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Effects of parsley (*Petroselinum crispum*) extract versus glibornuride on the liver of streptozotocin-induced diabetic rats

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Abstract

Parsley (*Petroselinum crispum*) is one of the medicinal herbs used by diabetics in Turkey. The aim of this study is to investigate the effects of parsley (2 g/kg) and glibornuride (5 mg/kg) on the liver tissue of streptozotocin-induced diabetic rats. Swiss albino rats were divided into six groups: control; control + parsley; control + glibornuride; diabetic; diabetic + parsley; diabetic + glibornuride. Diabetes was induced by intraperitoneal injection of 65 mg/kg streptozotocin (STZ). Parsley extract and glibornuride were given daily to both diabetic and control rats separately, until the end of the experiment, at day 42. The drugs were administered to one diabetic and one control group from days 14 to 42. On day 42, liver tissues were taken from each rat. In STZ-diabetic group, blood glucose levels, serum alkaline phosphatase activity, uric acid, sialic acid, sodium and potassium levels, liver lipid peroxidation (LPO), and non-enzymatic glycosylation (NEG) levels increased, while liver glutathione (GSH) levels and body weight decreased. In the diabetic group given parsley, blood glucose, serum alkaline phosphatase activity, sialic acid, uric acid, potassium and sodium levels, and liver LPO and NEG levels decreased, but GSH levels increased. The diabetic group, given glibornuride, blood glucose, serum alkaline phosphatase activity, serum sialic acid, uric acid, potassium, and liver NEG levels decreased, but liver LPO, GSH, serum sodium levels, and body weight increased. It was concluded that probably, due to its antioxidant property, parsley extract has a protective effect comparable to glibornuride against hepatotoxicity caused by diabetes.

Keywords: Parsley; Glibornuride; Streptozotocin; Liver; Serum

1. Introduction

Diabetes mellitus is a major endocrine disorder, affecting nearly 10% of the population all over the world. In spite of the introduction of hypoglycemic agents, diabetes and the related complications continue to be a major medical problem (Nammi et al., 2003). Diabetes is associated with the generation of reactive oxygen species (ROS), causing oxidative damage particularly to various tissues (Mohamed et al., 1999). Glucose level was found to increase the production of free radicals, as determined by cell damage markers, such as malonaldehyde and conjugated dienes (Cuncio et al., 1995). Hyperglycemia can cause oxidative stress, which, in turn, may result in cellular tissue damage. The harmful influence of diabetes on metabolism of tissues and organs is well known. Likewise, uncontrolled hyperglycemia can lead to disturbances in the structure and functions of organs (Gupta et al., 2004). Insulin and oral hypoglycemic agent are the main ways to treat diabetes mellitus and are effective in controlling hyperglycemia, but these kinds of drugs also have prominent side effects. The main reason to look for new antidiabetic agents is the fact that currently many

Abbreviations: ALP, alkaline phosphatase; ANOVA, analysis of variance; GSH, glutathione; LPO, lipid peroxidation; MDA, malondialdehyde; NEG, non-enzymatic glycosylation; ROS, reactive oxygen species; STZ, streptozotocin; TBARS, thiobarbituric acid-reactive substances; WHO, World Health Organization

