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Research Article

Antidiabetic activity of the aqueous extracts of *Foeniculum vulgare* on streptozotocin-induced diabetic rats

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ABSTRACT

Objective: Diabetes mellitus is a clinical syndrome associated with an abnormal high blood glucose concentration due to insufficient insulin secretion or defective in insulin action. The present study was attempted to evaluate the antidiabetic effects of Foeniculum vulgare in streptozotocin-induced diabetic rats. Methods: The effects of daily oral administration of an aqueous extract of Foeniculum vulgare (150 mg, 300 mg/kg) for 35 days on blood glucose, hemoglobin (Hb), HbA1c, liver glycogen and some carbohydrate metabolic enzymes were evaluated in normal and streptozotocin-induced diabetic rats. Various biochemical parameters such as hexokinase activity, succinate dehydrogenase, serum and tissue proteins, urea, creatinine were also determined as per the standard protocol available from the literature. Results: Administration of the aqueous extract of Foeniculum vulgare to diabetic rats corrected the hyperglycaemia from 339.3±0.48 mg/dl to $101.4\pm$ 0.34 mg/dl and the levels of HbA1c from 11.09 \pm 0.56 mg/dl to 6.26 \pm 0.2 mg/dl. Further the extract decreased total cholesterol, triglycerides, LDL, VLDL levels and increased HDL levels. Oral administration of 300 mg/kg extract modulated all the parameters evaluated to levels seen in control rats. Also, improved the pathological changes noticed in their kidney and liver. Conclusion: The present investigation suggested that the treatment with Foeniculum vulgare exhibited antidiabetic activity in streptozotocin-induced diabetes in male albino rats and could be considered for further evaluation in drug development.

Key words: Foeniculum vulgare, antidiabetic activity, aqueous extract, Streptozotocin-induced diabetic rats.

1. INTRODUCTION

In folk medicinal practice many plants are used to treat diabetes mellitus in south India. Most of these medicinal plants are scientifically validated for their therapeutic efficacy and safety. In modern medicine no satisfactory and effective therapy is available to cure diabetes mellitus, which is a syndrome resulting from a variable interaction of hereditary and environmental factors and characterized by abnormal insulin secretion or insulin receptor or post receptor events affecting metabolism involving carbohydrates, proteins, and fats in addition to damaging β -cells of pancreas, liver and kidney in some cases¹. Diabetes mellitus is a clinical syndrome associated with an abnormal high blood glucose concentration due to insufficient insulin secretion or defective in insulin action. Approximately more than 150 million people were reported to have diabetes mellitus worldwide².

Fennel is one of the important spices that cure many diseases. Fennel (Foeniculum vulgare) is a plant species in the genus Foeniculum. It is highly aromatic and flavorful herb with culinary and medicinal uses, and is one of the primary ingredients of absinthe. It is a hardy, perennial, umbelliferous herb, with yellow flowers and feathery leaves, grow wild in most part of Europe, but are generally considered indigenous to the shores of the Mediterranean (botanical.com). Fennel contains and 90% trans anethole, up to 20% fenchone and also contain small amounts of limonene, camphor, alphapinene and about six additional minor volatile compounds³. The ethanolic extract of dried ripe fruit of Foeniculum vulgare (500 mg/kg) was tested for diuretic, analgesic, antipyretic, antimicrobial, cytotoxic activities and its effect on bile secretion in rats⁴.

Multi herbal formulations containing aqueous extract of fennel were analyzed for glucose content by using glucose oxidase peroxidase (GOD-POD) method using a visible spectrophotometer at 505 nm⁵. The essential oils obtained from Crithmum maritimum L. (marine fennel) and two samples of Foeniculum vulgare M. (common fennel) were analyzed by GC-MS and assayed for their antioxidant and antibacterial activities⁶. The *in vitro* antioxidant activity of natural (essential oils, vitamin E) or synthetic substances (tert-butyl hydroxy anisole (BHA), trolox) has been evaluated by monitoring volatile carbonyl compounds released in model lipid systems subjected to peroxidation⁷. Hepatoprotective activity of fennel essential oil (FEO) was studied using carbon tetrachloride (CCl₄) induced liver injury model in rats⁸. Essential oil obtained from *F. vulgare*, and its main component anethole reported as a safe antithrombotic may be due to their broad spectrum antiplatelet activity, clot destabilizing effect and vasorelaxant activity⁹. The present study was aimed to evaluate the antidiabetic effects of F. vulgare in diabetic rats.

2. MATERIALS AND METHODS

2.1. Plant material

Seed materials were collected from local super market in Erode, Tamilnadu, India and kept it under shade for drying and crushed into a powder form using a blender. The powdered material was used for phytochemical analysis. *Foeniculum vulgare* were further dried over a polythene cover under shade drying method with the help of fan at room temperature (21°C) and pulverized using a mixer grinder. The coarse powder of the seed was used for the preparation of various extracts.

