Anethum Graveolens supplementation improves insulin sensitivity and lipid abnormality in type 2 diabetic patients

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Abstract: Introduction: Diabetes Mellitus (DM) characterized by hyperglycemia, insulin resistance and dyslipidemia. The use of herbs as complementary medicine for treatment of diseases has been prevailed. This study was aimed to investigate the effects of Anethum supplementation on insulin sensitivity, fasting blood glucose (FBS) and lipid profile in type 2 diabetic patients. **Methods:** This randomized, double blind, placebo-controlled clinical trial was conducted on 60 diabetic patients in Tabriz, Iran in 2012. Eligible subjects randomly divided to intervention and placebo groups. Intervention and placebo groups received 3.3 g/day powder of Anethum and starch, respectively, for 8 weeks. For assessing the primary variables, including insulin, fasting blood glucose, Triglyceride (TG), Total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C) and high-density lipoprotein-cholesterol (HDL-C) levels 5 cc blood samples was collected at onset and at the end of study. Serum insulin level was determined by ELISA method. HOMA-IR as an index of insulin resistance calculated as fasting concentrations of blood glucose (mg/dL) * insulin (μU/mL) / 405. Other variables were determined by enzymatic colorimetric method. **Results:** A significant reduction in insulin level was observed in intervention group at the end of study (p=0.003) and this result confirmed after adjusting for baseline and confounding variables. TC and LDL-C decreased significantly at the end of study (p=0.016, p=0.009, respectively). Changes in HDL-C, TG and HOMA-IR were not apparent. Surprisingly, FBS increased in the intervention group but it did not reach to significant value (p=0.142). **Conclusion:** Considering the novelty nature of this study, further scientific efforts with large sample size and longer duration of intervention are needed to confirm these results.
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1. Introduction

Along with cancer, cardiovascular and cerebrovascular diseases, Diabetes mellitus (DM), is one of the most challenging diseases facing health care professionals today (Qi, 2010). There was approximately 194 million adults with diabetes mellitus aged between 29-79 years in 2003 worldwide and it is estimated to increase over 333 million by 2030 (International Diabetes Federation, 2005). The prevalence of diabetes in Iran, has been reported 7.7% in 2008 (Esteghamati, 2008).

Obesity, impaired insulin action, insulin secretory dysfunction and increased endogenous glucose output are the major and important characteristics of type 2 diabetic patients (Abdul-Ghani, 2006). Lipid abnormalities can be observed in type 2 diabetes (Mooradian, 2009). According to the previous studies, there was a relationship between lipid abnormality and insulin resistance in type 2 diabetes (Adiels, 2006; Krentz, 2003; Farmer, 2007). Although the causes of type 2 diabetes appear to be multifactorial, it has been strongly established that diet can play a major role in the incidence and progression of the disease (Hu, 2001). Considering many harmful side effects of long-term consumption of drugs, use of complementary and alternative medicine seems logical and effective approach to prevent or treat different abnormalities in type 2 diabetes (Yeh, 2002).

Anethum Graveolens L. known as Dill, is one of the most common herbs with a long history of applying as a remedy and spices in foods (Moshfekus, 2010; Yazdanparast, 2008). This herb is an annual herb, belongs to Apiaceae family (Husain, 1988). It is growing in the Mediterranean region, Europe, central, southern Asia and widely cultured in southeastern region of Iran (Yazdanparast, 2008).

All segments of freshly plant including stem, leaves, seed and fruit are widely used for as condiment in foods and in various medicinal productions (Moshfekus, 2010). Anethum leaves are a source of mineral, protein and fiber (Rekha, 2010). Anethoferon, carvone and limonene are the most important components of Anethum oil with a variety of biological roles (Zheng, 1992).

Beside many beneficial effects of Anethum Graveolens including anti-cancer, anti-spasmodic, anti-hypolipidemic and anti hypercholesterolemia, prevention of colic (in babies) and improving bad breath, galactagogue effects (in nursing mothers) (Jeet Kaur, 2010), antimicrobial (Aggarwal, 2002; Pascal, 2002), anti-inflammatory (Naseri, 2012; Valadi, 2010), little attention has been paid to evaluate the effect of Anethum Graveolens on insulin sensitivity and blood biochemical parameters in type 2 diabetic patients. Therefore, this study was aimed to investigate the effects of Anethum Graveolens supplementation on the insulin sensitivity; fasting blood glucose and lipid profile in type 2 diabetic patients.

