# Hypoglycemic Effect of Ethanolic Extract of *Carum carvi* L. Seeds in Normal and Streptozotocin-induced Diabetic Rats

**Eidi A (Ph.D.)[1*], Eidi M (Ph.D.)[2], Haeri Rohani A (Ph.D.)[1], Basati F (M.Sc.)[1]**

1- Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran
2- Department of Biology, Varamin Branch, Islamic Azad University, Varamin, Iran
*Corresponding author: Department of Biology, Science and Research Branch, Islamic Azad University, P.O.Box: 16535 - 446, Tehran, Iran
Tel: +98 - 912 - 3380064, Fax: +98-21- 44865939
Email: eidi@srbiau.ac.ir

**Receive:** 3 Jul 2010 **Acceptance:** 23 Aug. 2010

## Abstract

**Background: Herbal medicine has been used for many years by different cultures around the world for the treatment of diabetes.**

**Objective: The hypoglycemic effect of caraway ethanolic extract (*Carum carvi* L.) was investigated in normal and streptozotocin-induced diabetic rats.**

**Methods: Intraperitoneal administration of caraway ethanolic extract seeds (0.1, 0.2, 0.4 and 0.6 g/kg body wt.) on the level of serum glucose and insulin in normal and streptozotocin-induced diabetic rats were evaluated. Before administration and 1, 3 and 5 h after administrations of the ethanolic extract, blood samples were drawn from the retro-orbital sinus. Serum glucose and insulin levels were determined.**

**Results: The results showed that the caraway ethanolic extract seeds at doses 0.2, 0.4 and 0.6 g/kg body wt. significantly decreased serum glucose and insulin in diabetic rats in 3 and 5 h but not in healthy rats.**

**Conclusions: It could be proofed that the traditional use of caraway as a hypoglycemic agent is justified and that extract from this plant show a dose-dependent hypoglycemic activity.**

**Keywords: Caraway, C*arum carvi* L., Streptozotocin, Diabetes, Rat**

[ Downloaded from jmp.ir on 2026-10-31 ]

[ DOR: 20.1001.1.2717204.2010.9.35.12.2 ]

## Introduction

Diabetes is one of the most challenging diseases facing health care professionals today. Its increasing prevalence puts a large burden on society and the public health sector [1]. Type 1 diabetes is characterized by an absolute deficiency of insulin secretion, associated with auto-immune destruction of pancreatic β-cells, and this disease is more likely to occur in relatives of an affected person [2]. Type 2 diabetes, which accounts for more than 90% of cases, is caused by a combination of resistance to insulin action and impaired insulin secretion [3]. Plants have been reported as an exemplary source of drugs, and many of the currently available drugs have been derived directly or indirectly from them. In recent years, there has been renewed interest in plant medicine [4-6] for the treatment against different diseases as herbal drugs are generally out of toxic effect [7,8] reported from research work conducted on experimental model animal. Although in human, whether there is any toxic effect are not investigated. It is reported that about 800 plants may possess anti-diabetic potential [9]. Isolated studies screened various plants having "folk medicine reputation" by biochemical test for this antidiabetogenic effect [10].

The dried ripe fruits of *Carum carvi* L. Apiaceae (Umbelliferae) (caraway) are used in folk medicine as a carminative, found to be effective against spasmodic gastrointestinal complaints, flatulence, irritable stomach, indigestion, lack of appetite, and dyspepsia in adults [11-13], and in relieving flatulent colic of infants [14]. In Moroccan traditional medicine, an aqueous extract of caraway is used as an aperitif, tranquilizer, carminative, diuretic, emenagogue, galactagogue, spasmolytic, gastric stimulant and as an aphrodisiac [15]. The plant extract and the volatile oils from *Carum carvi* have also been used as an antiulcerogenic agent [16]. Furthermore, experimental studies have shown its antitumor [17], antiproliferative [18], antihyperglycemic [19], and antimicrobial [20] activities. So, the purpose of this research was to experimentally assess the hypoglycemic effect of caraway alcoholic extract used in normal and streptozotocin-induced diabetic rats.

