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HYPOLIPIDEMIC ACTIVITIES OF *FICUS RACEMOSA* LINN. BARK IN ALLOXAN INDUCED DIABETIC RATS

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Abstract

Ficus racemosa (Moraceae family) is used in traditional system of medicine for the treatment of several disorders including diabetes mellitus. The aim of the study was to investigate the antihyperglycemic and hypolipidemic activities of ethanolic extract of *Ficus racemosa* bark (FrEBet) in alloxan-induced diabetic rats. A total number of 30 animals were divided into 5 groups of six each. Diabetes mellitus was induced by single intraperitoneal injection of freshly prepared solution of alloxan monohydrate (150 mg/kg bw) dissolved in physiological saline in overnight fasted wistar rats. Dose dependent studies for FrEBet (100-500mg/kg bw) was carried out to find out the effective pharmacological dose (antidiabetic and hypolipidemic) to alloxan-induced diabetic rats. Blood glucose, plasma insulin, total cholesterol, phospholipids, triglycerides, free fatty acids, HDL cholesterol and LDL cholesterol levels in plasma, erythrocyte membranes, liver and kidney were determined by specific colorimetric methods. An increase in blood glucose was accompanied by an increase in total cholesterol, phospholipids, triglycerides, FFA and decrease in HDL choleterol in diabetic rats. Oral administration of FrEBet (300mg/kg bw) to diabetic rats restrored the status of blood glucose, lipids and lipoproteins to near normal range. Our investigation thus shows that FrEBet has potent antidiabetic and hypolipidemic effects in alloxan-induced diabetic rats and these effects were much comparable to that of the standard reference drug, glibenclamide.

Key words: Diabetes mellitus, Alloxan, Lipids, Lipoproteins

Introduction

Diabetes is the world's largest endocrine disease associated with increased morbidity and mortality rate and can be manifested by chronic hyperglycemia due to defects in insulin secretion, insulin action and /or both (O'Brine and Granner, 1996). Currently, 170 million people worldwide affected by diabetes mellitus. Statistical projections about India suggest that 57 million Indians will be affected by diabetes mellitus by the year 2025 making the country with highest number of diabetics in the world (Boyle et al., 2001).

Alloxan is widely employed to induce diabetes mellitus in experimental animals due to the fact that it causes severe necrosis of pancreatic β-cells with consequent lack of insulin secretion. Increased oxidative stress induced by alloxan is another possible mechanism of its diabetogenic action (Szkudelski, 2001). Lipids play an important role in maintaining the integrity of biomembrane structure and functions. Alterations in cholesterol-phospholipid molar ratio results in an increased red cell membrane permeability, fragility and reduced fluidity. Altered lipids and lipoprotein metabolism in chronic diabetes mellitus is associated with pathogenesis of atherosclerosis and other cardiovascular diseases (Manninen et al., 1992). Abnormalities in plasma lipids and

lipoprotein patterns due to defect in insulin insufficiency has been well documented, in both type I and type II diabetes mellitus (Das and Mohan, 2003).

A wide number of traditional medicinal plants are still being used to treat diabetes mellitus. Several beneficial roles such as correcting altered carbohydrate metabolism, maintaining integrity and function of β-cells, insulin-secreting activity, enhancing glucose uptake and utilization and antioxidant properties present in the traditional medicinal plants and their constituents offer exciting opportunity to develop them into novel therapeutics (Ashok et al., 2002).

Ficus racemosa is a medium tall tree with quite rich green foliage that provides good shade. It is popularly known as "Country fig" in English and "Atti" in Tamil. The leaves, bark and fruits of *F. racemosa* are employed in native medicine to treat several diseases (Joshi, 2000). Experimental studies have demonstrated its anti-inflammatory, hepatoprotective and hypoglycemic effects (Li et al., 2004; Mandal et al., 1999; Bhaskara Rao et al., 2002). However, there were no reports on antihyperlipidemic effect of *F. racemosa* bark in alloxan-induced diabetic rats. In view of the above, it seems necessary to investigate the hypolipidemic activities of ethanolic extract of *F. racemosa* bark in alloxan-induced diabetic rats.

