ORIGINAL ARTICLE

The Effect of Foeniculum VULgare (Fennel) Extract on Lipid Profile, Lipid Peroxidation and Liver Enzymes of Diabetic Rat

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Abstract

Objective: Diabetes Mellitus (DM) is one of the leading causes of death, illness, and economic loss in the world. The present study was attempted to evaluate extract of Foeniculum vulgare (fennel) on lipid profile, lipid peroxidation and activities of amino transferase enzymes in streptozocin induced diabetic adult male rats.

Materials and Methods: The effects of daily oral administration of Foeniculum vulgare extract (50 ,75,100mg/kg) for 30 days on blood glucose ,cholesterol, triglyceride, LDL-cholesterol, HDL-cholesterol, malondialdehyde (MDA), aspartate amino transferase (AST) and alanine aminotranferase (ALT) were evaluated in normal and streptozotocin induced diabetic rats.

Results: Administration of Foeniculum vulgare extract to diabetic rats decreased blood glucose, total cholesterol, triglycerides, LDL, HDL, MDA, AST, ALT and increased HDL levels.

Conclusion: The present investigation suggested that the treatment with Foeniculum vulgare exhibited beneficial effects on lipid profile, lipid peroxidation and aminotranferase enzymes in streptozotocin induced diabetes in male rats and could be considered for further evaluation in drug development.

Keywords: Foeniculum vulgare, Streptozotocin-induced diabetic rats, Lipid profile, Lipid peroxidation, Aminotransferase enzymes.

Introduction

Natural remedies and herbal medicines are cost-effective methods of disease treatment (1,2) Nowadays herbal medicines are good alternative to chemical drugs, one of the major reason for this is low side effect (3,4). The World Health Organization (WHO) estimated that 80% of populations in developing countries rely on traditional medicines, mostly herbal medicines for their primary health care needs (5).

Diabetes mellitus (DM) is an example of a disease that has been treated with herbal medicines (6). DM prevalence is increasing rapidly in most parts of the world (7). In 1995, the WHO reported, 150 million persons worldwide suffer from DM, and may be double by 2025 (8).

Foeniculum vulgare (Fennel) is one of the important spices that cure many diseases. Fennel 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 (9).

Fennel contains 90% trans anethole, up to 20% fenchone and also contain small amounts of limonene, camphor, alphapinene and about six additional minor volatile compounds (9). This plant has anti-inflammatory, antispasmodic, antiseptic, carminative, diuretic and analgesic effect and is effective in gastrointestinal disorder treatment. Also with its anti-ulcer and anti-oxidant properties it is used to treat neurological disorders (10,11). According to importance of fennel as a medicinal herb, the aim of the present study was to evaluate the seed extract of Foeniculum vulgare (fennel) on lipid profile, lipid peroxidation and activities of aminotransferase enzymes in streptozocin induced diabetic adult male rats.

Materials and methods

Extraction of plant seeds
Fennel seeds were purchased in Yazd, Iran. Then the seeds were powdered .The extraction of powdered material was done with 70% ethanol and then put on shaker at 35 °C. After filtering the extract, dehydrated by rotator

Animals
Male albino rats with weight of 150-200 gm were kept in an air-conditioned animal room (a 12 hour light/dark cycle) and fed on a standard diet and tap water.

Study design
Male albino rats were injected streptozocin (65 mg/kg BW) by using one ml solution in 0.1 M citrate buffer with PH 4.5.We measured non fasting blood glucose concent-ration for detection of diabetes. Three days after injection of streptozotocin (STZ/Zanosar), rats with a blood glucose level over 250 mg/dl were considered as diabetic rats.

The rats were weighed and divided into eight experimental groups each of five rats as follows: Group I; normal rats treated with distilled water as control of non diabetic groups, Group II; normal rats treated with 50 mg/kg of plant extract, Group III ; normal rats treated with 75 mg/kg of plant extract, Group IV; normal rats treated with 100 mg/kg of plant extract Group V; diabetic rats treated with only distilled water as control of diabetic groups, Group VI; diabetic rats treated with 50 mg/kg of plant extract, Group VII ; diabetic rats treated with 75 mg/kg of plant extract, Group VIII; diabeticl rats treated with 100 mg/kg of plant extract.

