to 200 mg and 400 mg of the crude drug per kilogram body weight were calculated and suspended in 1% w/v tween 80 solutions for the experiment.

Streptozotocin (STZ)-induced diabetes in rats

After fasting 18 h, the rats were injected intraperitoneal injection through tail vein with a single dose of 40 mg/kg Streptozotocin (Sigma, St. Louis, Mo, USA), freshly dissolved in citrate buffer (pH 4.5). After injection, the rats had free access to food and water and were given 5% glucose solution to drink overnight to counter hypoglycemic shock. Diabetes in rats was observed by moderate polydipsia and marked polyuria. The diabetes was confirmed by estimating the blood glucose level after

3 days by glucometer based on glucose oxidation method. Rats having blood glucose level more than 250 mg/dl were selected for further study.[11]

Experimental design of antidiabetic study of leaves and bark

To assess the antidiabetic activity, the animals were divided into 15 groups of six animals in each group.

Group 1: Normal control, 0.9% NaCl-treated animals, Group 2: Diabetic control, STZ-treated rats (40 mg/kg body weight), Group 3: Treated with Pet. ether extract of leaves of FR (200 mg/kg body weight), Group 4: Treated with Pet. ether extract of leaves of FR (400 mg/kg body weight), Group 5: Treated with chloroform extract of leaves of FR (200 mg/kg body weight), Group 6: Treated with chloroform extract of leaves of FR (400 mg/kg body weight), Group 7: Treated with ethyl acetate extract of leaves of FR (200 mg/kg body weight), Group 8: Treated with ethyl acetate extract of leaves of FR (400 mg/kg body weight), Group 9: Treated with ethanolic extract of leaves of FR (200 mg/kg body weight), Group 10: Treated with ethanolic extract of leaves of FR (400 mg/kg body weight), Group 11: Treated with methanolic extract of leaves of FR (200 mg/kg body weight), Group 12: Treated with methanolic extract of leaves of FR (400 mg/kg body weight), Group 13: Treated with aqueous extract of leaves of FR (200 mg/kg body weight), Group 14: Treated with aqueous extract of leaves of FR (400 mg/kg body weight), and Group 15: Standard drug, glibenclamide-treated rats (5 mg/kg body weight). The test drug and reference drug were administered orally at two dose level for 21 days from starting day of diabetes. Similar experiment was done for bark.

Blood collection and biochemical estimations in serum

On the 22nd day, fasting blood samples were collected from the tail vein of all the groups of rats. Whole blood was collected for estimation of blood glucose using the glucometer (Easy Gluco, Morepen Laboratories Ltd.; New Delhi).[12]

Determination of parameters for hypolipidemic activity

Then, serum samples were also used to analyze for serum total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and very low-density lipoprotein cholesterol (VLDL-C).

Statistical Analysis

The analysis of variance was carried out in triplicate for all data and the results of the triplicate were expressed as mean ± standard error of the mean using GraphPad Prism v5.01 software. Significance of the differences was defined as $P < 0.05$, $P < 0.01$, and $P < 0.001$ for one-way ANOVA. The difference in mean was compared using Kramer's t-test.

RESULTS

Phytochemical Screening

Maximum yield was obtained in ethanolic extract of leaves and bark and minimum was found in ethyl acetate of leaves and petroleum ether bark [Table 1]. Phytochemical screening of different extracts showed the presence of different phytochemical, i.e. alkaloids, terpenoids, flavonoids, carbohydrate, steroids, phenolic compounds, etc. [Table 2]. The study was done according to the standard procedure of Ayurvedic Pharmacopoeia, India.

Antidiabetic Activity

Effect of different extracts of leaves and bark on blood glucose level

Antidiabetic potential of FR (leaves and bark) shown in Tables 3 and 4. The induction of diabetes with STZ increases the blood glucose level significantly ($P < 0.001$) in Group II rats as compared to normal rats. The Study was performed for 21-day. Glibenclamide the standard drug restored the blood glucose level significantly ($P < 0.001$) in 14 days, whereas Ficus recemosa methanolic extract (200 and 400 mg/kg) reduced the glucose level moderately ($P < 0.01$) and highly significantly ($P < 0.001$) respectively compared to standard drug Glibenclamide. Petroleum ether, chloroform, ethyl acetate, and ethanolic extracts had moderately significant effects ($P < 0.01$) on 14th and 21st days. However, aqueous extracts did not show any significant decrease in glucose levels. The results are shown in Table 3.