2.2 Chemicals

Streptozotocin was obtained from Sigma (St Louis, MO, USA). All other chemicals and reagents used were of analytical grade (Ranchem, Mumbai, India).

2.3. Experimental Animals

Adult male rats of swiss albino strain were procured from Salem, Tamilnadu, India. They were acclimatized to laboratory condition for one week in the animal housing facility owned by the Research & PG Department of Biochemistry of Muthayammal College of Arts & Science, Tamilnadu, India. Rats were housed in polypropylene cages (47x34x20 cm) lined with husk (renewed every 24 h) under a 12 h light-dark cycle at approximately 22 °C. Rats had free access to tap water and food (standard pellet diet; Pranav Agro Industries, Maharashtra, India). The pellet diet consisted of 23% protein, 5% lipids, 4% crude fiber, 8% ash, 1% calcium, 0.6% phosphorus, 3.4% and 55% nitrogen-free glucose, extract (carbohydrates). Experiments were performed according to the guidelines of the Committee for the Purpose of Control and Supervision of Experiment on Animals (CPCSEA). New Delhi. India, and were approved by the Animal Ethics Committee of Muthayammal College of Arts & Science, Tamilnadu, India.

2.4. Preparation of plant extract

The powdered materials are subjected for extraction using various solvents such as like ether, benzene, diethyl ether. petroleum chloroform, ethyl acetate, acetone, methanol, ethanol, butanol, water. The method involves soaking 30 gm dried powder of Foeniculum vulgare in 100 ml of selected solvent in a separating funnel for 24 h with intermittent shaking. The seed extracts were then collected and filtered through Whatmann No. 1 filter paper separately. From the filtrates, solvents were dried by heating on water bath. The dried powders of the seed extracts were stored at 40 °C in air tight bottle. These extracts were used for phytochemical analysis and aqueous extract was used for animal studies.

2.5. Phytochemical analysis

The extracts obtained as above were then subjected to qualitative chemical tests for the identification of various phytoconstituents present in the plant material. The tests include detecting alkaloids, flavanoids, tannins - phenolic compounds, saponins, steroids, thiols and resins. The test procedures are followed as per the standard protocol adopted from various literature reports. The test results indicated the presence of active constituents in maximum proportion as reported earlier.

2.6. Experimental set up

The rats were weighed and divided into five experimental groups each of five rats as follows: (i) Group I, normal rats treated with saline; (ii) Group II, normal rats treated with 300 mg/kg of plant extract which serve as positive control; Group III, diabetic rats by an intra peritonial (ip) injection of single dose of streptozotocin (40 mg/kg body wt); Group IV, treated with the aqueous extract of F. vulgare at a dose of 150 mg/kg body wt; Group V, the same extract in different concentration (300 mg/kg body wt) was given. After 35 days of treatment, all rats were decapitated after an overnight fast. Blood was collected from the animals by retro-orbital bleeding at the end of the study period into heparinised tubes (plasma) and non-heparinized tubes (sera) for the determination of biochemical parameters. Tissues (liver and kidney) were also collected in ice-cold normal saline for the analysis of various biochemical parameters.

2.7. Preparation of tissue homogenate

Tissue samples from animals were rinsed thoroughly in cold physiological saline and blotted dry on filter paper. Tissues were then weighed and homogenized using a glass homogenizer with a Teflon pestle in 5 mL buffer solution (0.1 M Tris-HCl buffer, pH 7.4). The homogenate was centrifuged at 2500 rpm for 5 min. The supernatant was used for the estimation of various biochemical parameters.

2.8. Biochemical analysis

After 35 days, rats were killed by mild ether anesthesia and tissues were collected for the subsequent biochemical analysis. Blood samples were collected by cardiac puncture and were separated to obtain blood constituents. After autopsy under mild ether anesthesia, serum was separated and analyzed¹⁰⁻³⁰. Various biochemical parameters evaluated in the present study was shown in Table-1.

2.9. Statistical analysis:

Statistical analyses were performed using one-way analysis of variance (ANOVA) in the SPSS software package (version 17.0; SPSS, Chicago, IL, USA). The results were expressed in mean \pm SE for each parameter under for different groups was tested using student's t- test at 1% level and 5% levels. The result is significant at 1% level if P<0.001 and significant at 5% level if P<0.05. Results obtained at the end of the experiments were compared with those of the control and diabetic groups and differences were considered significant at P < 0.001.

3. RESULTS

The results of phytochemical analysis of the extracts were presented in Table-2 and scavenging activity of extract of *Foeniculum vulgare* was expressed in Table-3. Various biochemical parameters were evaluated and the results are presented in Tables 4-12. The aqueous extract of *F. vulgare* has showed hypoglycaemic activity in streptozotocin-induced diabetic rats. Administration of the extract to diabetic rats corrected the hyperglycaemia from 339.3 ± 0.48 mg/dl to $101.4\pm$ 0.34 mg/dl and the levels of HbA1C from 11.09 ± 0.56 mg/dl to 6.26 ± 0.2 mg/dl.