Materials and Methods

Animals

Albino wistar male rats 7 to 8 weeks old and weighing 150-200g were used for the present study. The animals were obtained from Central Animal House, Rajah Muthiah Institute of Health Sciences, Annamalai University, India and were maintained at 12h light and 12h dark cycles. The animals were randomized into experimental and control groups and were housed 4 or 5 in a polypropylene cage. Standard pellets obtained from Mysore Snack Feed Ltd, Mysore, India, were used as a basal diet during the experimental period. The control and experimental animals were provided food and drinking water ad libitum

Chemicals

Alloxan was purchased from Sigma Aldrich Chemicals, Pvt., Ltd., Bangalore. All other chemicals and reagents used were of analytical grade.

Hypoglycemic drug

Glibenclamide was purchased from Rajah Muthiah Medical College and hospital [RMMC & H] Drugs home, Annamalai University.

Plant material

F. racemosa bark was collected in and around Chidambaram, Tamil Nadu and identified by the Botanist Dr. S. Sivakumar, Department of Botany, Annamalai University. A voucher specimen (AU 04152) was deposited in the Department of Botany, Annamalai University.

Phytochemical studies

Preliminary phytochemical examination of *F. racemosa* revealed the presence of glycosides, 8-sitosterol and lupeol,in the root bark. Tannins and psoralens were also detected.

Preparation of plant extract

Ethanolic extract preparation [FrEBet]

The ethanolic extract of *F. racemosa* bark was prepared according to the method of Hossain et al., (1992). 500g of fresh bark of *F. racemosa* was dried, powdered and then soaked in 1500 ml of 95% of ethanol overnight. After filtration, the residue obtained was again resuspended in equal volume of 95% ethanol for 48 h and filtered again. The above two filtrates were mixed and the solvent was evaporated in a rotavapor at 40°-50°C under reduced pressure. A 7% semisolid dark brown material obtained was stored at 0-4°C until used.

The ethanolic residual extract of *F. racemosa* bark (300mg/kg bw) was suspended in 2ml-distilled water and was orally administered to the animals by gastric intubation using a force-feeding needle during the experimental period.

Induction of diabetes mellitus

Diabetes mellitus was induced by single intraperitoneal injection of freshly prepared solution of alloxan monohydrate (150 mg/kg. bw) dissolved in physiological saline in over night fasted wistar rats (Al-Shamaony et al., 1994). The diabetes was assessed in alloxan-induced rats by determining the blood glucose concentration 3 days and 5 days after injection of alloxan. The rats with blood glucose level above 260mg/dl were selected for the experimental study.

Dose dependent studies for FrEBet

Different doses of (100, 200, 300, 400 and 500 mg/kg.bw) FrEBet were assessed to find out the effective antidiabetic dose in alloxan induced diabetic rats. The antidiabetic effect was assessed by giving the different doses of extract (100 to 500mg/kg.bw) daily for 45 days, to severely diabetic rats [blood glucose 260 mg/dl and urinary sugar (+++)] and studying their effects on fasting blood glucose and urine sugar. A dose of 300 mg/kg.bw FrEBet brought about significant reduction in FBG and urine sugar after 45 days of treatment as compared to diabetic rats treated with 100 and 200 mg/kg.bw. A higher dose of 400 and 500 mg/kg.bw FrEBet had more or less the same effect as that of 300 mg/kg.bw. Due to this reason, we chose the FrEBet at a dose of 300 mg/kg.bw, to assess the antihyperglycemic and antilipidperoxidative effects in alloxan induced diabetic rats.