Hypolipidemic Activity

Effect of different extracts of leaves and bark on lipid level

Untreated diabetic rats showed significant hypercholesterolemia, hypertriglyceridemia, elevated LDL-C, VLDL-C, and decrease in HDL-C in comparison to that of normal group. Methanolic extract of leaves showed a very good effect on lipid profile. It showed highly significant

Table 1: %Yield of different extracts of *Ficus racemosa*

Solvents	*Ficus racemosa*	
	Leaves	Bark
Petroleum ether	5.29±0.006	3.12±0.017
Chloroform	5.18±0.012	4.15±0.012
Ethyl acetate	5.14±0.012	6.34±0.017
Ethanol	11.28±0.012	9.56±0.006
Methanol	5.28±0.012	8.56±0.017
Aqueous	9.80±0.012	4.67±0.006

Table 2: Phytochemical screening of *Ficus racemosa*

Test	Petroleum ether	Chloroform	Ethyl acetate	Ethanol	Methanol	Aqueous
Carbohydrate						
Molish test	-	-	-	-	+	+
Felling test	-	-	-	-	+	+
Glycosides						
Bontrager's test	-	-	+	-	+	+
Alkaloid						
Mayer test	-	+	+	-	+	-
Hager test	-	+	+	-	+	-
Phytosterol+Triterpinoids						
Salkowski test	-	+	-	+	+	-
Protein+Amino acid						
Biuret test	-	-	-	-	-	-
Ninhydrin test	-	-	-	-	-	-
Phenolic test						
Ferric test	-	+	+	+	+	-
Lead acetate test	-	+	+	+	+	-
Flavonoids						
Alkaline test	-	-	+	+	+	+
Saponin						
Foam test	-	-	-	-	+	+
Mucilage						
Iodine test	-	-	-	-	-	+
Ethanol test	-	-	-	-	-	+

-: Abscent, +: Present

Table 3: Effect of different extracts of *Ficus racemosa* (leaves) on glucose level in streptozotocin-induced diabetic rats

Group No.	Group	Blood sugar level				
		Long-term study (days)				
		Before inducing diabetes	3	7	14	21
1	Normal control	80.3±0.46	82.2±0.17	81.4±1.7	81.9±0.57	80.11±0.18
2	Diabetic control	82.4±0.81	241.7±1.89	273.8±1.43***	268.3±3.07***	291.1±0.24***
3	Pet. ether extract (200 mg/kg)	79.4±0.92	241.6±1.44	239.9±2.11**	234.8±2.98**	226.6±0.20**
4	Pet. ether extract (400 mg/kg)	83.77±1.08	243.4±3.04	223.3±2.89**	217.8±3.09**	203.4±0.49**
5	Chloroform extract (200 mg/kg)	81.4±0.84	243.6±1.46	224.9±2.19	217.8±2.99**	215.6±1.80**
6	Chloroform extract (400 mg/kg)	79.4±0.22	244.6±1.39	222.2±2.18	215.8±2.88**	214.6±3.20**
7	Ethyl acetate extract (200 mg/kg)	78.4±0.89	243.6±1.39	264.9±2.09	255.6±2.88*	256.6±0.20*
8	Ethyl acetate extract (400 mg/kg)	79.4±0.92	244.5±1.38	258.9±2.18	251.8±2.94*	247.6±0.20*
9	Ethanolic extract (200 mg/kg)	79.4±0.92	240.7±1.69	226.3±1.41	218.3±3.09**	218.1±0.34**

(Contd...)

