Diabetes & Metabolic Syndrome: Clinical Research & Reviews 3 (2009) 40–44

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original paper

Antidiabetic effects of sage (*Salvia officinalis* L.) leaves in normal and streptozotocin-induced diabetic rats

Akram Eidi [a,*], Maryam Eidi [b]

[a] Department of Biology, Science and Research Branch, Islamic Azad University, P.O. Box 16535-446, Tehran, Iran
[b] Department of Biology, Varamin Branch, Islamic Azad University, Tehran, Iran

ARTICLE INFO

Keywords:
Salvia officinalis
Sage
Streptozotocin
Diabetes
Rat

ABSTRACT

Background: Sage (*Salvia officinalis* L.) has a wide range of biological activities, such as anti-oxidative properties, anti-bacterial, hypoglycemic, anti-inflammatory, fungistatic, virustatic, astringent, eupeptic and anti-hydrotic effects. This study was designed to examine the antidiabetic effect of sage ethanolic extract in normal and streptozotocin-induced diabetic rats.
Methods: Oral administration of sage extract (0.1, 0.2, and 0.4 g/kg body weight) and glibenclamide (600 μg/kg) for 14 days on the level of serum glucose, triglycerides, total cholesterol, urea, uric acid, creatinine, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in normal and streptozotocin-induced diabetic rats were evaluated.
Results: Oral administration of 0.2 and 0.4 g/kg body wt. of the sage extract for 14 days exhibited a significant reduction in serum glucose, triglycerides, total cholesterol, urea, uric acid, creatinine, AST, ALT and increased plasma insulin in streptozotocin-induced diabetic rats but not in normal rats. Glibenclamide was used as reference and showed similar antidiabetic effect.
Conclusions: It is concluded that the traditional use of *S. officinalis* as an antidiabetic agent is justified and that extracts from this plant show a dose-dependent activity which is comparable to the standard antidiabetic drug glibenclamide.

1. Introduction

Diabetes mellitus (DM) is a chronic disease caused by inherited or acquired deficiency in insulin secretion and by decreased responsiveness of the organs to secreted insulin [1]. DM is currently one of the most costly and burdensome chronic diseases and is a condition that is increasing in epidemic proportions throughout the world [2]. Diabetes affects about 5% of the global population [3] and the management of diabetes without any side effects is still a challenge to the medical system [4,5]. Renewed attention in recent decades to alternative medicines and natural therapies has stimulated a new wave of research interest in traditional practices. The plant kingdom has become a target for the search for new drugs and biologically active "lead" compounds [6]. Ethnobotanical information indicates that more than 800 plants are used as traditional remedies for the treatment of diabetes [7,8], but only a few have received scientific scrutiny.

Salvia, the largest genus of the Lamiaceae family, includes about 900 species, spread throughout the world, some of which are economically important since they have use as spices and flavoring agents in perfumery and cosmetics. Many species of *Salvia*, including *Salvia officinalis* L. (sage), have been used as traditional herbal medicine against a variety of diseases. The plant is reported to have a wide range of biological activities, such as anti-oxidative properties [9], anti-bacterial [10], hypoglycemic [11], anti-inflammatory [12], fungistatic, virustatic, astringent, eupeptic and anti-hydrotic effects [13,14]. Despite the folk medicine use, so far, there has been no scientific evidence to support the antidiabetic effect of sage. The objective of this investigation was to ascertain the scientific basis for the use of this plant in the management of diabetes, using streptozotocin (STZ)-induced diabetic rats.

2. Materials and methods

2.1. Subjects

Male Wistar rats initially weighing 200–250 g were used. The animals were housed in groups of 5 per cage with free access to

* Corresponding author. Tel.: +98 21 77068793; fax: +98 21 77068794.
E-mail addresses: eidi@sr.iau.ir, akram_eidi@yahoo.com (A. Eidi).

1871-4021/$ – see front matter © 2009 Published by Elsevier Ltd on behalf of Diabetes India.
doi:10.1016/j.dsx.2008.10.007

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 a.m. to 19 p.m. and relative air humidity of 40–60%. The study was conducted in accordance with ethical procedures and policies approved by the Animal Care and Use Committee of Islamic Azad University, Tehran, Iran.

2.2. Extraction of ethanolic plant material

Sage leaves were collected from Karaj area in summer and identified in the Department of Botany of Teacher Training University (Voucher number: 037420; deposited in: Farabi Herbarium; Director: Dr. F. Ghahremani Nejad). The leaves were dried at 40 °C and finely powdered. The powder (60 g) was extracted with 300 mL aqueous 80% ethanol in a Soxhlet apparatus for 72 h. After extraction, the solvent was filtered and then evaporated by Rotavapor. The extract yield was 16%. The obtained sage alcoholic extract was stored at −20 °C until usage.