## Materials and Methods

Plant material

Caraway seeds purchased from a retail food store (Tehran, Iran) in June 2009. The seeds were ground with a blender, and the powder was kept in nylon bags in a deep freezer (−20°C) until the time of experiments. Ground seeds (about 60 g) were submitted to extraction with 300 ml ethanol (80%) in a Soxhlet apparatus for 72 h. After extraction, the solvent was filtered and then evaporated under reduced pressure by Rotavapor. The obtained dried caraway alcoholic extract was stored at −20°C until usage.

### Animals

Male Wistar rats initially weighing 200 to 250 g were used. The animals were housed in groups of 5 per cage with free access to standard laboratory chow (35% carbohydrates, 25% proteins, 7% lipids, and 3% vitamins) and tap water. The diet was purchased from Pars-Dam food service, Tehran, Iran. The animal room was maintained at 22 ± 2°C with timed lighting on from 7 AM to 19 PM and relative air humidity of 40 to 60%.

### Preparation of diabetic rat

The animals were injected with streptozotocin (70 mg/kg, i.p.). Five days after injection, the rats with fasting blood glucose



[ Downloaded from jmp.ir on 2026-10-31 ]

[ DOR: 20.1001.1.2717204.2010.9.35.12.2 ]

higher than 300 mg/dl were used for the experiments. The food was removed 12 h before blood sampling. Six rats were used in each experiment. Each animal was used once only in all of experiments. The food was removed from cages 12 h before testing.

**Experimental design**

In the present experiment, 60 rats (30 diabetic, 30 normal rats) were used. The rats were divided into ten groups. Six rats were used in each group.

Group 1: Normal control rats were administrated saline.

Groups 2-5: Normal rats were administrated caraway ethanolic extract (0.1, 0.2, 0.4 and 0.6 g/kg body wt.) intraperitoneally.

Group 6: Diabetic control rats were administrated saline.

Groups 7 - 10: Diabetic rats were administrated caraway ethanolic extract (0.1, 0.2, 0.4 and 0.6 g/kg body wt.) intraperitoneally.

**Blood sampling and Biochemical assays**

Before administration and 1, 3 and 5 h after administrations of the ethanolic extract, rats were anesthetized with sodium pentothal (intraperitoneally), and 1 ml of blood was withdrawn through the retro-orbital plexus using a glass capillary (Micro Hematocrit Capillaries, Mucaps) and collected in polystyrene tubes without the anticoagulant [21]. Serum was separated by centrifugation at 3000 rpm for 10 min. Samples were stored at −20 °C until assayed. Blood glucose levels were determined by the glucose oxidase method [22]. Plasma insulin was determined by using a rat insulin radioimmunoassay kit (DiaSorin, Saluggia, Italy), in a gamma counter (Peckard, USA) based on the method of Ram et al. [23]. Serum glucose and insulin levels were considered as control values before administration.

**Statistical analysis**

All the data were expressed as mean ± S.E.M. Statistical analysis was carried out using one-way ANOVA followed by Tukey post hoc test. The criterion for statistical significance was $p<0.05$.

# Results

There was a significant elevation in serum glucose while the serum insulin level significantly decreased in the diabetic rats. Intraperitoneal administration of caraway ethanolic extract seeds produces a significant decrease in serum glucose level only in streptozotocin-induced diabetic rats (Fig. 1) but not in healthy fasted rats (Fig. 2). Intraperitoneal administration of caraway ethanolic extract seeds significantly increased serum insulin levels in diabetic (Fig. 3) but not in healthy rats (Fig. 4).

# Discussion

The results demonstrated that the ethanolic extract of caraway seeds exerted a significant and potent anti-hyperglycemic activity in STZ-diabetic rats. This strong effect was first demonstrated in this study realized in diabetic rats, an experimental model of type 1 diabetes mellitus [24]. It is now well established that STZ selectively destroys the pancreatic cells and produces hyperglycemia [25], which is evidenced by the decreased level of plasma insulin. STZ is commonly used in chemically induced diabetic animal model. The timing of STZ injection is important and will affect the type of diabetes that subsequently develops. If STZ is injected to adult animals (i.e. 3 months or older), type 1 diabetes results. However, if



[ Downloaded from jmp.ir on 2026-10-31 ]

[ DOR: 20.1001.1.2717204.2010.9.35.12.2 ]