4. **DISCUSSION**

The present investigation was taken up to assess the antidiabetic effect of aqueous extract of *Foeniculum vulgare* against Streptozotocin induced diabetes in male albino rats. Phytochemical investigation revealed that there was high concentration of phytochemical constituents present in aqueous seed extract of *Foeniculum vulgare*. Present investigation showed that the presence of free radical scavenging activity in various seed extract of *Foeniculum vulgare*.

The level of serum glucose was significantly increased in Streptozotocin-induced diabetic rats, while the pretreatment of aqueous extract of *Foeniculum vulgare* leads to decrease in their levels. The level of liver glycogen was significantly increased in streptozotocin-induced diabetic rats, while the pretreatment of aqueous extract of *Foeniculum vulgare* leads to decrease in their levels. The level of insulin was significantly decreased in diabetic rats, while the pretreatment of aqueous extract of aqueous extract of *Foeniculum vulgare* leads to decrease in their levels. The level of insulin was significantly decreased in diabetic rats, while the pretreatment of aqueous extract of *Foeniculum vulgare* leads to the recovery of the normal levels.

Streptozotocin induced diabetic rats showed a significant increase in the level of glycosylated hemoglobin while the pretreatment of *Foeniculum vulgare* showed decrease in the glycosylated hemoglobin level. Streptozotocin-induced diabetic rats showed a significant decrease in the level of hexokinase, in liver and kidney, while the pretreatment of *Foeniculum vulgare* showed a significant increase in the hexokinase level. Streptozotocin-induced diabetic rats showed a significant decrease in the hexokinase level. Streptozotocin-induced diabetic rats showed a significant decrease in the level of serum and tissue protein, while the pretreatment of *Foeniculum vulgare* showed a significant increase in the protein levels.

Streptozotocin induced diabetic rats showed a significant increase in the level of urea and creatinine, while the pretreatment of *Foeniculum vulgare* showed a significant decrease in the urea and creatinine levels. Streptozotocin induced diabetic rats showed a significant decrease in the level of succinate dehydrogenase, while the pretreatment of *Foeniculum vulgare* showed a

significant increase in the succinate dehydrogenase level.

In the present study, streptozotocin induced diabetic rats showed a significant increase in the liver, kidney and serum marker enzymes such as ALP, ACP, ALT, AST and LDH while the pretreatment of aqueous extract of Foeniculum vulgare showed a significant decrease in the marker enzymes which shows that the extract possess protective action against tissue damage. From the present investigation, streptozotocininduced diabetic rats shows the serum lipid profile such as total cholesterol, triglycerides, LDL, VLDL levels, were significantly increased with a desirable feature of decreasing the HDL levels. Pretreatment of aqueous extract of Foeniculum vulgare leads to the recovery of the normal levels. This feature moderately shows the hypolipidemic effects.

Enzymatic antioxidants such as Catalase, SOD and GPX, were decreased significantly and the nonenzymatic antioxidant such as Vitamin C were also significantly decreased in streptozotocin-induced diabetic rats, while the oral pretreatment of aqueous extract of *Foeniculum vulgare* leads to significant increase in the enzymatic and non enzymatic antioxidants. In conclusion, our observation suggested that the treatment with *Foeniculum vulgare* exhibited antidiabetic activity in streptozotocin-induced diabetes in male albino rats. Further work need to be done to isolate and purify the active constituents present in the seed extract of *Foeniculum vulgare*, which is responsible for its antidiabetic activity.

Conflict of interest statement

We declare that we have no conflict of interest.

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 Table-1.

 Various biochemical parameters determined for the aqueous extract of *Foeniculum vulgare*

S. No.	Biochemical parameter	Reference
1	Serum glucose (GOD/POD method)	[10]
2	Liver glycogen	[11]
3	Plasma insulin (Ubi-Magiwel kit)	[12]
4	Glycosylated haemoglobin (monozyme Hemoglobin A ₁ C Chromatographic-Spectrophotometric method)	[13]
5	Hexokinase (rate of disappearance of glucose at 37 °C was measured)	[14]
6	Succinate dehydrogenase	[15]
7	Protein content	[16]
8	Urea	[17]
9	Creatinine	[18]
10	Acid phosphatise	[19]
11	Alkaline phosphatise	[19]
12	Aspartate transaminases	[20]
13	Alanine transaminases	[20]
14	Lactate dehydrogenase	[19]
15	Cholesterol (colourimetry method)	[21]
16	High density liprotein (HDL)	[22]
17	Triglycerides	[23]
18	Superoxide dismutase	[24]
19	Catalase	[25]
20	Glutathione peroxidase	[26]
21	Ascorbic acid	[27]
22	Scavenging of nitric oxide radical	[28]
23	Scavenging of hydroxy radical	[29]
24	Scavenging of superoxide anion	[30]