Table 3: (*Continued*)

Group No.	Group	Blood sugar level				
		Long-term study (days)				
		Before inducing diabetes	3	7	14	21
10	Ethanolic extract (400 mg/kg)	80.3±0.82	242.6±1.42	221.9±2.19	217.8±2.88**	215.6±2.30**
11	Methanolic extract (200 mg/kg)	84.27±1.09	244.4±3.05	219.2±2.89***	205.8±3.08***	198.2±0.29***
12	Methanolic extract (400 mg/kg)	87.78±1.09	245.6±3.09	208.2±2.79***	194.6±3.02***	178.3±0.82***
13	Aqueous extract (200 mg/kg)	82.4±0.91	240.7±1.49	271.8±1.33	271.3±3.12	283.1±0.34
14	Aqueous extract (400 mg/kg)	83.4±0.81	241.7±1.89	268.2±1.33	265.3±3.11	262.1±1.35
15	Glibenclamide (5 mg/kg)	83.25±0.97	244.8±2.54	198.4±3.49**	167.3±2.77***	159.8±0.24***

Where *P<0.05, **P<0.01, ***P<0.001 compared with diabetic control versus treated groups

Table 4: Effect of different extracts of *Ficus racemosa* (Bark) on glucose level in streptozotocin-induced diabetic rats

Group No.	Group	Blood sugar level				
		Long-term study (days)				
		Before inducing diabetes	3	7	14	21
1	Normal control	80.3±0.46	82.2±0.17	81.4±1.7	81.9±0.57	80.11±0.18
2	Diabetic control	82.4±0.81	241.7±1.89	273.8±1.43***	268.3±3.07***	291.1±0.24***
3	Pet. ether extract (200 mg/kg)	78.4±0.92	241.6±1.44	239.9±2.11**	232.8±2.98**	224.6±0.20**
4	Pet. ether extract (400 mg/kg)	83.77±1.08	243.4±3.04	223.3±2.89**	217.8±3.09**	210.4±0.49**
5	Chloroform extract (200 mg/kg)	81.4±0.84	243.6±1.46	224.9±2.19	216.8±2.99**	215.6±1.80**
6	Chloroform extract (400 mg/kg)	79.4±0.22	244.6±1.39	222.2±2.18	216.8±2.88**	215.6±3.20**
7	Ethyl acetate extract (200 mg/kg)	78.4±0.89	243.6±1.39	264.9±2.09	256.6±2.88*	255.6±0.20*
8	Ethyl acetate extract (400 mg/kg)	79.4±0.92	244.5±1.38	258.9±2.18	250.8±2.94*	246.6±0.20*
9	Ethanolic extract (200 mg/kg)	79.4±0.92	240.7±1.69	226.3±1.41	217.3±3.09**	219.1±0.34**
10	Ethanolic extract (400 mg/kg)	80.3±0.82	242.6±1.42	221.9±2.19	216.8±2.88**	214.6±2.30**
11	Methanolic extract (200 mg/kg)	84.27±1.09	244.4±3.05	214.2±1.89***	201.8±2.08***	190.2±0.29***
12	Methanolic extract (400 mg/kg)	87.78±1.09	245.6±3.09	201.2±3.79***	190.6±2.02***	170.3±0.82***
13	Aqueous extract (200 mg/kg)	82.4±0.91	240.7±1.49	271.8±1.33	270.3±3.12	282.1±0.34
14	Aqueous extract (400 mg/kg)	83.4±0.81	241.7±1.89	267.2±1.33	264.3±2.11	261.1±1.35
15	Glibenclamide (5 mg/kg)	83.25±0.97	244.8±2.54	198.4±3.49**	167.3±2.77***	159.8±0.24***

Where *P<0.05, **P<0.01, ***P<0.001 compared with diabetic control versus treated groups

($P < 0.001$) effect on lipid profile in comparison to that of diabetic group. Methanolic extract also showed a highly significant effect on various lipids and also increased HDL level as compared to disease group or diabetic animals. Results are summarized in Tables 5 and 6.

DISCUSSION

Traditionally, there are various herbs are being used for the treatment of diabetes mellitus, from which merely some have been evaluated as per the modern system of medicine. The methanolic extract of FR produced a marked decrease in blood glucose levels at 200 mg/kg and 400 mg/kg body weight in STZ diabetic rats after 21 days treatment. The antidiabetic effect of FR may be due to increased release of insulin from the existing β-cells of pancreas similar to that observed after glibenclamide administration. STZ-induced diabetes is characterized by a severe loss in body weight.[13] The decrease in body weight is due to the loss or degradation of structural proteins, since structural proteins are known to contribute to the body weight. Previous reports show that protein synthesis is decreased in all tissues due to decreased production of ATP and absolute or relative deficiency of insulin.[14] The rise in plasma triacylglycerols, cholesterol, and LDL-C levels in the present study indicate derangement of lipid metabolism and increased incidence of cardiac dysfunction in diabetic rats. On the other hand, glucagon and other hormones enhance lipolysis. The marked hyperlipidemia that characterizes the diabetic state may, therefore, be regarded as a consequence of uninhibited actions of lipolytic hormones on the fat deposits.[15] Studies on STZ-induced diabetes in experimental animals have suggested that an increase in circulatory VLDL and their associated TG are largely due to defective clearance of these particles from the circulation.[16]