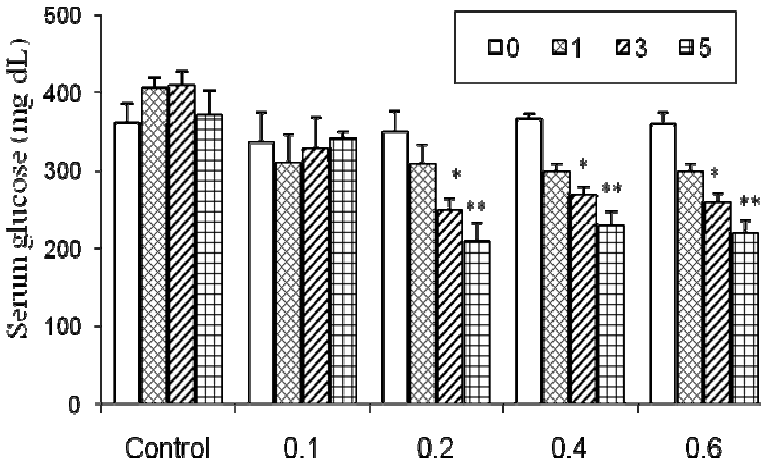



**Fig. 1. Effect of intraperitoneally administration of caraway ethanolic extract seeds at doses of 0.1, 0.2, 0.4 and 0.6 g/kg body weight on serum glucose in streptozotocin-induced diabetic fasted rats for 1, 3 and 5 h after administration. Each point represents mean ± SEM for six rats. Serum glucose levels at zero time or before administrations were considered as control values. *p< 0.05, **p< 0.01 different from zero time. Control group was administered with saline as a vehicle**

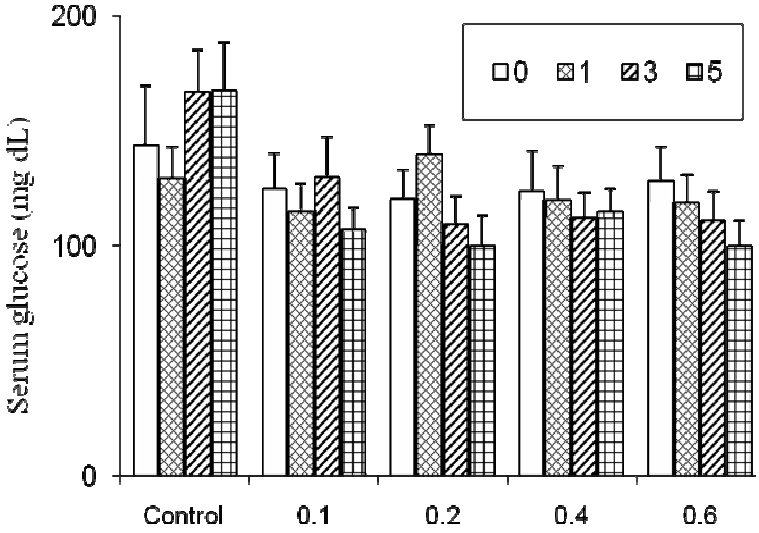



**Fig. 2- Effect of intraperitoneally administration of caraway ethanolic extract seeds at doses of 0.1, 0.2, 0.4 and 0.6 g/kg body weight on serum glucose in healthy fasted rats for 1, 3 and 5 h after administration. Each point represents mean ± SEM for six rats. Serum glucose levels at zero time or before administrations were considered as control values. Control group was administered with saline as a vehicle.**

[ Downloaded from jmp.ir on 2026-10-31 ]

[ DOR: 20.1001.1.2717204.2010.9.35.12.2 ]