2. Material and Methods

Study design:

This randomized, double blind, placebo-controlled clinical trial was conducted on 60 type 2 diabetic patients. Subjects were recruited from diabetes association in Tabriz, Iran between Januarys to March in 2012. The regional ethics committee of Tabriz University of Medical Sciences approved the research protocol by the number of 9043. Insulin therapy at the onset or during the study, smoking and use of alcohol, pregnant and breastfeeding women, consumption of Anethum and other herbal supplements, antioxidants, etc during 3 month ago, presence the acute and chronic diseases including kidney, liver, cardiovascular and gastrointestinal diseases were exclusion criteria of study. After explanation of nature of study, finally a written informed consent was taken from all participants with the ages between 18-65 years.

Sample size was determined based on data from previous study (20). By considering the confidence interval of 95%, $\alpha = 0.05$ and power of 80%, using formula $N= ((Z1-\alpha/2 + Z1-B)^2 (SD_1^2+SD_2^2)) /\Delta^2$, 25 diabetic patients were computed per group. Regarding a possible loss in follow-up period, a margin of 20% was determined, and finally 30 patients were allocated in each group.

Tablets preparation

Fresh and green Anethum Graveolens herbs (leaves, stems) were purchased from local market and after washing were dried to make powders. The powders were delivered to a pharmaceutical lab (Tabriz university of medical science, Iran) to prepare tablets containing 1.1 gr powder of Anethum in each. Starch was used to make placebo. The color and shape of Anethum and placebo tablets were similar together. A third person who not directly involved in the study was placed tablets in the same bottles. This person labeled the bottles with 2 cods which retained unknown for researchers until the end of intervention. To evaluate the compliance of patients, participants who consumed more than 90% of tablets were included in statistically analysis and bottles containing tablets were given monthly.

Treatment:

After recruited 74 diabetic patients, 60 eligible patients were selected to take part in the study. These 60 patients, then, were randomly divided to intervention groups (n=30) and placebo group (n=30) based on a random block procedure produced by Random Allocation Software (RAS) (Saghaei 2004). Intervention group received one tablet of Anethum after each meal (breakfast, lunch and dinner) and placebo group received the same amount starch for 8 weeks. Participants were asked to continue their usual diet and medications according to physician prescription. During the study, 8 patients did not complete the study and data analysis were done on 52 patients (26 in each group) who carefully completed follow-up period and protocol of study. Figure 1 display the protocol of study.

Anthropometric and Biochemical assessments:

Anthropometric measurements including weight, height, waist and hip circumference were measured at the baseline and after intervention. The body weights were measured without shoes and light clothing by a Seca scale (Seca, Hamburg, Germany). Heights were also measured using a statiometer (Seca) without shoes. BMI was calculated as the weight in kilogram divided by the square of the height in meter. Waist and hip circumference was measured with a non-elastic tape.

Blood samples (5cc) were collected at the beginning and at the end of 8 weeks after 10-12hr fasting state and the serum samples were obtained by high-speed centrifugation at least 10 minute and were frozen immediately at −70°C until assay. Serum

concentration of FBS, TG, TC, LDL-C and HDL was determined by enzymatic colorimetric method (Parsazmun and Shimatso kits) (Abbott, model Alcyon 300, USA). Serum insulin concentration was determined by ELISA method.

Insulin resistance was estimated according to the Homeostasis Model Assessment (HOMA) calculated as: HOMA-IR = fasting concentrations of glucose (mg/dL) * insulin (μU/mL) / 405 (Matthews, 1985).

Statistical analysis:

The data were analyzed by SPSS software (version 13.0; SPSS Inc, Chicago, IL). Normality of data was evaluated using the Kolmogorov-Smirnov test. Continuous variables were expressed as mean (standard deviation) and qualitative data were presented as frequency (percentage).Paired t-test was used to compare the differences within group before and after the supplementation. Analysis of covariance (ANCOVA) was used for the comparison of post treatment values of variables after adjusting for baseline values and confounding variables (age, gender, type of consumed hypoglycemic drug and use of hypolipidemic drugs) between groups. In addition, Chi-square test was examined the differences in gender variable in both groups. P value less than 0.05 considered statistically significant.