Normally, circulating LDL-C undergoes reuptake in the liver through specific receptors and gets cleared from the

Table 5: Effect of different extracts of leaves of *Ficus racemosa* on different lipid level

Group No.	Groups	Parameters				
		Totalcholesterol (mg/dl)	Triglycerides (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)	HDL-C (mg/dl)
1	Normal control	78.11±2.31	77.15±2.49	16.50±2.19	16.223±1.36	50.43±2.31
2	Diabetic control	107.24±2.62***	106.33±1.32***	55.27±1.96***	23.18±1.12**	33.14±1.16**
3	Pet. ether extract (200 mg/kg)	91.34±1.13*	90.33±2.21*	32.20±2.84**	21.19±0.14*	34.35±1.34*
4	Pet. ether extract (400 mg/kg)	90.14±1.13*	89.33±2.21*	30.10±2.24**	19.29±0.14*	36.35±1.34*
5	Chloroform extract (200 mg/kg)	90.24±1.13*	95.33±3.11*	35.48±1.24***	21.19±0.14*	40.35±1.34*
6	Chloroform extract (400 mg/kg)	89.14±1.13*	91.43±21.41*	32.61±3.54***	20.69±0.14*	43.35±1.34*
7	Ethyl acetate extract (200 mg/kg)	94.34±1.13*	95.33±2.21*	33.20±2.84*	20.29±0.14*	43.35±1.34**
8	Ethyl acetate extract (400 mg/kg)	91.24±0.13*	91.43±2.21*	30.20±1.84*	18.39±0.14*	45.35±1.34**
9	Ethanolic extract (200 mg/kg)	91.34±1.13*	91.33±2.21*	32.20±2.84***	21.29±0.14*	43.35±1.34**
10	Ethanolic extract (400 mg/kg)	91.24±0.13*	91.43±2.21*	30.20±1.84*	18.39±0.14*	45.35±1.34**
11	Methanolic extract (200 mg/kg)	90.44±2.03**	92.43±2.01**	30.20±2.84***	20.39±0.13*	42.25±2.74**
12	Methanolic extract (400 mg/kg)	82.33±1.27***	86.34±2.19***	22.66±1.90***	15.27±0.90***	45.10±1.92***
13	Aqueous extract (200 mg/kg)	91.34±1.13*	91.33±2.21*	32.20±2.84*	21.29±0.14*	43.35±1.34*
14	Aqueous extract (400 mg/kg)	80.21±1.17**	85.24±2.11*	20.22±1.50*	14.37±0.40*	42.23±1.32*
15	Glibenclamide (5 mg/kg)	81.21±2.10***	81.32±2.16***	19.03±1.06***	13.32±1.12***	46.75±3.23***

Where *P<0.05, **P<0.01, ***P<0.001 compared with diabetic control versus treated groups. HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, VLDL-C: Very low-density lipoprotein cholesterol

Table 6: Effect of different extracts of bark of *Ficus racemosa* on different lipid level