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patients are poorly controlled, resulting in the development of long-term macrovascular and microvascular complications. Plants have always been utilizable sources of drug and many of the currently available drugs have been directly or indirectly obtained from plants. In accordance to the recommendations of the WHO Expert Committee on Diabetes Mellitus, it seems important to investigate the hypoglycemic agents from plant origin, which were used in traditional medicine (Alarcon-Aguilera et al., 1998). Parsley (*Petroselinum crispum*) is a member of the Umbelliferae family that has been employed in the food, pharmaceutical, perfume, and cosmetic industries (Lopez et al., 1999). Parsley is widely distributed in Turkey and this plant is grown in gardens and fields. As a traditional medicine for diabetes, parsley has been used in Turkey (Yanardag et al., 2003a) and the world (Noel et al., 1997). Parsley is used as a hypoglycemic agent by diabetic patients in Turkey. In folk medicine, parsley is used to treat a wide variety of conditions (Yanardag et al., 2003a). Parsley seeds have a strong diuretic activity due to its high essential oil content (Darias et al., 2001). The hypoglycemic activity of parsley has been investigated in many studies (Yanardag and Ozsoy, 2000). Phytochemical screening of parsley has revealed the presence of flavonoids (apiin, luteolin, and apigenin-glycosides) (Fejes et al., 2000), carotenoids (Francis and Isaksen, 1989), ascorbic acid (Davey et al., 1996), tocopherol (Fiad and El Hamidi, 1993), volatile compounds (myristicin, apiole), coumarines (bergapten, imperatorin) (Fejes et al., 2000), phthalides, furanocoumarins, and sesquiterpenes (Spraul et al., 1991). Glibornuride is a sulphonylurea derivative, which has been used as a hypoglycemic agent in diabetes mellitus (Logie and Stowers, 1975). The main action of sulphonylureas is stimulation of insulin secretion, although extra-pancreatic effects may contribute. This drug, when given orally, is rapidly and almost completely (98%) absorbed from intestines and is highly but reversibly protein-bound (95%) in the circulation. It is non-toxic, safe and effective in the treatment of maturity onset diabetes (Logie and Stowers, 1975).

The purpose of this study was to investigate the biochemical effects of administration of parsley extract and glibornuride on the liver of normal and STZ-induced diabetic rats.

2. Materials and methods

2.1. Plant material

Parsley leaves were collected from Buyukçekmece, Istanbul (Turkey), and carefully washed with tap water and left to dry in the dark at room temperature. They were stored in well-closed cellophane bags.

2.2. Preparation of aqueous plant extract

The air-dried leaves (100 g) were extracted by adding 1000 mL of distilled water and boiled for 30 min. The extract was then filtered, and the filtrates were evaporated, using a rotary evaporator under reduced pressure to dryness. The extract was dissolved in distilled water before the administration to normal and STZ-diabetic rats.

Table 1
Diet composition

Ingredients	%
Wheat	10
Corn	22
Barley	15
Wheat bran	8
Soybean	26
Fish flour	8
Meat-bone flour	4
Pelted	5
Salt	0.8
Vitamin mineral mix	0.2

2.3. Administration of parsley extract and glibornuride

Fourteen days after the experimental animals were rendered STZ-diabetic, the parsley extract was given by gavage technique to rats at a dose 2 g/kg, to one of the diabetic groups and also one of the control groups, daily for 28 days. Fourteen days after the experimental animals were made diabetic, 5 mg/kg body weight glibornuride (Roche, Turkey) dissolved in distilled water was given by gavage method, to one of the diabetic groups and also one of the control groups, daily for 28 days.

2.4. Preparation of diabetic rats

Diabetes was induced by intraperitoneal of STZ in a single dose of 65 mg/kg body weight. STZ was dissolved in a freshly prepared 0.01 M citrate buffer (pH 4.5).

2.5. Animals

The experiments were reviewed and approved by the Institute's Animal Care and Use Committee of Istanbul University; 6–6.5-month-old male Swiss Albino rats, weighing 150–200 g, were used. The animals were fed laboratory pellet chows (Table 1) and given water ad libitum. All rats were clinically healthy. The animals were divided into six groups—Group I: untreated, non-diabetic animals; Group II: control animals given parsley extract; Group III: control animals given glibornuride; Group IV: diabetic animals; Group V: diabetic animals given parsley extract; Group VI: diabetic animals given glibornuride.

2.6. Biochemical assays

In this study, biochemical investigations were made in blood, serum and liver tissue. Blood samples from rats were collected from the tail vein at days 0, 14, and 42. Fasting blood glucose levels (after 18 h period of fasting) were determined by *o*-toluidine methods (Relander and Raiha, 1963).

At day 42, serum ALP activity was estimated by two-point (Walter and Schütt, 1974) methods. ALP catalyzes the hydrolysis of *p*-nitro phenyl-phosphate forming phosphate and free *p*-nitrophenol, which are colorless in dilute acid solutions. Under alkaline conditions, this is converted to the nitrophenolate ion, which assumes a quinoid structure with a very intense yellow