After 30 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 non-heparinized tubes (sera) for the determination of biochemical parameters . Serum cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol, and activity of AST and ALT were measured by auto-analyzer and enzymatic kit. Serum malondialdehyde was measured by thiobarbituric acid reactive substance (TBARS).

Statistical analyses were performed using one-way analysis of variance (ANOVA) in the SPSS software package (version 15.0). The results were expressed in mean ± SE for each parameter. Differences were considered significant at P<0.05.

Results
Various biochemical parameters were evaluated and the results are presented in Tables 1 and 2. Table (1) shows the effect of consuming 3 doses of fennel extract on serum glucose, Lipid profiles and lipid peroxidation in non diabetic and diabetic rats before and after intervention and also between groups. As shown, the mean value of blood glucose, total cholesterol triglyceride, LDL- cholesterol, and MDA of diabetic and non diabetic rats after consumption of fennel extract significantly decreased (*P*=0.000) especially in diabetic groups. The mean value of HDL-C of diabetic and non diabetic rats after consumption of fennel extract significantly increased (*P*=0.000) especially in diabetic groups. The

Table 1. Effect of treating 3 doses of fennel on FBS, serum lipids and Malondialdehyde in non diabetic and diabetic rats

Parameters	Non diabetic groups				Diabetic groups			
	Control	50 mg/kg (BW)	75 mg/kg (BW)	100 mg/kg (BW)	Control	50 mg/kg (BW)	75 mg/kg (BW)	100 mg/kg (BW)
FBS	96.00	94.60	93.40	93.20	314.80	264.40	193.80	129.40
(mg/dl)	±1. 58	1.81 [b]±	±2.07 [b]	±2.58 [b]	±3.42 [a b]	±3.84 [a b]	±3.96 [a b]	±3.84 [a b]
Before	96.00	93.40	91.40	90.20	314.80	147.40	140.80	97.00
After	±1.58	2.07±	±2.07 [a]	±2.58 [a]	±3.71	±2.96 [a b]	±2.77 [a b]	±4.84 [a b]
P-Value	NS	0.004	NS	NS	NS	0.000	0.000	0.000
TC	104.54	103.55	102.60	101.84	186.02	184.08	179.91	178.16±
(mg/dl)	±1.82	1.77 [b]±	±1.39 [b]	±1. 51 [b]	±2.56 [a]	±2.55 [a]	±2.55 [ab]	1.49 [ab]
Before	104.32	101.35	98.49	96.59	185.83	180.74	174.06	171.07
After	±1.77	1.67 [a]±	±1.77 [a]	±1. 34 [a]	±2.59 [a]	±2.4 [ab]	±2.53 [ab]	±1.2 [ab]
P-Value	0.195	0.000	0.000	0.000	0.031	0.000	0.000	0.000
TG	75.50	73.66	69.77	66.58	205.38	198.04	196.16	193.84
(mg/dl)	±1.88	±1.34 [b]	±1.79 [ab]	±1.55 [ab]	±2.00 [a]	±1.71 [ab]	±1.40 [ab]	±1.45 [ab]
Before	75.16	71.41	67.04	62.45	205.12	191.91	187.98	183.79
After	±2.05	±1.4 [a]	±1.82 [a]	±1.55 [a]	±1.94	±1.34	±1.67 [ab]	±1.59 [ab]
P-Value	0.187	0.000	0.001	0.000	0.006	0.000	0.000	0.000
LDL-C	46.26	43.26	39.39	34.27	127.72	102.52	99.71	97.67
(mg/dl)	±1.02	±1.04 [b]	±0.99 [a b]	±1.17 [ab]	±2.82 [a]	±2.8 [ab]	±2.53 [ab]	±2.63 [ab]
Before	46.27	40.71	36.31	29.02	127.06	96.53	92,73	86.7
After	±1.14	±0.73	±1.23	±1.57 [a]	±2.72 [a]	±2.74 [ab]	±3.16 [ab]	±2.71
P-Value	0.986	0.000	0.000	0.000	0.152	0.000	0.026	0.000
HDL-C	26.38	27.70	28.50	32.24	27.24	28.24	32.55	36.98
(mg/dl)	±1.60	±1.72	±0.91 [a]	±1.09 [b]	±1.01	±1.03	±1.06 [ab]	±1.09 [ab]
Before	26.26	28.65	31.19	35.62	27.25	31.54	37.25	43.10
After	±1.72	±1.89 [ab]	±0.86 [ab]	±1.30 [ab]	±1.05	±1.15 [ab]	±1.50 [ab]	±1.19 [ab]
P-Value	0.369	0.003	0.000	0.000	0.916	0.000	0.000	0.000
MDA	0.11	0.097	0.089	0.077	0.318	0.27	0.196	0.114
(µM/L)	±0.014	±0.001 [b]	±0.001 [b]	±0.001 [ab]	±0.008 [a]	±0.01 [ab]	±0.013 [ab]	±0.005 [b]
Before	0.109	0.092	0.082	0.073	0.312	0.202	0.118	0.056
After	±0.013	±0.001	±0.001	±0.009	±0.011 [a]	0.016 [ab]	±0.011 [ab]	±0.006 [ab]
P-Value	0.658	0.000	0.000	0.377	0.070	0.000	0.000	0.000