Group No.	Groups	Parameters				
		Total cholesterol (mg/dl)	Triglycerides (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)	HDL-C (mg/dl)
1	Normal control	78.11±2.31	77.15±2.49	16.50±2.19	16.223±1.36	50.43±2.31
2	Diabetic control	107.24±2.62***	106.33±1.32***	55.27±1.96 ***	23.18±1.12**	33.14±1.16**
3	Pet. ether extract (200 mg/kg)	92.14±1.13*	91.33±2.21*	33.20±1.84**	22.19±1.14*	36.15±1.34*
4	Pet. ether extract (400 mg/kg)	89.14±1.13*	88.33±1.21*	31.10±1.24**	20.29±0.14*	34.35±1.34*
5	Chloroform extract (200 mg/kg)	92.24±1.13*	94.33±2.11*	38.18±1.24***	23.19±0.14*	42.35±1.34*
6	Chloroform extract (400 mg/kg)	90.14±1.13*	90.23±1.41*	34.61±3.54***	22.69±0.14*	44.15±1.34*
7	Ethyl acetate extract (200 mg/kg)	94.14±1.13*	94.33±1.21*	33.60±2.24*	21.29±0.14*	44.35±1.34**
8	Ethyl acetate extract (400 mg/kg)	90.24±0.13*	91.23±1.41*	31.20±1.84*	19.39±0.14*	49.35±1.34**
9	Ethanolic extract (200 mg/kg)	94.24±1.13*	97.33±2.21*	33.20±2.84*	27.29±0.14*	45.35±1.34*
10	Ethanolic extract (400 mg/kg)	89.24±0.13*	92.73±2.21*	29.20±1.84*	22.39±0.14*	48.35±1.34*
11	Methanolic extract (200 mg/kg)	90.44±2.03**	92.43±2.01**	30.20±2.84***	20.39±0.13**	42.25±2.74**
12	Methanolic extract (400 mg/kg)	82.33±1.27***	83.34±2.19***	20.66±1.90***	12.27±0.90***	53.10±1.92***
13	Aqueous extract (200 mg/kg)	91.34±1.13*	91.33±2.21*	32.20±2.84*	21.29±0.14*	43.35±1.34*
14	Aqueous extract (400 mg/kg)	80.21±1.17**	85.24±2.11*	20.22±1.50*	14.37±0.40*	42.23±1.32*
15	Glibenclamide (5 mg/kg)	81.21±2.10***	81.32±2.16***	19.03±1.06***	13.32±1.12***	46.75±3.23***

Where *P<0.05, **P<0.01, ***P<0.001 compared with diabetic control versus treated groups. HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, VLDL-C: Very low-density lipoprotein cholesterol

circulation.[17] HDL-C is protective by reversing cholesterol transport, inhibiting the oxidation of LDL-C and by neutralizing the atherogenic effects of oxidized LDL-C. The increased levels of LDL-C and VLDL-C decreases HDL-C as there is a reciprocal relationship between the concentration of VLDL-C and LDL-C. In diabetic rats treated with methanolic and ethyl acetate extract showed an elevation in HDL-C and reduction in LDL-C and VLDL C. As there is a close relationship between the TC level of elevated plasma and the occurrence of atherosclerosis, the ability of methanolic and ethyl acetate extract is reflected in the selective reduction of TC through the reduction of VLDL and LDL components. It could be beneficial in preventing atherosclerotic conditions, thereby reducing the possibility of coronary heart disease (CHD). It is therefore noteworthy that the effect of α-amyrin and rosmarinic acid on plasma HDL, clearly shows that the level of this lipoprotein fraction increased with methanolic and ethyl acetate extract administration.

Cholesterol is a powerful risk factor for many CHD. The degree of hypercholesterolemia is directly proportional to severity in diabetes. In this study, we have observed higher levels of cholesterol in tissues of diabetic rats. The increased level of cholesterol in tissues could be due to the decreased level of HDL-C. This, in turn, results in decreased level of cholesterol from extra hepatic tissues by the HDL cholesterol.[18,19] Administration of methanolic and ethyl acetate extract to STZ diabetic rats normalizes plasma levels of cholesterol due to the decrease in cholesterol absorption from the intestine, by binding with bile acids in the intestine and increasing bile acids excretion.

CONCLUSION

The present study revealed promising antidiabetic and hypolipidemic capacities in FR extracts which could be

used as an efficient natural source of antidiabetics. Among all tested extracts, the methanol extract was found to possess highest antidiabetic and hypolipidemic capacity and this extract was further investigated for high-performance liquid chromatography/gas chromatography/mass spectrometry chemometric profiling. In total, the accession of the study lies within methanol extract of FR which was found to have promising antidiabetic and hypolipidemic capacities. It is evident from the study that the FR is a reservoir of novel compounds and could be sustainably utilized as an immense wealth for the discovery of novel drugs against a variety of human ailments, specifically diabetic stress-induced disorders.

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