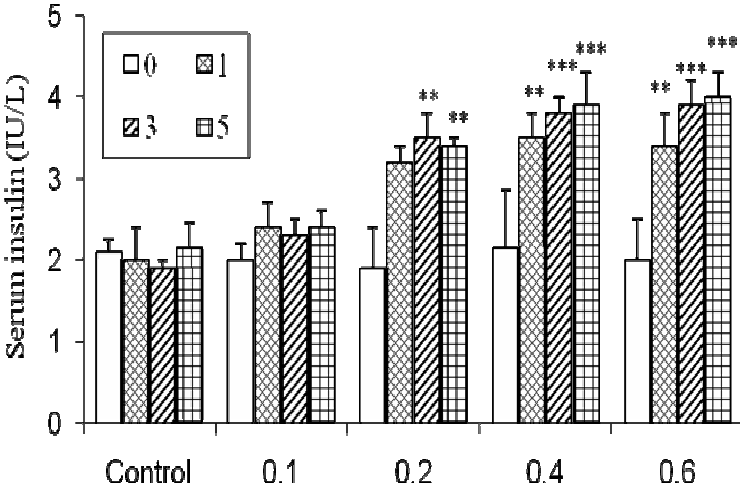



**Fig. 3- Effect of intraperitoneally administration of caraway ethanolic extract seeds at doses of 0.1, 0.2, 0.4 and 0.6 g/kg body weight on serum insulin in streptozotocin-induced diabetic fasted rats for 1, 3 and 5 h after administration. Each point represents mean ± SEM for six rats. Serum insulin levels at zero time or before administrations were considered as control values. **p< 0.01, ***p< 0.001 different from zero time. Control group was administered with saline as a vehicle**

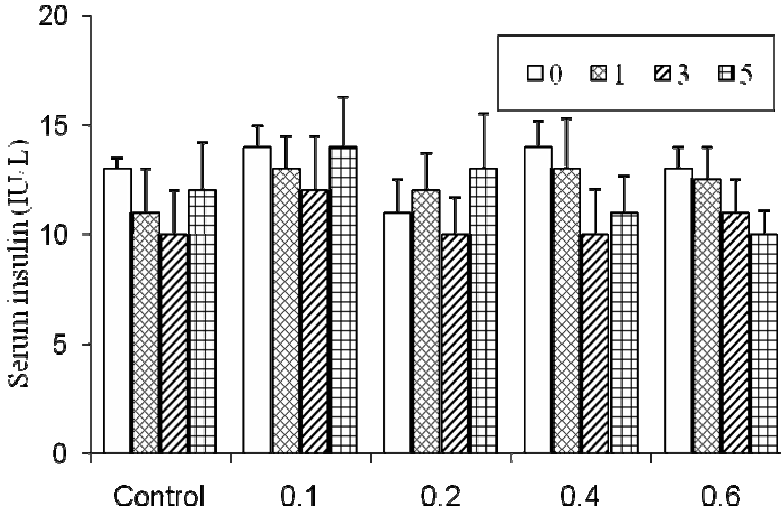



**Fig. 4- Effect of intraperitoneally administration of caraway ethanolic extract seeds at doses of 0.1, 0.2, 0.4 and 0.6 g/kg body weight on serum insulin in healthy fasted rats for 1, 3 and 5 h after administration. Each point represents mean ± SEM for six rats. Serum insulin levels at zero time or before administrations were considered as control values. Control group was administered with saline as a vehicle**

injected during the first week of birth while the capacity of pancreatic -cell regeneration remains in the animals, type 2 diabetes develops [25, 26].



[ Downloaded from jmp.ir on 2026-10-31 ]

[ DOR: 20.1001.1.2717204.2010.9.35.12.2 ]

The known main constituents of caraway have been demonstrated to be carvone (40 – 60%), limonene, carveol, dihydrocarveol, thymol in addition to glucosides and flavonoids [27-30]. Flavonoids are considered as active principles in many medicinal plants and natural products with positive effect for human health [31].

The caraway extract seeds had increasing effect on basal plasma insulin concentrations in diabetic rats. It appears that the fruit extracts of these plants exerts a hypoglycemic effect dependently of insulin secretion. Recent-onset insulinopenia in STZ-diabetic rats was associated with glucose overproduction in the basal (hyperglycemic) state [32]. The hypoglycemic activity of this plant may therefore be due to inhibition of hepatic glucose production [32] and/or stimulation of glucose utilization by peripheral tissues, especially muscle and adipose tissue. The plant extracts could also act as inhibitors of tubular renal glucose reabsorption [33].

As a result, it may be concluded that, ethanolic extract of caraway seeds is effective in attenuate of increasing serum glucose and decreasing serum insulin resulting from the damage of STZ-induced diabetic rats. It could be proofed that the plant must be considered as excellent candidate for future studies on diabetes mellitus. In addition, further comprehensive pharmacological investigations, including experimental chronic studies, should be carried out.

## Acknowledgement

We would like to thank Deputy Research of the Science and Research Branch, Islamic Azad University for financial support of the project.