Experimental protocol

The local institutional animal ethics committee, Annamalai University, Annamalai Nagar, India, approved the experimental design. In the experiment a total number of 30 rats (18 diabetic rats, 12 normal rats) were used. The rats were divided in to five groups of six each. Group I served as control animals and received 2ml of distilled water (instead of FrEBet) by gastric intubation using force-feeding needle. Group II animals were treated with 'FrEBet' (300 mg/kg. bw) alone for 45 days in order to evaluate the hypoglycemic effect of the 'FrEBet' in control rats. Group III animals were treated with single intraperitoneal injection of alloxan monohydrate (150 mg/kg. bw) after overnight fast for 12h. Determining the blood glucose concentration 3 days and 5 days after alloxan treatment assessed the diabetic condition. The rats with blood glucose level above 260 mg/dl and urinary sugar (+++) were selected for experimental study. Group IV animals were received 2ml of the water solution of the residual ethanolic extract of bark of *F. racemosa* (FrEBet) (300mg/kg. bw) once daily, for 45 days after the diabetic state was assessed in alloxan induced diabetic rats. Group V animals were received the reference drug glibenclamide (600 μg/kg. bw) in 2ml of distilled water once daily for 45 days after diabetic state was assessed in alloxan induced diabetic rats.

Biochemical estimations

After the experimental period, all animals were anesthetized and sacrificed by cervical dislocation and biochemical studies were conducted in blood, plasma, erythrocyte membrane, liver and kidney of control and experimental animals in each group.

Liver and kidney samples from animals were weighed and homogenized using appropriate buffer in an all glass homogenizer with Teflon pestle using specified medium and then used for biochemical estimations. We have used specific manual methods to evaluate the levels of glucose, lipids and lipoproteins. Insulin level was estimated by using Boehringer Mannheim kit.

After plasma separation, the buffy coat was removed and the packed cells were washed thrice with physiological saline. 1.0ml of erythrocytes were lysed with hypotonic phosphate buffer at pH 7.4. The hemolysate was separated by centrifugation at 10,000 rpm for 15 minutes at 20^{o}C. The erythrocyte membrane was isolated according to the procedure of Dodge et al., (1968) with a change in buffer according to Quist (1980). Blood glucose was determined by the method of Sasaki et al., (1972) using O-toluidine reagent. Plasma insulin was determined by ELISA method using Boehringer Mannheim Kit (Anderson et al., 1993). Total cholesterol and phospholipids were assayed in plasma, erythrocyte membranes, liver and kidney according to the methods of Parekh and Jung (1970), Zilversmit and Davis (1950). Free fatty acids and triglycerides were estimated in plasma, liver and kidney by the

methods of Falholf et al (1973) and Foster and Dunn (1973) respectively. HDL cholesterol was estimated by the method of Gidez et al (1950).

LDL cholesterol was calculated using the formula

$$\text{LDL cholesterol} = \text{Total cholesterol} - \text{HDL} + \left(\frac{TG}{5}\right) \text{ and}$$

VLDL cholesterol was calculated using the formula $\left(\frac{TG}{5}\right)$.

Statistical analysis

The data are expressed as mean ± SD. Statistical comparisons were performed by one way analysis of variance (ANOVA) followed by Duncan's multiple range test (DMRT). The results were considered statistically significant if the p values were 0.05 or less.

Results

Table 1 shows the body, liver and kidney weight in control and experimental animals in each group. The mean body and liver weight was significantly decreased ($P < 0.05$) whereas kidney weight was increased ($p < 0.05$) in diabetic rats as compared to control animals. The body, liver and kidney weight were normalized in diabetic rats after treatment with FrEBet and glibenclamide.

Table 2 shows the status of blood glucose and plasma insulin in control and experimental animals in each group. Blood glucose level was significantly increased ($P < 0.05$) whereas plasma insulin level was decreased ($p < 0.05$) in diabetic animals as compared to control animals. The status of blood glucose, and plasma insulin were normalized in diabetic rats after treatment with FrEBet and glibenclamide. The FrEBet showed comparable effect to that of glibenclamide. Control rats treated with FrEBet alone showed no significant difference in blood glucose and plasma insulin levels as compared to control rats.