3. Results

The mean (±SD) ages of participated patients were 53.11±7.51 years. No statistically significant differences observed between genders and other variables including age and anthropometric measurements at baseline (p>0.05).Table 1 shows demographic characteristics of participants in the onset of study.

Table 1: Demographic characteristics of participates in the onset of study (n=52)

Variables	Intervention group (N=26)	Placebo group (N=26)	P
Age (year)	53.11±7.23	53.11±7.93	1.000
Male Gender N (%)	11(42.3)	13(50.0)	0.582
Weight (Kg)	74.13±12.83	79.38±16.97	0.214
BMI (Kg/m^2)	28.20±3.93	30.63±5.19	0.062
Waist circumference(cm)	96.53±10.78	100.92±11.22	0.157
Hip circumference (cm)	107.73±8.64	108.73±8.63	0.678

Table 2 depicted the results of biochemical markers (Insulin, HOMA-IR, FBS, TG, TC, LDL-C, HDL-C) at baseline and at the end of study in both groups. Total cholesterol and LDL-C decreased significantly in intervention group at the end of study (respectively p=0.016, PC= -12.12 and p=0.009, PC= -13.75). However, these results did not approve after adjusting for baseline and confounding variables by AVCOVA test. Regarding other lipid profile markers (TG and LDL-C), the results manifested any significant changes in intervention group. Surprisingly, FBS increased slightly and non-significant in intervention group (p=0.142).

Insulin concentration decreased in intervention group significantly (p=0.003, PC= -8.94). This result also confirmed by ANCOVA test after adjusting for baseline and confounding variables (p=0.001). HOMA index increased slightly due to the effects of increased FBS.

4. Discussions

Type 2 diabetes is a heterogeneous metabolic disorder characterized by the impairment of insulin secretion from pancreatic β-cells, insulin resistance in peripheral tissues and lipid abnormality (Butler, 2003; Hanley, 2010).

The use of herbs for treatment or prevention of insulin resistance in diabetic patients has been common, recently.

Cinnamon and Cortidis Rhizoma are examples of herbs recognized for insulin secretagogues effects (Ko, 2005; Kirkham, 2009).

In present study, insulin concentration decreased significantly at the end of study. It was shown that green vegetables such as Anethum are rich in antioxidant components including vitamin C, polyphenols and carotenoieds (Agte, 2000; Duthie, 2003; Kidmose, 2001).

Reactive oxygen species (ROS) are associated with the inflammatory response and oxidative stress as other complication of type 2 diabetes (Agrawal, 2010 Ceriello, 2006). Beside the neutralizer of ROS properties of antioxidant and flavonoid components of Anethum, these components can be involved in repairing of damaged β-cells and insulin secretion (Teuber and Herrmann, 1978; Rashidlamir, 2012; Madani, 2005).

Supplementation of Anethum resulted in significant decreasing in serum total cholesterol and LDL-C concentration, however, no obvious changes were observed in serum triglyceride and HDL-C level. Several human and experimental studies reported controversial results about the effect of

Anethum on lipid profile biomarkers. Hajhashemi and Abbasi (Hajhashemi and Abbasi, 2008) showed that supplementation of 16 hypercholesterolemic wistar male rats with 10% Anethum powder for 2 weeks resulted in a significant reduction in TC, LDL-C and TG and a significant increasing in HDL-C levels. In Madani et al, (Madani, 2005) survey, fifteen male rats in three five group, were used to supplementation with dill extract for 48 hours.

The control group, received physiological serum, diabetic control group (DCG), diabetes was induced using Alloxan monohydrate at a dose of 120 mg/kgbw and the treated diabetic control group (TDCG) rats were dosed with 300 mg/kgbw hydroalcoholic Anethum graveolens extract. The results indicated significant reduction in glucose, total cholesterol, triglyceride, LDL and VLDL levels in TDCG rats compared to DCG rats. Due to the use of dill extract, HDL level was significantly increased. In other study yazdanparast et al., (Yazdanparast, 2008) displayed that supplementation of 18 male rats in three groups normal diet, high fat diet and high fat diet with 1 mg Anethum extract equivalent 500 mg of the plant powder for up to 10 and/or 30 day decreased serum TC, TG and LDL-C compared to rats which were fed high fat diet, and the concentration of serum HDL-C increased significantly after 30 days. In contrast, Kojuri et al., (Kojuri, 2007) represented 650 mg Anethum supplementation in hyperlipidemic patients twice daily for six weeks, have significant changes on the mean TC and LDL-C. But, triglyceride level increased and HDL-C reduced.