## References

**1.** Leroith D, Smith DO. Monitoring glycemic control: the cornerstone of diabetes care. *Clinical Therapeutics* 2005; 27: 1489 - 99.

**2.** Bottini N, Vang T, Cucca F, Mustelin T. Role of PTPN22 in type 1 diabetes and other autoimmune diseases. *Seminars in Immunol.* 2006; 18: 207 - 13.

**3.** Warren RE. The stepwise approach to the management of type 2 diabetes. *Diabetes Research and Clinical Practice* 2004; 65: 53-8.

**4.** Dubey GP, Dixit SP, Alok S. Alloxan-induced diabetes in rabbits and effect of herbal formulation D–400. *Indian J. Pharmacol.* 1994; 26: 225 - 6.

**5.** Prince PS, Menon VP, Pari L. Hypoglycemic activity of *Syzigium cuminii* seeds: effect on lipid peroxidation in alloxan diabetes rats. *J. Ethnopharmacol.* 1998; 61: 1 - 7.

**6.** Ladeji O, Omekarah I, Solomon M. Hypoglycemic properties of aqueous bark extract of *Ceiba pentandra* in streptozotocin-induced diabetic rats. *J. Ethnopharmacol.* 2003; 84: 139 - 42.

**7.** Geetha BS, Biju CM, Augusti KT. Hypoglycemic effects of leucodelphinidin derivative isolated from *Ficus bengalensis* (Linn.). *Indian J. Pharmacol.* 1994; 38: 220 - 2.

**8.** Rao BK, Sudarshan PR, Rajasekhar MD, Nagaraju N, Rao CA. Antidiabetic activity of *Terminalia pallida* fruit in alloxan induced diabetic rats. *J. Ethnopharmacol.* 2003; 85: 169 - 72.



[ Downloaded from jmp.ir on 2026-10-31 ]

[ DOR: 20.1001.1.2717204.2010.9.35.12.2 ]

**9.** Grover JK, Yadav S, Vats V. Medicinal plants of India with antidiabetes potential. *J Ethnopharmacol* 2002; 81: 81-100.

**10.** Vats V, Grover JK, Rathi SS. Evaluation of antihyperglycemic effect of *Trigonella foenum-graecum* Linn., *Occium sanctum* Linn. and *Pterocarpus marsupium* Linn., in normal and alloxanised diabetic rats. *J. Ethnopharamcol.* 2002; 79: 95 - 100.

**11.** Holtmann G, Haag S, Adam B, Funk P, Wieland V, Heydenreich CJ. Effects of a fixed combination of peppermint oil and caraway oil on symptoms and quality of life in patients suffering from functional dyspepsia. *Phytomedicine* 2003; 10: 56 - 7.

**12.** Madisch A, Holtmann G, Mayr G, Vinson B, Hotz J. Treatment of functional dyspepsia with a herbal preparation: a double-blind, randomized, placebo-controlled, multicenter trial. *Digestion* 2004; 69: 45 - 52.

**13.** Thompson Coon J, Ernst E. Systematic review: herbal medicinal products for non-ulcer dyspepsia. *Alimen Pharmacol Therap* 2002; 16: 1689 - 99.

**14.** Reynolds JEF. The Extra Pharmacopoeia, 30th ed. Pharmaceutical Press, London, 1993, pp: 1349 - 50.

**15.** Bellakhdar J. La Pharmacop´ee Marocaine Traditionnelle, M´edecine Arabe Ancienne et Savoirs Populaires. Edition Ibis Press, 1997, pp: 150.

**16.** Khayyal MT, El-Ghazaly MA, Kenawy SA, Seif-El-Nasr M, Mahran LG, Kafafi YA, Okpanyi SN. Antiulcerogenic effect of some gastrointestinally acting plant extracts and their combination. *Arzneimittelforschung* 2001; 51: 545 - 53.

**17.** Zheng G, Kenney PM, Lam LKT. Anethofuran, carvone, and limonene: potential cancer chemopreventive agents from dill weed oil and caraway oil. *Planta Med.* 1992; 58: 338 - 41.