Table 3 shows the lipid profile (cholesterol, triglycerides, phospholipids and free fatty acids) in plasma of control and experimental animals in each group. Cholesterol, triglycerides, phopholipids and free fatty acids levels were significantly increased ($p < 0.05$) in alloxan-induced diabetic rats as compared to control rats. Treatment of alloxan-induced diabetic rats with ethanolic extract of bark (FrEBet) for 45 days resulted in a marked decrease in cholesterol, triglycerides, phospholipids and free fatty acids. The FrEBet showed comparable effect to that of glibenclamide. Control rats treated with FrEBet showed no significant difference in lipids level as compared to normal rats.

Table 4 shows the levels of cholesterol and phospholipids in erythrocyte membrane of control and experimental animals. Total cholesterol was increased ($p < 0.05$) whereas phopholipids was decreased ($p < 0.05$) in erythrocyte membrane of diabetic animals as compared to control animals. Oral administration of FrEBet to diabetic rats significantly normalized the levels of erythrocyte membrane cholesterol and phospholipids. The FrEBet showed comparable effect to that of glibenclamide. Control rats treated with FrEBet showed no significant difference in levels of cholesterol and phospholipids in erythrocyte membrane as compared to normal rats.

Table 5 shows the levels of HDL cholesterol, LDL cholesterol, and VLDL cholesterol in plasma of control and experimental animals in each group. LDL cholesterol and VLDL cholesterol levels were significantly increased ($p < 0.05$) whereas HDL cholesterol was decreased ($p < 0.05$) in diabetic animals as compared to control animals. However, the levels of HDL cholesterol, LDL cholesterol and VLDL cholesterol were returned to near normal range in diabetic rats treated with FrEBet. Rats treated with FrEBet alone showed no significant difference in HDL cholesterol, LDL cholesterol and VLDL cholesterol levels as compared to control rats.

Table 6 shows the lipid profile (cholesterol, triglycerides, phospholipids and free fatty acids) in liver of control and experimental animals in each group. Cholesterol, triglycerides, phopholipids and free fatty acids levels were significantly increased ($p < 0.05$) in alloxan-induced diabetic rats as compared to control rats. Treatment of alloxan-induced diabetic rats with FrEBet for 45 days resulted in a marked decrease in cholesterol, triglycerides, phospholipids and free fatty acids. The FrEBet showed comparable effect to that of glibenclamide. Control rats treated with FrEBet showed no significant difference in lipids level as compared to normal rats.

Table 7 shows the lipid profile (cholesterol, triglycerides, phospholipids and free fatty acids) in kidney of control and experimental animals in each group. Cholesterol, triglycerides, phopholipids and free fatty acids levels

were significantly increased ($p < 0.05$) in alloxan-induced diabetic rats as compared to control rats. Treatment of alloxan-induced diabetic rats with FrEBet for 45 days resulted in a marked decrease in cholesterol, triglycerides, phospholipids and free fatty acids. The FrEBet showed comparable effect to that of glibenclamide. Control rats treated with FrEBet showed no significant difference in lipids level as compared to normal rats.

Table 1: Body, liver and kidney weight of control and experimental animals in each group Values are expressed as mean ± SD (n=6 rats). Values not sharing a common superscript letter differ significantly at P< 0.05 (DMRT) FrEBet – *Ficus racemosa* ethanolic bark extract.

Groups	Body weight (g)		Liver weight (g)	Kidney weight (g)
	Initial	Final		
Group I – Control	190.51± 17.6[a]	215.6± 17.1[a]	6.38±0.52[a]	1.11±0.06[a]
Group II - Control + FrEBet [300 mg/kg bw]	187.3±19.1[a]	218.7±16.9[a]	6.49±0.49[a]	1.17±0.07[a]
Group III - Diabetic control	193.8±18.1[a]	157.58±17.3[b]	4.71±0.42[b]	1.31±0.15[a]
Group IV - Diabetic + FrEBet [300 mg/kg bw]	190.8±18.6[a]	186.9±18.1[a]	5.51±0.48[a]	1.05±0.05[a]
Group V - Diabetic + glibenclamide [600 µg/kg bw]	188.7±16.9[a]	178.6±16.9[a]	5.28±0.42[a]	1.03±0.08[a]

Table 2: Blood glucose and Plasma Insulin levels in control and experimental animals in each group.