Table-2.									
P	hytochemi	ical constitue	ents prese	ent in vario	ous extr	act of <i>Foe</i>	eniculum	vulgare	
Phytoconstituent	Pet. ether	Chloroform	Acetone	Methanol	Water	Benzene	Ethanol	Butanol	Ethyl Acetate
Alkaloids	-	+	-	-	+	-	+	+	-
Flavanoids	-	-	-	+	-	+	+	-	-
Steroids	+	+	-	-	-	+	+	+	-
CardiacGlycosides	-	-	++	-	-	-	+	+	+
Saponins	+	-	+	+	+	+	-	-	-
Tannins	+	+	+	+	+	+	+	+	+
Phenols	-	+	+	+	+	-	+	+	+
Thiols	-	-	-	-	-	-	+	-	-
Resins	+	-	-	-	-	-	-	-	-
Glycosides	-	-	-	+	+	+	+	+	-
Triterpenoids	-	-	-	-	-	+	+	+	-

Table-2.

(++) – Dark colors; (+) - Presence; (-) - Absence

Table-3.

Scavenging activity of various extract of Foeniculum vulgare

S. No.	Scavenging activity	Petroleum ether extract	Chloroform extract	Methanol extract
1	Nitric oxide	+	+	+
2	Hydroxy radical	+	+	+
3	Superoxide anion	+	+	+

(+) – Presence; (-) – Absence

Table-4.
Effect of aqueous seed extract of <i>Foeniculum vulgare</i> pretreated on
serum glucose, liver glycogen, serum insulin and HbA1c levels in control & experimental rats

S. No.	GROUPS	GLUCOSE	GLYCOGEN mg/g	INSULIN	HbA1C mg/dl
		mg/dl	tissue	μU/ml	
1	Group I (Normal control)	75.5 <u>+</u> 0.15	53.5 <u>+</u> 0.13	11.3 <u>+</u> 0.19	4.65 <u>+</u> 0.17
2	Group II (positive control)	70.6 ± 0.08^{NS}	50.6 ± 0.31^{NS}	11.6 ± 0.09^{NS}	4.10 ± 0.19^{NS}
3	Group III (Diabetic control)	339.3 <u>+</u> 0.48*	23.3 <u>+</u> 0.6**	14.9 <u>+</u> 0.52**	11.09 <u>+</u> 0.56**
4	GroupIV (Diabetic+Extract) (150mg/kgbw)	110.4 <u>+</u> 0.64**	39.1 <u>+</u> 0.44**	17.7 <u>+</u> 0.23**	7.57 <u>+</u> 0.22**
5	GroupV (Diabetic+Extract) (300mg/kgbw)	101.4 <u>+</u> 0.34**	42.2 <u>+</u> 1.25**	18.5 <u>+</u> 0.28**	6.26 <u>+</u> 0.2**

Statistical significance: * - P<0.05; ** - P<0.001; NS - Not significant Values are expressed by mean \pm SE (n = 5 rats in each group).

Table-5. Effect of aqueous seed extract of Foeniculum vulgare pretreated on liver and kidney hexokinase and succinate dehydrogenase activities in control and experimental rats.

S. No.	GROUPS	HEXOKINASE		SUCCINATE DHase		
		LIVER ^a	KIDNEY ^a	LIVER ^b	KIDNEY ^b	
1	Group I (Normal control)	266.6 <u>+</u> 0.4	171.6 <u>+</u> 0.24	1.22 <u>+</u> 0.39	1.38 <u>+</u> 0.27	
2	Group II (positive control)	265.6 ± 0.23^{NS}	169.6 <u>+</u> 0.21 ^{NS}	1.05 ± 0.06^{NS}	1.09 ± 0.05^{NS}	
3	Group III (Diabetic control)	131.5 <u>+</u> 0.66**	120.4 <u>+</u> 0.40**	0.68 <u>+</u> 0.13**	0.74 <u>+</u> 0.04*	
4	GroupIV (Diabetic+ Extract) (150mg/kg BW)	216.2 <u>+</u> 0.54**	156.6 <u>+</u> 0.38**	0.85 <u>+</u> 0.03**	0.88 <u>+</u> 0.01**	
5	Group V (Diabetic+ Extract) (300mg/kg BW)	204.5 <u>+</u> 0.26**	160.8 <u>+</u> 0.40**	0.94 <u>+</u> 0.01**	0.96 <u>+</u> 0.02**	

a. n moles of glu-6-phosphate formed/hr/mg protein; b- n moles of SDHase liberated/litre Statistical significance: * - P<0.05; ** - P<0.001; NS - Not significant

Values are expressed by mean \pm SE (n = 5 rats in each group).