Table2: The results of biochemical markers in baseline and at the end of study in intervention and placebo groups (n=52)

	Intervention group (N=26)		p^a	PC Lower to upper	Placebo group (N=26)		p^a	PC Lower to upper	p^b
	Baseline	After			Baseline	After			
Insulin (μU/ml)	11.59±2.66	10.47±2.73	0.003*	-15±24, -2.64	11.86±3.21	12.55±3.47	0.150	-1.17±16.67	0.001*
FBS (mg/dl)	141.07±44.02	155.42±60.90	0.142	-0.42,26.67	141.26±44.20	164.38±48.95	0.005*	6.82,31.85	0.732
HOMA-IR	3.98±1.80	4.04±1.87	0.833	-10.21, 23.60	4.14±1.93	5.13±2.39	0.005*	11.71,46.40	0.075
TG (mg/dl)	148.76±58.86	136.76±69.72	0.361	-15.45,3.55	120.38±48.72	155.11±57.60	0.006*	-2.70,37.11	0.072
TC (mg/dl)	152.76±30.09	129.84±37.19	0.016*	-24.00,-0.24	152.50±37.32	144.96±44.79	0.472	-12.91,9.90	0.191
LDL-C (mg/dl)	87.07±20.19	71.57±23.08	0.009*	-28.48,0.98	91.23±21.10	84.65±6.12	0.119	-15.07,2.06	0.089
HDL-C (mg/dl)	45.42±8.77	42.80±7.75	0.164	-11.50,4.17	45.65±6.56	43.88±6.56	0.250	-9.87,5.08	0.682

*statistically significant a Paired t-test, b: ANCOVA test between two groups with adjusting for baseline values and confounding variables (age, gender, type of consumed hypoglycemic drug, use of hypolipidemic drugs)

The possible underlying mechanism by which Anethum can exert its lipid lowering activities is not completely elucidated. However, several fundamental effective mechanisms have been proposed: 1) phenolic components mainly flavonoids in Anethum graveolens that can modify LDL/HDL ratio (Yazdanparast, 2008), 2) increasing LDL receptors and uptake of LDL and inhibition the activity of acetyl-CoA carboxylase (Slater, 1980) 3) reduction in cholesterol absorption from intestine by binding to bile acids 4) decreasing HMG-COA reductase activity and suppression cholesterol and fatty acids synthesis (Yazdanparast, 2008).

Fasting blood glucose increased slightly after intervention in our study. In agreement of our findings, Piri et al, (Piri, 2010) demonstrated the supplementation of diabetic and normal rats (88 Wistar male rats) which were fed high fat diet with Anethum extract (50, 100, 200 mg/kg) for 3 weeks increased significantly plasma blood glucose in diabetic rats compared with normal rats in a dose-dependent manner ($p<0.001$).

In contrast, Madani et al,. (Madani, 2005) investigation showed a significant reduction in blood glucose with supplementation of male diabetic rats with receiving 300 mg/kg/w hydroalcoholic extract of Anethum graveolens for 10 day (200-250g). It was reported that Anethum has some kind of coumarin components with phototoxicity effects that can aggravate oxidative stress and encourage destruction on β-cells that have role in increasing endogenous glucose output (Ojala, 1999; Gonzalez and Pathak, 1996).

Conclusion:

To the best of our knowledge, this was the first study investigated the effect of Anethum graveolens supplementation on the insulin sensitivity and fasting blood glucose, insulin resistance index (HOMA) and lipid profile biomarkers in type 2 diabetic patients. The results showed an improving in

the insulin sensitivity as a major complication of type 2 diabetes. Moreover total cholesterol and LDL-C concentration deceased significantly at the end of study in supplemented group; however, fasting blood glucose, HDL-C, triglyceride and HOMA index did not change significantly. Regarding to the novelty and preliminary nature of this study, further scientific efforts with large sample size and in safe dose of Anethum are certainly needed to confirm our results.