Groups	Fasting blood glucose (mg/dl)	Plasma Insulin (µU/ml)
Group I – Control	91.77 ± 8.52 [a]	14.43 ± 1.15[a]
Group II - Control + FrEBet [300 mg/kg bw]	85.48 ± 7.93 [a]	14.81 ± 1.06 [a]
Group III - Diabetic control	317.70 ± 27.73 [b]	8.47 ± 0.67 [b]
Group IV - Diabetic + FrEBet [300 mg/kg bw]	108.98 ±10.12 [c]	12.92 ± 1.02 [c]
Group V - Diabetic + glibenclamide [600 µg/kg bw]	128.41 ± 8.82 [d]	11.64 ± 0.83 [d]

Values are expressed as mean ± SD (n=6 rats). Values not sharing a common superscript letter differ significantly at P< 0.05 (DMRT) FrEBet – *Ficus racemosa* ethanolic bark extract.

Table 3: Plasma lipid profile in control and experimental animals in each group.

Groups	Cholesterol (mg/dl)	Phospholipids (mg/dl)	Triglycerids (mg/dl)	Freefatty acids (mg/dl)
Group I – Control	99.15 ± 8.43^{a}	86.42 ± 5.53^{a}	87.19 ± 5.58^{a}	7.90 ± 0.67^{a}
Group II - Control + FrEBet [300 mg/kg bw]	97.69 ± 8.88^{a}	83.17 ± 6.48^{a}	85.24 ± 6.64^{a}	7.23 ± 0.55^{a}
Group III - Diabetic control	176.46 ± 11.16^{b}	138.37 ± 11.78^{b}	159.37 ± 10.94^{b}	16.59 ± 1.41^{b}
Group IV - Diabetic + FrEBet [300 mg/kg bw]	124.16 ± 10.08^{c}	91.49 ± 7.96^{ac}	92.38 ± 8.03^{ac}	8.98 ± 0.72^{c}
Group V - Diabetic + glibenclamide [600 μg/kg bw]	140.30 ± 11.26^{d}	105.71 ± 9.25^{d}	105.59 ± 9.24^{d}	10.15 ± 0.61^{d}

Values are expressed as mean ± SD (n=6 rats). Values not sharing a common superscript letter differ significantly at P< 0.05 (DMRT). FrEBet – *Ficus racemosa* ethanolic bark extract.

Table 4: Levels of cholesterol and phospholipids in erythrocyte membrane of control and experimental animals in each group.

Groups	Cholesterol (μg/mg Protein)	Phospholipids (μg/mg Protein)
Group I – Control	143.90 ± 10.72^{a}	317.25 ± 26.98^{a}
Group II - Control + FrEBet [300 mg/kg bw]	141.59 ± 9.53^{a}	322.90 ± 25.16^{a}
Group III - Diabetic control	176.11 ± 12.45^{b}	236.34 ± 20.13^{b}
Group IV - Diabetic + FrEBet [300 mg/kg bw]	148.25 ± 11.42^{ac}	304.09 ± 26.46^{ac}
Group V - Diabetic + glibenclamide [600 μg/kg bw]	160.08 ± 10.41^{d}	271.38 ± 23.75^{d}

Values are expressed as mean ± SD (n=6 rats). Values not sharing a common superscript letter differ significantly at P< 0.05 (DMRT). FrEBet – *Ficus racemosa* ethanolic bark extract.

Table-5: Plasma lipoproteins pattern in control and experimental animals in each group.