		Table-	J •							
	Effect of aqueous seed extract of <i>Foeniculum vulgare</i> pretreated on									
protein 1	levels (serum, liver and kid	lney) and urea	and creatinin	e levels in con	trol and exp	erimental rats.				
S.No.	GROUPS	SERUM g/dl	LIVER mg/g tissue	KIDNEY mg/g tissue	UREA mg/dl	CREATININE mg/dl				
1	Group I (Normal control)	7.09 <u>+</u> 0.06	243.2 <u>+</u> 3.07	216.1 <u>+</u> 0.16	15.2 <u>+</u> 0.12	0.66 <u>+</u> 0.44				
2	Group II (positive control)	6.81 ± 0.11^{NS}	247.7 ± 0.39^{NS}	216.3 ± 0.19^{NS}	14 4 +0 37 ^{NS}	0.63 ± 0.05^{NS}				

Table_6

2	Group II (positive control)	6.81 ± 0.11^{NS}	247.7 <u>+</u> 0.39 ^{NS}	216.3 <u>+</u> 0.19 ^{NS}	14.4 <u>+</u> 0.37 ^{NS}	0.63 ± 0.05^{NS}
3	Group III (Diabetic control)	3.28 <u>+</u> 0.12**	131.8 <u>+</u> 0.41*	139.9 <u>+</u> 0.67*	49.4 <u>+</u> 0.27**	0.95 <u>+</u> 0.03**
4	GroupIV (Diabetic+Extract) (150mg/kgBW)	5.26 <u>+</u> 0.10**	201.4 <u>+</u> 0.18**	179.3 <u>+</u> 0.18*	28.3 <u>+</u> 0.08 *	0.74 <u>+</u> 0.02**
5	GroupV (Diabetic+Extract) (300mg/kg BW)	6.24 <u>+</u> 0.01**	219.5 <u>+</u> 0.27**	201.2 <u>+</u> 0.02*	30.5 <u>+</u> 0.04*	0.70 <u>+</u> 0.56**

Statistical significance: * - P<0.05; ** - P<0.001; NS - Not significant

Values are expressed by mean \pm SE (n = 5 rats in each group).

Table-7. Effect of aqueous seed extract of Foeniculum vulgare pretreated on serum marker enzymes (AST, ACP, ALT, ALP and LDH) in control & experimental rats.

S. No.	GROUPS	Serum Marker Enzymes					
		ALT ^a	AST ^a	ACP ^b	ALP ^b	LDH ^a	
1	Group I (Normal control)	41.2 <u>+</u> 0.6	49.1 <u>+</u> 0.77	17.9 <u>+</u> 0.40	36.5 <u>+</u> 0.23	122.6 <u>+</u> 0.65	
•		40.4 0.40NS	514 045 NS	10.4 0.40 NS	20.0 0.27 NS	1057 0 70 NS	

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	2	Group II (positive control)	$43.4 \pm 0.49^{\text{NS}}$	51.4 ± 0.46^{NS}	$19.4 \pm 0.49^{\text{NS}}$	38.8 ± 0.37^{NS}	125.7 ± 0.79^{NS}
Γ	3	Group III (Diabetic control)	114.5 <u>+</u> 0.87*	68.3 <u>+</u> 0.87*	41.4 <u>+</u> 0.5**	63.1 <u>+</u> 0.16**	246.9 <u>+</u> 0.86**
	4	GroupIV (Diabetic+Extract)(150mg/kgbw)	69.1 <u>+</u> 0.64*	58.6 <u>+</u> 0.79**	30.5 <u>+</u> 0.48**	52.3 <u>+</u> 0.69*	181.1 <u>+</u> 0.50**
	5	GroupV (Diabetic+Extract) (300mg/kgbw)	61.4 <u>+</u> 0.58*	55.8 <u>+</u> 0.74**	27.3 <u>+</u> 0.40**	49.5 <u>+</u> 0.86*	175.8 <u>+</u> 1.22**
	0 11 1000	les of avanuate liberated/litre buy moles of ab	an al lib anatad/lite	a			

a- μ moles of pyruvate liberated/litre, b- μ moles of phenol liberated/litre Statistical significance: * - P<0.05; ** - P<0.001; NS - Not significant

Values are expressed by mean \pm SE (n = 5 rats in each group).

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Table-8.