**18.** Nakano Y, Matsunaga H, Saita T, Mori M, Katano M, Okabe H. Antiproliferative constituents in Umbelliferae plants II. Screening for polyacetylenes in some Umbelliferae plants, and isolation of panaxynol and falcarindiol from the root of *Heracleum moellendorffii*. *Biol. Pharm. Bull* 1998; 21: 257 - 61.

**19.** Eddouks M, Lemhadri A, Michel JB. Caraway and caper: potential anti-hyperglycaemic plants in diabetic rats. *J. Ethnopharmacol.* 2004; 94: 143 - 8.

**20.** Iacobellis NS, Lo Cantore P, Capasso F, Senatore F. Antibacterial activity of *Cuminum cyminum* L. and *Carum carvi* L. essential oils. *J. Agric Food Chem.* 2005; 53: 57 - 61.

**21.** Madway W, Prier IE, Wilkinson JS. A Text Book of Veterinary Clinical Pathology. The Williams and Wilkins Co., Baltimore, 1969, p: 256.

**22.** Trinder P. Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. *Ann. Clin. Biochem.* 1969; 6: 24 - 8.

**23.** Ram JL, Fares MA, Standley PR, Sowers JR. Insulin inhibits vasopressin-elicited contraction of vascular smooth muscle cells**.** *J. Vasc Med. Biol.* 1993; 4: 250 - 5.

**24.** Burcelin R, Eddouks M, Maury J, Kande J, Assan R, Girard J. Excessive glucose production, rather than insulin resistance, accounts for hyperglycaemia in recent-onset streptozotocin-diabetic rats. *Diabetologia* 1995; 38: 283 - 90.

**25.** Elsner M, Guldbakke B, Tiedge M, Nunday R, Lenzen S. Relative importance of



[ Downloaded from jmp.ir on 2026-10-31 ]

[ DOR: 20.1001.1.2717204.2010.9.35.12.2 ]

transport and alkylation for pancreatic beta-cell toxicity of streptozotocin. *Diabetologia* 2000; 43: 1528 - 33.

**26.** Matsuda M, Kawasaka F, Mikami Y, Takeuchi Y, Saito M, Eto M, Kaku K. Rescue of beta-cell exhaustion by diazoxide after the development of diabetes mellitus in rats with steptozotocin-induced diabetes. *European J. Pharmacol.* 2002; 431: 141 - 8.

**27.** Matsumura T, Ishikawa T, Kitajima J. Water-soluble constituents of caraway: carvone derivatives and their glucosides. *Chemical and Pharmceutical Bulletin* 2002; 50: 66 - 72.

**28.** Gersbach PV, Reddy N. Non-invasive localization of thymol accumulation in Carum carvi copticum (Apiaceae) fruits by chemical shift selective magnetic resonance imaging. *Annals of Botany* (London) 2002; 90: 253 - 7.

**29.** Bouwmeester HJ, Gershenzon J, Konings MC, Croteau R. Biosynthesis of the Monoterpenes limonene and carvone in the fruit of caraway. *Plant Physiol.* 1998; 117: 901 - 12.

**30.** Kunzermann J, Herrmann K. Isolation and identification of flavon(ol)-O-glycosides in caraway (*Carum carvi* L.) fennel (*Foeniculum vulgare* Mill.), anise (*Pimpinelle anisum* L.), and coriander (*Coriandrum sativum* L.), and flavon-C-glycosides in anise. L. Phenolics of spices. *Zeitschrift fur Lebensmittel-untersuchung und-Forschung* 1977; 164: 194 - 200.

**31.** Havsteen BH. The biochemistry and medical significance of the flavonoids. *Pharmacology and Therapeutics* 2002; 96 (2 - 3): 67 - 202.

**32.** Eddouks M, Jouad H, Maghrani M, Lemhadri A, Burcelin R. Inhibition of endogenous glucose production accounts for hypoglycaemic effect of *Spergularia purpurea* in diabetic mice. *Phytomedicine* 2003; 10: 594 - 9.

**33.** Maghrani M, Lemhadri A, Jouad H, Michel JB, Eddouks M. Effect of the desert plant Retama raetam on glycaemia in normal and streptozotocin-induced diabetic rats**.** *J. Ethnopharmacol.* 2003; 87 (1): 21 - 5.

[ Downloaded from jmp.ir on 2026-10-31 ]

[ DOR: 20.1001.1.2717204.2010.9.35.12.2 ]