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References

1. Qi LW, Liu EH, Chu C, Peng YB, Cai HX, Li P(2010). Anti-Diabetic Agents from Natural Products—An Update from 2004 to 2009. Curr Top Med Chem; 10 (4): 434-457.
2. International Diabetes Federation (2005). Diabetes e-Atlas. Available at: http://www.eatlas.idf.org. Accessed July 14. 2005.
3. Esteghamati A, Gouya MM, Abbasi M, Delavari A, Alikhani S, Alaedini F, et al(2008). Prevalence of Diabetes and Impaired Fasting Glucose in the Adult Population of Iran. Diabetes Care; 31(1): 96–98.
4. Abdul-Ghani MA, Tripathy D, Deferonzo RA(2006). Contributions of Cell Dysfunction and Insulin Resistance to the Pathogenesis of Impaired Glucose Tolerance and Impaired Fasting Glucose. Diabetes Care; 29 (5): 1130-1139.
5. Mooradian AD(2009). Dyslipidemia in type 2 diabetes mellitus. Nat Clin Pract Endocrinol Metab; 5(3): 150-159.
6. Adiels M, Olofsson SO, Taskinen MR, Boren J(2006). Diabetic dyslipidaemia. Curr Opin Lipidol; 17 (3):238-246.
7. Krentz AJ(2003). Lipoprotein abnormalities and their consequences for patients with type 2 diabetes. Diabetes Obes Metab; 5(1):19-27.
8. Farmer JA(2007). Diabetic dyslipidemia and atherosclerosis: evidence from clinical trials. Curr Atheroscler Rep; 9(2): 162-168.
9. H FB, van Dam RM, Liu S(2001). Diet and risk of Type II diabetes: the role of types of fat and carbohydrate. Diabetologia; 44(7): 805-817.
10. Yeh GY, Eisenberg DM, Davis RB, Phillips RS(2002). Use of Complementary and Alternative Medicine Among Persons With Diabetes Mellitus: Results of a National Survey. Am J Public Health; 92(10): 1648-1652.
11. Moshfekus Saleh-e-In M, Sultana A, Husain M, Kumar Roy S(2010). Chemical Constituents of Essential Oil from Anethum sowa L. Herb (Leaf and Stem) Growing in Bangladesh. Bangladesh J Sci Ind Res; 45(2): 173-176.
12. Yazdanparast R, Bahramikia S(2008). Evaluation of the effect of Anethum graveolens L. crude extracts on serum lipids and lipoproteins profiles in hypercholesterolaemic rats. DARU; 16(2): 88-94.
13. Husain A(1988). Major essential oil-bearing plants of India. Central Institute of Medicinal and Aromatic Plants. 1988; 1-237.
14. R MN, Yadav AR, Dharmesh Sh, Chauhan AS, Ramteke RS(2010). Evaluation of Antioxidant properties of dry soup mix extracts containing Dill (Anethum sowa L.) leaf. Food Bioprocess Technol; 3(3): 441-449.
15. Zheng GQ, Kenney PM, Lam LK(1992). Anethofuran, Carvone, and Limonene: Potential Cancer Chemoprotective Agents from Dill Weed Oil and Caraway Oil. Planta Med; 58(4): 338-341.
16. Jeet Kaur G and Singh Arora D(2010). Bioactive potential of Anethum graveolens, Foeniculum vulgare and Trachyspermum ammi belonging to the family Umbelliferae - Current status. J Med Plants Res; 4(2): 87-94.
17. Aggarwal KK, Khanuja SPS, Ahmad A, Santha Kumar TR, Gupta VK and Kumar S(2002). Antimicrobial activity profiles of the two enantiomers of limonene and carvone isolated from the oils of Mentha spicata and Anethum sowa. Flavour Fragr J; 17: 59–63.
18. Pascal JD, Stanich B and Mazza G(2002). Antimicrobial activity of individual and mixed fractions of dill, cilantro, coriander and eucalyptus essential oils. Int J Food Microbiol; 74 (1-2): 101–109.
19. Naseri M, Mojab F, Khodadoost M, Kamalinejad M, Choopani R, Hasheminejad A, et al(2012). The study of anti-inflammatory activity of oil-based Dill (Anethum graveolens L.) extract used topically in formalin-induced