Groups	HDL – C (mg/dl)	LDL – C (mg/dl)	VLDL – C (mg/dl)
Group I – Control	44.85 ± 3.25[a]	33.69 ± 3.25[a]	17.65 ± 1.73[a]
Group II - Control + FrEBet [300 mg/kg bw]	46.82 ± 3.28[a]	30.83 ± 2.38[a]	17.28 ± 1.72[a]
Group III - Diabetic control	19.67 ± 1.82[b]	83.44 ± 7.17[b]	31.66 ± 2.16[b]
Group IV - Diabetic + FrEBet [300 mg/kg bw]	37.86 ± 2.41[c]	37.72 ± 3.12[c]	18.28 ± 1.51[ac]
Group V - Diabetic + glibenclamide [600 μg/kg bw]	27.34 ± 2.52[d]	51.24 ± 4.88[d]	22.75 ± 1.77[d]

Values are expressed as mean ± SD (n=6 rats). Values not sharing a common superscript letter differ significantly at P< 0.05 (DMRT),FrEBet – *Ficus racemosa ethanolic* bark extract.

Table – 6: Levels of lipids in liver of control and experimental animals in each group.

Groups	Cholesterol (mg/100 g tissues)	Phospholipids (g/100 g tissues)	Triglycerids (mg/100 g tissues)	Freefatty acids (mg/100 g tissues)
Group I – Control	298.50 ± 22.53[a]	1.28 ± 0.08[a]	342.68 ± 24.59[a]	542.84 ± 38.83[a]
Group II - Control + FrEBet [300 mg/kg bw]	285.83 ± 20.60[a]	1.21 ± 0.08[a]	335.58 ± 21.30[a]	518.33 ± 39.40[a]
Group III - Diabetic control	485.00 ± 32.71[b]	2.75 ± 0.18[b]	478.01 ± 26.66[b]	814.60 ± 63.74[b]
Group IV - Diabetic + FrEBet [300 mg/kg bw]	316.66 ± 30.11[ac]	1.53 ± 0.09[c]	370.35 ± 28.54[ac]	620.44 ± 52.10[c]
Group V - Diabetic + glibenclamide [600 μg/kg bw]	349.16 ± 29.15[d]	1.69 ± 0.13[d]	408.86 ± 29.99[d]	751.54 ± 61.35[d]

Values are expressed as mean ± SD (n=6 rats). Values not sharing a common superscript letter differ significantly at P< 0.05 (DMRT). FrEBet – Ficus *racemosa* ethanolic bark extract

Table – 7: Levels of lipids in kidney of control and experimental animals in each group.

Groups	Cholesterol (mg/100 g tissues)	Phospholipids g/100 g tissues)	Triglycerids (mg/100 g tissues)	Freefatty acids (mg/100 g tissues)
Group I – Control	370.31 ± 33.68^{a}	1.13 ± 0.09^{a}	255.60 ± 21.74^{a}	390.55 ± 27.00^{a}
Group II - Control + FrEBet [300 mg/kg bw]	363.02 ± 28.29^{a}	1.05 ± 0.08^{a}	245.20 ± 19.11^{a}	382.06 ± 33.81^{a}
Group III - Diabetic control	505.17 ± 37.95^{b}	1.94 ± 0.15^{b}	474.38 ± 35.64^{b}	612.96 ± 52.90^{b}
Group IV - Diabetic + FrEBet [300 mg/kg bw]	402.79 ± 29.46^{ac}	1.29 ± 0.10^{c}	305.05 ± 26.54^{c}	410.06 ± 36.34^{ac}
Group V - Diabetic + glibenclamide [600 μg/kg bw]	453.94 ± 39.73^{cd}	1.49 ± 0.09^{d}	380.42 ± 33.30^{d}	452.22 ± 40.77^{d}

Values are expressed as mean ± SD (n=6 rats). Values not sharing a common superscript letter differ significantly at $P < 0.05$ (DMRT). FrEBet – *Ficus racemosa* ethanolic bark extract

Discussion

We found an elevated blood glucose concentration accompanied by increase in total cholesterol, phospholipid, triglycerides, free fatty acids and decrease in HDL cholesterol in alloxan-induced diabetic rats as compared to control animals. Oral administration of FrEBet normalized the levels of blood glucose, plasma insulin, lipids and lipoprotein in alloxan induced diabetic rats. The potent antidiabetic effect of the plant extract suggests the presence of potent antidiabetic active principles, which produced antihyperglycemic effect in diabetic rats. The *F. racemosa* bark not only showed antihyperglycemic effect but also increased the plasma insulin level, which suggests its ability to potentiate insulin secretion from remnant parcreatic β-cells, which could correct other essential metabolic alterations.