Effect of aqueous seed extract of Foeniculum vulgare pretreated on

liver marker enzymes (AST, ACP, ALT, ALP, LDH) in control & experimental rats

S.No.	GROUPS	Liver Marker Enzymes				
		ALT ^a	AST ^a	ACP ^b	ALP ^b	LDH ^a
1	Group I (Normal control)	192.5 <u>+</u> 0.34	30.5 <u>+</u> 0.38	24.4 <u>+</u> 0.24	24.4 ± 0.26	16.2 <u>+</u> 0.29
2	Group II (positive control)	196.5 ± 0.33^{NS}	32.2 ± 0.67^{NS}	24.5 ± 0.37^{NS}	25.6 ± 0.39^{NS}	$17.3 \pm 0.31^{\text{NS}}$
3	Group III (Diabetic control)	466 <u>+</u> 0.40*	185.9 <u>+</u> 0.97*	87.1 <u>+</u> 0.18**	72.7 <u>+</u> 0.14**	63.5 <u>+</u> 0.07**
4	GroupIV (Diabetic+Extract) (150mg/kgbw)	312.5 <u>+</u> 0.35*	86.1 <u>+</u> 0.59**	39.5 <u>+</u> 0.42**	42.6 <u>+</u> 0.31**	17.6 <u>+</u> 0.38**
5	Group V (Diabetic+Extract)	295.9 + 0.65*	83.8 + 0.19**	35.2 + 0.11**	40.8+ 0.36**	15.2 + 0.39**
5	(300mg/kgbw)	255.5 1 0.05	05.0 - 0.17	<u>55.2 -</u> 0.11	10.0 1 0.50	10.2 - 0.57

a- μ moles of pyruvate liberated/litre, b- μ moles of phenol liberated/litre Statistical significance: * - P<0.05; ** - P<0.001; NS - Not significant

Values are expressed by mean \pm SE (n = 5 rats in each group).

Table-9. Effect of aqueous seed extract of Foeniculum vulgare pretreated on kidney marker enzymes (AST, ACP, ALT, ALP, LDH) in control & experimental rats

S. No.	GROUPS	Kidney Marker Enzymes					
		ALT ^a	AST ^a	ACP ^b	ALP ^b	LDH ^a	
1	Group I (Normal control)	18.7 <u>+</u> 0.37	56.3 <u>+</u> 0.22	24.4 <u>+</u> 0.24	83.6 <u>+</u> 0.42	12.5 <u>+</u> 0.5	
2	Group II (positive control)	19.2 <u>+</u> 0.18 ^{NS}	64.3 <u>+</u> 0.23 ^{NS}	24.5 ± 0.27 ^{NS}	81.4 <u>+</u> 0.78 ^{NS}	42.9 <u>+</u> 0.03 ^{NS}	
3	Group III (Diabetic control)	55.8 <u>+</u> 0.14*	206.5 <u>+</u> 0.09**	57.2 <u>+</u> 0.62*	97.5 <u>+</u> 0.42**	13.7 <u>+</u> 0.19**	
4	GroupIV (Diabetic+Extract) (150mg/kgbw)	38.5 <u>+</u> 0.11**	121.6 <u>+</u> 0.34*	39.6 <u>+</u> 0.3**	89.2 <u>+</u> 0.18**	24.3 <u>+</u> 0.35**	
5	GroupV (Diabetic+Extract) (300mg/kgbw)	35.4 <u>+</u> 0.24**	177.8 <u>+</u> 0.22**	35.6 <u>+</u> 0.37**	87.2 <u>+</u> 0.14**	21.3 <u>+</u> 0.12**	

a- µ moles of pyruvate liberated/litre, b- µ moles of phenol liberated/litre

Statistical significance: * - P<0.05; ** - P<0.001; NS - Not significant

Values are expressed by mean \pm SE (n = 5 rats in each group).

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lipid profile in control & experimental rats						
S.No.	GROUPS	TC mg/dl	TG mg/dl	LDL mg/dl	VLDL mg/dl	HDL mg/dl
1	Group I (Normal control)	105.9 <u>+</u> 0.13	64.2 <u>+</u> 0.08	21.5 <u>+</u> 0.23	21.3 <u>+</u> 0.65	26.1 <u>+</u> 0.82
2	Group II (positive control)	102.5 ± 0.14^{NS}	66.5 ± 0.07^{NS}	22.6 ± 0.06^{NS}	20.3 ± 0.19^{NS}	26.4 ± 0.26^{NS}
3	Group III (Diabetic control)	184.3 <u>+</u> 0.25**	196.6 <u>+</u> 0.14**	136.4 <u>+</u> 0.25**	34.7 <u>+</u> 0.19**	13.5 <u>+</u> 0.04*
4	Group IV (Diabetic+Extract) (150mg/kgbw)	187.6 <u>+</u> 0.37**	126 <u>+</u> 0.10**	78.7 <u>+</u> 0.4**	30.6 <u>+</u> 0.18**	18.7 <u>+</u> 0.15**
5	Group V (Diabetic+Extract) (300mg/kghw)	180.8 <u>+</u> 0.18**	121.9 <u>+</u> 0.97*	76.4 <u>+</u> 0.52**	27.3 <u>+</u> 0.87**	16.9 <u>+</u> 0.01*

 Table-10.

 Effect of aqueous seed extract of *Foeniculum vulgare* pretreated on linid profile in control & experimental rats

Statistical significance: * - P<0.05; ** - P<0.001; NS - Not significant

Values are expressed by mean \pm SE (n = 5 rats in each group).