2.3. Preparation of diabetic rats

Diabetes in rats was induced with a single injection of STZ (70 mg/kg body weight [wt]) by intraperitoneal route. The STZ was freshly dissolved in physiological saline solution. Diabetes was confirmed by the determination of fasting blood glucose concentration with the help of a glucometer on the fifth day after administration of STZ. Rats exhibiting blood glucose levels 300 mg/dL or more were segregated and kept into cages marked with groups 5–9. The drug preparations were fed orally by gastric intubation to rats of respective groups once daily for 14 days. Control animals (groups I and V) received the same amount of distilled water.

2.4. Experimental design

Rats were randomly divided into the following nine groups, each group consisting of eight animals.

Group I	Non-diabetic control rats treated with distilled water
Groups II–IV	Non-diabetic rats treated with sage extract (0.1, 0.2 and 0.4 g/kg wt., respectively)
Group V	Diabetic control rats treated with distilled water
Groups VI–VIII	Diabetic rats treated with sage extract (0.1, 0.2 and 0.4 g/kg wt., respectively)
Group IX	Diabetic rats treated with glibenclamide (600 μg/kg wt.)

The volume of administration was 1 mL, and the treatments lasted for 14 days. The animals were carefully monitored every day and weighed every week.

2.5. Biochemical assays

At the end of the experiment (14 days), rats were fasted overnight and blood samples were withdrawn through the retro-orbital plexus under light ether anesthesia using a glass capillary and collected in tubes. Blood was allowed to clot and serum separated by centrifugation at 3500 rpm for 10 min. Serum glucose, insulin, total cholesterol, triglycerides, urea, uric acid, creatinine, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were determined. Serum glucose was estimated by oxidase method [15]. The serum insulin level was estimated by using a radioimmunoassay kit (DiaSorin, Saluggia, Italy), total cholesterol and triglycerides by the method of Rifai et al. [16]. Urea in the serum was estimated by using the diagnostic kit based on the method of Tomas [17]. Uric acid in the plasma was measured estimated by using the diagnostic kit based on the enzymatic method described by Fossati et al. [18]. Creatinine in the serum was estimated using the diagnostic kit based on the methods of Tomas [17]. The activities of serum AST and ALT were assayed by using commercially available kits by the method of Moss and Henderson [19].

2.6. 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 $p < 0.05$.

3. Results

There was a significant elevation in serum glucose, total cholesterol, triglycerides, urea, uric acid, creatinine, AST and ALT while the serum insulin level significantly decreased in the diabetic control rats as compared with non-diabetic control group.

Changes in initial and final body weight in control and experimental groups are shown in Table 1. Significant weight loss was observed in diabetic rats compared to control non-diabetic rats. Treatment with sage extract or glibenclamide improved the body weight as compared to control diabetic rats.

Fig. 1 showed the levels of serum glucose and insulin of normal and experimental animals. There was a significant ($p < 0.001$) elevation in serum glucose, while the level of insulin significantly ($p < 0.001$) decreased in the diabetic control animals as compared with non-diabetic control group. The effect of administration of sage extract at 0.1, 0.2 and 0.4 g/kg body wt. and glibenclamide tended to bring serum glucose and insulin towards normal values, while normal rats did not exhibit any significant alterations in serum glucose and insulin levels duration of the experiment. The effect of sage leaves extract was similar to that observed for glibenclamide. The administration of the sage leaves extract (0.1, 0.2 and 0.4 g/kg body wt.) did not significantly change serum glucose and insulin levels in normal rats.

Table 1
Changes in the body weight in nondiabetic and diabetic rats after administration with different doses of sage extract for 14 days.

	Non-diabetic control rats distilled water	Non-diabetic rats Extract (g/kg)			Diabetic control rats distilled water	Diabetic rats Extract (g/kg)			Diabetic rats glibenclamide
		0.1	0.2	0.4		0.1	0.2	0.4	
Initial (g)	217 ± 12.3	221 ± 15.1	211 ± 8.4	224 ± 17.1	228 ± 19.4	225 ± 13.6	226 ± 10.3	229 ± 9.5	231 ± 17.9
Final (g)	249 ± 15.8	243 ± 12.7	248 ± 19.3	239 ± 16.7	165 ± 13.1*	173 ± 11.6	198 ± 14.3+	207 ± 12.8++	212 ± 15.1++

Values are mean ± S.E.M. of 8 rats.
* $p < 0.05$ different from non-diabetic control rats.
+ $p < 0.05$ different from diabetic control rats.
++ $p < 0.01$ different from diabetic control rats.