In the present study diabetic animals had lowered body and liver weight and increased kidney weight as compared to control rats. The decrease in body weight could be due to excess breakdown of tissue proteins. Increased breakdown of glycogen and pronounced gluconeogenesis in diabetes might be responsible for reduction in liver weight of diabetic animals. Glomerular cell proliferation accompanied with glomerular enlargement caused an increase in kidney weight of alloxan induced diabetic rats. Oral administration of FrEBet to diabetic rats significantly increased their body and liver weight and decreased their kidney weight, which suggests that FrEBet considerably improved the health status and glycemic control mechanism in diabetic rats.

In recent years, considerable interest has been directed towards the investigation of plasma lipids and lipoproteins pattern in diabetes mellitus due to the fact that abnormal lipid level leads to the development of coronary artery disease in diabetic patients (Sarti and Gallagher, 2006). Reduced insulin secretion and defect in insulin function results in enhanced metabolism of lipids from adipose tissue to the plasma. Impairment in insulin sensitivity due to high concentration of lipids in the cells is responsible for the elevated cardiovascular risk in diabetes mellitus (EL-Hazmi and Warsy, 1999; Frayn, 2002). As insulin has a profound role in the regulation of key enzymes involved in the lipid and lipoprotein metabolism, its deficiency causes major changes in the activity of these enzymes and thereby affecting overall lipid metabolism and lipid profile of various tissues (Mironava et al, 2000). Insulin has also profound influence on the synthesis and expression of apolipoproteins in hepatic and extra hepatic tissues (Krishnaswami, 1996). Thus, the altered lipid and lipoprotein pattern observed in diabetic rats could be due to defect in insulin secretion and/or action.

Hypercholesterolemia and hypertriglyceridemia have been reported to occur in alloxan-induced diabetic rats. Accumulation of cholesterol and phospholipids in liver due to elevated plasma free fatty acids has been

reported in diabetic rats (Das, 2003). The higher concentration of plasma total cholesterol observed in diabetic rats is probably due to mobilization of free fatty acids from the peripheral fat depots (Das and Baliarshinaha, 1997). Alterations in the erythrocyte membranes lipid composition may be a reflection of alterations in the plasma lipid profile. HDL removes cholesterol from non-hepatic tissues to liver through the process known as reverse cholesterol transport. Several studies have documented reduction in plasma HDL cholesterol in diabetic rats and diabetic patients due to defect in reverse cholesterol transport (Khan et al, 2003). Our results support these observations.

Liver plays an important role in the catabolism and excretion of cholesterol. Profound increases in plasma and tissue lipids (cholesterol, phospholipids, triglycerides and free fatty acids) were reported in diabetic animals. Triglycerides accumulation in the liver of diabetic rats is due to enhanced synthesis or decreased output from liver as VLDL or combination of both.

Oral administration of FrEBet restored the levels of lipids and lipoproteins in diabetic rats. The hypolipidemic effect of the *F. racemosa* bark extract is due to inhibition of endogenous synthesis of lipids probably by potentiating the secretion of insulin. The hypolipidemic effect of FrEBet may also be due to the presence of several bioactive hypolipidemic principles and their synergistic properties.

Conclusion

We concluded that the oral administration of the ethanolic bark extract of *Ficus racemosa* significantly reduced the blood sugar level (80%) and restored the status of lipids and lipoproteins (60-70%) to near normal range. The present study also warrants further studies to isolate and characterizing potent molecules for diabetes mellitus and its lipids associated complications.

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