Values are expressed by mean ± SE

NS= Not significant

a = significance ≤0.05 as compared with non diabetic control

b = significance≤0.05 as compared with diabetic control

P-value= difference between before and after intervation in each group (paired T-test)

mean value of blood glucose, total cholesterol (TC) and LDL- C of diabetic control group and diabetic rats treated with the 3 doses of fennel extract 50, 75 and 100 mg/kg were significantly (P=0.000) lower than the non diabetic control group after intervention.

Also the mean value of blood glucose, TC and LDL-C of 50, 75 and 100 mg/kg treated groups in diabetic rats were significantly (P=0.000) lower than that of the diabetic control group after intervention. The triglyceride (TG) level of non diabetic group treated with 50,75 and 100 mg/kg dose of fennel extract and diabetic control group were significantly (P=0.000) lower than that of the non diabetic control group. The mean value of TG of 3 doses of fennel extract treated groups

in diabetic rats were significantly (P=0.000) lower than that of the diabetic control group after intervention. The level of HDL-cholesterol was significantly (P=0.000) increased in non diabetic and diabetic rats treated with 50,75 and 100 mg/kg doses of fennel extract as compared to control group of non diabetic and diabetic rats after intervention. The mean value of serum MDA in non diabetic group treated with 100 mg/kg of fennel extract ,diabetic control group and diabetic rats treated with 3 doses of fennel extract were decreased significantly (P=0.000) as compared to non diabetic control group after intervention. Also the mean value of serum MDA in diabetic group treated with 3 doses of fennel extract decreased significantly

Table 2. Effect of treating 3 doses of fennel extract on serum liver enzymes in non diabetic and diabetic rats

Parameters	Non diabetic groups				Diabetic groups			
	Control	50 mg/kg (BW)	75 mg/kg (BW)	100 mg/kg (BW)	Control	50 mg/kg (BW)	75 mg/kg (BW)	100 mg/kg (BW)
AST	48.43	47.56	45.74	42.68	64.09	60.47	55.30	48.95
(IU/L)	±1.15	0.50±[b]	±1.09 [a,b]	±0.92[a,b]	±0.93[a]	±0.82[a,b]	±0.69 [a,b]	±1.00 [a,b]
Before	48.28	44.60	41.73	37.63	63.91	53.46	48.13	38.73
After	±1.25	±0.59	±1.19	±1.02	±1.06	±0.87	±0.53	±1.46
P-Value	0.044	0.000	0.000	0.000	0.052	0.000	0.378	0.000
ALT	43.14	41.34	38.42	34.40	115.11	100.07	97.13	93.11
(IU/L)	±1.52	±1.43 [b]	±1.63 [b]	±1.49 [b]	±0.93[a]	±0.84[a,b]	±1.04[a,b]	±1.16[a,b]
Before	42.99	38.22	34.30	29.27	114.90	95.20	92.33	85.13
After	±1.53	±1.61	±1.36	±1.36	±0.95	±0.96	±4.08	±0.82
P-Value	0.001	0.000	0.000	0.000	0,061	0.000	0.074	0.000