inflammation male rat paw. IJPR; 11(4): 1169-1174.
20. Valadi A, Nasri S, Abbasi N, Amin GR(2010). Antinociceptive and anti-inflammatory effects of hydroalcholic extract of Anethum Gravolens L. seed. J Med Plants; 9 (34):124-130.
21. Saghaei M(2004). Random allocation software for parallel group randomized trials. BMC; 4 (26): 1-6.
22. Matthews DJ, Hoskers JP, Rudenski AS, Naylor BA, Trencher DF and Turner RC(1985). Homeostasis model assessment: Insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia; 28(7): 412-419.
23. Butler AE, Janson J, Bonner-Weir S, Ritzel R, Rizza RA, Butler PC(2003). Beta-cell deficit and increased beta-cell apoptosis in humans with type 2 diabetes. Diabetes; 52 (1):102–110.
24. Hanley SC, Austin E, Assouline-Thomas B, Kapeluto J, Blaichman J, Moosavi M, et al(2010). Beta Cell mass dynamics and islet cell plasticity in human type 2 diabetes. Endocrinology; 151(4): 1462–1472.
25. Ko BS, Choi SB, Park SK, Jang JS, Kim YE, Park S(2005). Insulin Sensitizing and Insulinotropic Action of Berberine from Cortidis Rhizoma. Biol Pharm Bull; 28(8): 1431-1437.
26. Kirkham S, Akilen R, Sharma S, Tsiami A(2009). The potential of cinnamon to reduce blood glucose levels in patients with type 2 diabetes and insulin resistance. Diabetes Obes Metab; 11 (12): 1100–1113.
27. Agte VV, Tarwadi KV, Mengale S, Chiplonkar SA(2000). Potential of traditionally cooked green leafy vegetables as natural sources for supplementation of eight micronutrients in vegetarian diets. J Food Comp Anal; 13 (6), 885–891.
28. Duthie GG, Gardner PT, Kyle JA(2003). Plant polyphenols: are they the new magic bullet. Proc Nutr Soc; 62 (3): 599–603.
29. Kidmose U, Knuthsen P, Edelenbos M, Justesen U, Hegelund E(2001). Carotenoids and flavonoids in organically grown spinach (Spinacia oleracea L.) genotypes after deep frozen storage. J Sci Food Agric; 81: 918–923.
30. Agrawal N, Singh SK, Singh N, Kalra S, Srivastava G(2010). Oxidative stress and diabetes. Int J Geriatr Gerontol; 6(1): DOI: 10.5580/981.
31. Ceriello A(2006). Oxidative Stress and diabetes-associated compliactions. Endocr Pract; 12 (1): 60-62.
32. T, Herrmann K(1978). Flavonol glycosides of leaves and fruits of dill (Anethum graveolens L.). II. Phenolics of spices. Z Lebensm Unters Forsch; 167(2): 101-104.
33. Rashidlamir A, Gholamian S, Hashemi Javaheri A, Dastani M(2012). The effect of 4-weeks aerobic training according with the usage of Anethum Graveolens on blood sugar and lipoproteins profile of diabetic women. Annal Biological Res; 3 (9): 4313-4319.
34. Madani H, Mahmoodabady N, Vahdati A(2005). Effects of hydroalchoholic extract of anethum graveolens (Dill) on plasma glucose and lipid levels in diabetes induced rats. IJDLD; 5 (2): 109-116.
35. H, Abbasi N(2008). Hypolipidemic activity of Anethum graveolens in rats. Phytother Res; 22(3):372-5.
36. K J, Vosoughi AR, Akrami M(2007). Effects of anethum graveolens and garlic on lipid profile in hyperlipidemic patients. Lipids Health Dis; 6(5): 5.
37. Slater HR, Packard CJ, Bicker S, Shepherd J(1980). Effects of cholestyramine on receptor mediated plasma clearance and tissue uptake of human low density lipoprotein in the rabbit. J Biol Chem; 255 (21):10210–10213.
38. Piri M, Shahin M, Oryan SH(2010). The effects of Anethum on plasma lipid and lipoprotein in normal and diabetic rats fed high fat diets. J Shahrekord Univ Med Sci; 11 (4): 15-25.
39. O, Vuorela P, Kiviranta J, Vuorela H, Hiltunen R(1999). A bioassay using Artemia salina for detecting phototoxicity of plant coumarins. Planta Med; 65(8): 715-718.
40. G, Pathak MA(1996). Inhibition of ultraviolet-induced formation of reactive oxygen species, lipid peroxidation, erythema and skin photosensitization by polypodium leucotomos. Photodermatol Photoimmunol Photomed; 12(2): 45-56.

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