Table-11.
Effect of aqueous seed extract of <i>Foeniculumvulgare</i> pretreated on
zymatic antioxidants (liver and kidney) in control and experimental rats.

S.No.	GROUPS	Enzymatic antioxidant in liver		Enzymatic antioxidant in Kidney			
		SOD ^a	CATALASE ^b	GPX ^c	SOD ^a	CATALASE ^b	GPX ^c
1	Group I (Normal control)	13.7 <u>+</u> 0.09	34.4 <u>+</u> 0.18	5.67 <u>+</u> 0.01	7.25 <u>+</u> 0.09	29.4 <u>+</u> 0.1	4.57 <u>+</u> 0.03
2	Group II (positive control)	13.4 ± 0.10^{NS}	34.3 <u>+</u> 0.08 ^{NS}	5.37 ± 0.2^{NS}	$8.42 \pm 0.03^{\text{NS}}$	28.5 ± 0.18^{NS}	4.59 ± 0.07 ^{NS}
3	Group III (Diabetic control)	7.7 <u>+</u> 0.06**	20.6 <u>+</u> 0.18**	3.46 <u>+</u> 0.3**	5.52 <u>+</u> 0.16**	22.5 <u>+</u> 0.2**	2.57 <u>+</u> 0.02**
4	GroupIV (Diabetic+Extract) (150mg/kgBW)	11.7 <u>+</u> 0.05**	30.6 <u>+</u> 0.17**	4.14 <u>+</u> 0.06*	7.37 <u>+</u> 0.09*	25.6 <u>+</u> 0.07**	3.63 <u>+</u> 0.03**
5	GroupV (Diabetic+Extract) (300mg/kgBW)	9.5 <u>+</u> 0.15**	32.1 <u>+</u> 0.04**	3.30 <u>+</u> 0.19*	6.5 <u>+</u> 0.16*	27.5 <u>+</u> 0.04**	4.04 <u>+</u> 0.10**

a. 50% inhibition of nitrite/min/mg protein; b. n moles of H₂O₂ decomposed/min/mg protein;

 $c{\textbf{.}}\,\mu$ moles of GSH/min/mg protein

Statistical significance: * - P<0.05; ** - P<0.001; NS - Not significant

Values are expressed by mean \pm SE (n = 5 rats in each group).

Table-12.

Effect of aqueous seed extract of *Foeniculum vulgare* pretreated on liver and kidney Non enzymatic anti oxidants in control and experimental rats

S.No.	GROUPS	Vitamin - C	
		LIVER µg/mg protein	KIDNEY µg/mg protein
1	Group I (Normal control)	3.36 <u>+</u> 0.20	2.68 <u>+</u> 0.31
2	Group II (positive control)	3.35 ± 0.12^{NS}	2.62 <u>+</u> 0.31 ^{NS}
3	Group III (Diabetic control)	2.53 <u>+</u> 0.14**	1.59 <u>+</u> 0.2**
4	GroupIV (Diabetic+ Extract) (150mg/kg BW)	3.52 <u>+</u> 0.26**	2.51 <u>+</u> 0.24**
5	Group V (Diabetic+ Extract) (300mg/kg BW)	2.89 <u>+</u> 0.31**	1.96 <u>+</u> 0.14**

Statistical significance: * - P<0.05; ** - P<0.001; NS - Not significant

Values are expressed by mean \pm SE (n = 5 rats in each group).

REFERENCES

- 1. Ghosh R, Sharatchandra Kh, Rita S, Thokchom IS. Hypoglycemic activity of Ficus hispida (bark) in normal and diabetic albino rats. Indian J Pharmacol. 2004; 4: 222-225.
- Ramachandran A, Snehalatha C. Current scenario of diabetes in India. J Diabetes 2009; 1: 18-28.
- 3. Diaaz-Maroto MC, Pearez-Coello MS, Esteban J, Sanz J. Comparison of the volatile

composition of wild fennel samples (Foeniculum vulgare Mill.) from central Spain. J Agric Food Chem. 2006; 54: 6814-6818.

4. Tanira MOM, Shah AH, Mohsin A, Ageel AM, Qureshi S. Pharamacological and toxicological investigations on Foeniculum vulgare dried fruit extract in experimental animals. Phytother. Res. 1996; 10: 33-36.