Values are expressed by mean±SE

a = significance ≤0.05 as compared with non diabetic control

b = significance≤0.05 as compared with diabetic control

P-value= difference between before and after intervention in each group (paired T-test)

(*P*=0.000) as compared to diabetic control group after intervention.

Table (2) shows the effect of consuming 3 doses of fennel extract on activities of AST and ALT in non diabetic and diabetic rats before and after intervention and also between groups. The mean activities of AST and ALT of diabetic and non diabetic rats after consumption of fennel seed extract significantly decreased (P=0.000) especially in diabetic groups. The mean activity of ALT in diabetic control group and diabetic rats treated with 3 doses of fennel extract were decreased significantly (*P*=0.000) as compared to non diabetic control group after intervention. Also the mean activity of ALT in diabetic rats treated with 3 doses of fennel extract were decreased significantly (*P*=0.000) as compared to diabetic control group.

Discussion

DM is an endocrine and metabolic disorder. DM is characterized by chronic hyperglycemia produces multiple biochemical impairments and oxidative stress especially an increased susceptibility to lipid peroxidation that play role in the progression of the symptoms of diabetes (12). Despite progress in the management of DM by synthetic drugs most of these drugs have side effects in the long run. So, the search for improved and safe natural anti-diabetic agents is ongoing and

WHO has also recommended the development of herbal medicine in this concern (5). Fennel has been used for centuries in the Mediterranean area as an aromatic herb and also in folk medicine (13).

Typically, fennel and its preparations are used to cure various disorders, such as diabetes, bronchitis chronic cough and kidney stones, etc (14). The results of our study showed that fennel have beneficial effects on reduction of blood sugar levels in Streptozotocin induced diabetes rats. Phytochemical tests of fennel revealed the presence of triterpens, steroids, saponins and phenol compounds (15). These components especially triterpens and phenols may alleviate diabetes and its complications via their antioxidant properties (16,15) and ability to stimulate insulin secretion (17,18). Abnormalities in lipid profile are common during diabetes. From the present investigation, streptozotocin induced diabetic rats showed the serum lipid profile such as total cholesterol, triglycerides, LDL 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.

Fennel is known as an excellent source of natural antioxidants. This plant can inhibit free radicals due to the high content of polyphenols

and flavonoids. Phenolic compounds in this herb such as caffeoylquinic acid, rosmarinic acid, eriodictyol-7-orutinoside, quercetin- 3-O-galactoside, kaempferol-3-O-glucoside showed antioxidant activity (19).

Insufficiency of antioxidant defense system leads to elevation in the levels of free radicals. Elevated level of free radicals may lead to disruption in cellular functions, oxidative damages to membranes and enhanced susceptibility to lipid peroxidation (20).

Regarding to the results of MDA, it showed a significant decrease which may be due to oxidative stress and depression of the antioxidant defense system. This results agreement with researches of Amin et al,Orsolic et al and Hemieda et al (20,21,22).

The liver is the main tissue for detoxification and metabolism of most chemicals. Liver enzymes including AST and ALT usually help to detect chronic liver diseases by monitoring their concentrations. Both AST and ALT are considered as indicator of liver injury (23). Elevation in serum activities of both transaminases as observed in diabetes suggest damage to liver cells (24). Administration of the Foeniculum vulgare extract attenuated the elevation of AST and ALT in diabetic rats.

Conclusion

Administration of the seed extract of Foeniculum vulgare showed anti-hyperglycemic, Anti-hyperlipidemic and anti-per oxidative activities in STZ- induced diabetes in rats. It also showed potential to restore hepatic complication of diabetes. Thus Foeniculum vulgare extract might be potential future herbal remedy for diabetes and its complications.

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