- Sushruta K, Satyanarayana S, Srinivas N, Raja Sekhar J. Evaluation of blood-glucose reducing effects of aqueous extract of the selected umbelliferous fruits used in culinary practices. Trop J Pharm. Res. 2006; 5: 613-617.
- Ruberto G, Baratta, MT, Deans SG, Dorman HJ. Antioxidant and antimicrobial activity of Foeniculum vulgare and Crithmum maritimum essential oils. Planta Med. 2000; 66: 687- 693.
- Stashenko EE, Puertas MA, Martinz JR. SPME determination of volatile aldehydes for evaluation of in-vitro antioxidant activity. Anal Bioanal Chem. 2002; 373: 70-74.
- 8. Ozbek H, Ugras S, Dulger H, Bayram I, Tuncer I, Ozturk G. Hepatoprotective effect of Foeniculum vulgare essential oil. Fitoterapia 2003; 74: 317-319.
- 9. Tognolini M, Ballabeni V, Bertoni S, Bruni R, Impicciatore M, Barocelli E. Protective effect of Foeniculum vulgare essential oil and anthole in an experimental model of thrombosis. Pharmacol Res. 2007; 56: 254-260.
- 10. Trinder P. Determination of glucose in blood using glucose oxidase with an alternative oxygen receptor. Ann Clin Biochem. 1969; 6: 24-27.
- Wieland OH. Methods of enzymatic analysis (Bergmeyer, H. U. edition). 3rd Edition, 1984; 6: 504-510, Verlag Chemie, Weinheim, Deerfield Beach/Florida, Basel.
- Bennion LJ, Grundy SM. Risk factors for the development of cholelithiasis in man. N Engl J Med. 1978; 299: 1161-1167.
- 13. Bannon P. The effect of pH on the elimination of labile fraction of glycosylated haemoglobin. Clin Chem. 1982; 28: 2183.
- 14. Branstrup N, Kirk JE, Bruni C. The hexokinase and phosphoglucoisomerase activities and aortic and pulmonary artery tissue in individuals of various ages. J Gerontol. 1957; 12: 166-171.
- 15. Monroy GC, Pullman ME. Preparation and properties of a naturally occurring inhibitor of mitochondrial ATPase. Methods Enzymol. 1967; 10: 510-515.
- 16. Lowry OH, Rosebrogh NJ, Farr AL, Randall RJ. Protein measurement with the Folin phenol reagent. J Biol Chem. 1951; 193: 265-275.
- 17. Natelson S, Scott ML, Beffa C. A rapid method for the estimation of urea in biological fluids by means of the reaction between diacetyl and urea. Am J Clin Pathol. 1951; 21: 275-281.

- Anderson DR, Williams CM, Krise GM, Dowben RM. Determination of creatinine in biological fluids. Biochem J. 1957; 67: 258-262.
- King J. The dehydrogenase or oxidoreductase-lactate dehydrogenase. In: Van D, editor. Practical clinical enzymology. London: Nostrand Company Limited; 1965; 83-93.
- 20. Reitman S, Frankel S. Colorimetric method for the determination of serum glutamic oxalo acetic, glutamic pyurvic transaminases. Am J Clin Pathol. 1957; 28: 56-63.
- Ireland JT. The colorimetric estimation of total cholesterol in whole blood, serum, plasma, and other biological material. Biochem. 1941; 35: 283-293.
- 22. Demacker PN, Hijmans AG, Vos-Janssen HE, van't Laar A, Jansen AP. A study of the use of polyethylene glycol in estimating cholesterol in high-density lipoprotein. Clin. Chem. 1980; 26: 1775-1779.
- 23. Sullivan DR, Kruijswijk Z, West CE, Kohlmeier M, Katan MB. Determination of serum triglycerides by an accurate enzymatic method not affected by free glycerol. Clin Chem. 1985; 31: 1227-1228.
- Kakkar P, Das B, Viswanathan PN. A modified spectophotometric assay of superoxide dismutase. Indian J Biochem Biophys. 1984; 21: 130-132.
- 25. Sinha AK. Calorimetric assay of catalase. Anal Biochem. 1972; 47: 389-394.
- 26. Rotruck JT, Pope AI, Ganther HE, Swanson AB, Hafeman DG, Hoekstra WG. Selenium: Biochemical as a role as a component of Glutathione peroxidase. Science 1973; 179: 588-590.
- 27. Omaye ST, Turnbull JD, Sauberlich HE. Selected methods for the determination of ascorbic acid in animal cells, tissues, and fluids. Methods Enzymol. 1979; 62: 3-11.
- 28. Senthilkumar R, Parimelazhagan T, Chaurasia OM, Srivastava RB. Free radical scavenging property and antiproliferative activity of Rhodiola imbricata Edgew extracts in HT-29 human colon cancer cells. Asian Pac J Trop Med. 2013; 11-19.
- 29. Vijayakumar M, Selvi V, Krishnakumari S, Priya K, Noorlidah A. Free radical scavenging potential of Lagenaria siceraria (Molina) Standl fruits extract. Asian Pac J Trop Med. 2012; 20-26.
- Moorthi S, Krishnakumari S, Thomas RA. Hypericum mysorense: A potential antioxidant and antidepressant folk medicinal plant of Nilgiris Biosphere-Western Ghats. Res J Biotech. 2010; 5: 68-73.