Antidiabetic Effect of *Scoparia dulcis*:
Effect on Lipid Peroxidation in Streptozotocin Diabetes

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Abstract. Oxidative damage has been suggested to be a contributory factor in the development and complications of diabetes. The antioxidant effect of an aqueous extract of Scoparia dulcis, an indigenous plant used in Ayurvedic medicine in India was studied in rats with streptozotocin-induced diabetes. Oral administration of Scoparia dulcis plant extract (SPEt) (200 mg/kg body weight) for 3 weeks resulted in a significant reduction in blood glucose and an increase in plasma insulin. The aqueous extract also resulted in decreased free radical formation in tissues (liver and kidney) studied. The decrease in thiobarbituric acid reactive substances (TBARS) and hydroperoxides (HPX) and increase in the activities of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), reduced glutathione (GSH) and glutathione-S-transferase (GST) clearly show the antioxidant properties of SPEt in addition to its antidiabetic effect. The effect of SPEt at 200 mg/kg body weight was better than glibenclamide, a reference drug.
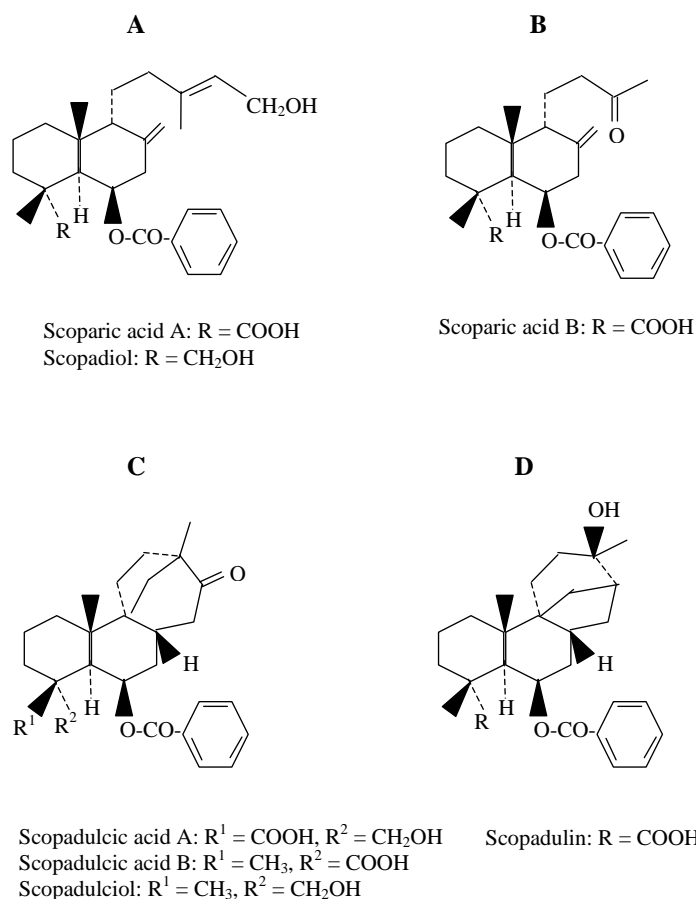
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Introduction

Scoparia dulcis (*Scrophulariaceae*), commonly known as sweet broomweed, is a perennial herb widely distributed in tropical and subtropical regions. In these regions, the fresh or dried plant of *Scoparia dulcis* has traditionally been used as one of remedies for stomach troubles (Satyanarayana 1969), hypertension (Chow et al. 1974), diabetes (Perry 1980), bronchitis (Freire et al 1993), and as an analgesic and antipyretic (Gonzales Torres 1986). A number of different principles include scoparic acid A, scoparic acid B (Fig. 1A and B) (Hayashi et al. 1993), scopadulcic acid A and B, scopadulciol (Fig. 1C) (Hayashi et al. 1991) and scopadulin

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A

B

Scoparic acid A: R = COOH
Scopadiol: R = CH$_2$OH

Scoparic acid B: R = COOH

C

D

Scopadulcic acid A: R^1 = COOH, R^2 = CH$_2$OH   Scopadulin: R = COOH
Scopadulcic acid B: R^1 = CH$_3$, R^2 = COOH
Scopadulciol: R^1 = CH$_3$, R^2 = CH$_2$OH

Figure 1. Biologically active compounds isolated from *Scoparia dulcis.*

(Fig. 1D) (Hayashi et al. 1990) that have been identified as contributor to the observed medicinal effect of the plant. Among them, scopadulcic acid B and sco- padulciol were found to be unique biomolecules with inhibitory effects on repli- cation of herpes simplex virus type 1 (Hayashi et al. 1993), gastric proton pump and bone resorption stimulated by parathyroid hormone (Hayashi et al. 1990). In addition, scopadulcic acid B showed antitumour promoting activities (Hayashi et al. 1991). Because of their unique carbon skeleton and many sided biological ac- tivities, they were paid much attention as chemical synthetic targets by organic synthetic chemists. In a previous study, Nath (1943) has studied the antidiabetic effect of *Scoparia dulcis* and obtained a glycoside, amellin from fresh plant and reported that it brought relief in other complications accompanied with diabetes (i.e., pyorrhoea, retinopathy, joint pain, susceptibility to cold etc.) within a very short period.

The elevated levels of blood glucose in diabetes produce oxygen-free radicals that cause membrane damage due to peroxidation of membrane lipids and protein glycation (Baynes 1991). Glucose auto-oxidize in the presence of transition metal ions generates oxygen-free radicals, which make the membrane vulnerable to oxidative damage (Hunt et al. 1990). The oxidative stress and resultant tissue damage are important component in the pathogenesis of diabetic complications (Baynes 1991). The free radicals react with biomembrane causing oxidative destruction of polyunsaturated fatty acids forming cytotoxic aldehydes by a process known as lipid peroxidation (LPO) (Wolff 1993). The extent of LPO was measured in terms of thiobarbituric acid reactive substances (TBARS) and lipid hydroperoxides (HPX), which are the end products of LPO. Several studies in human and animal models, using TBARS assay have shown increased LPO in membranes and lipoproteins in the diabetic state (Griesmacher et al. 1995; Krishnakumar et al. 1999). HPX formed by LPO have direct toxic effects on endothelial cells and also degrade to form hydroxyl radicals (OH*) (Testafamariam 1993). The action of streptozotocin produces reactive free radicals, which have been shown to be cytotoxic to the B-cells of the pancreas (Ivorra et al. 1989). As the diabetogenic action of streptozotocin is preventable by superoxide dismutase (SOD), catalase (CAT) and other OH* scavengers such as ethanol and dimethyl urea, there is evidence to suggest that the action of streptozotocin involve a superoxide anion and OH* (Asplund et al. 1984). Thus, streptozotocin-induced diabetes could elicit changes in the antioxidant defense systems in response to increased oxidative stress. The deleterious effects of superoxide radicals ($O_2^{\bullet-}$) and OH^* in oxidative stress can be counteracted by antioxidant enzymes such as SOD, CAT and glutathione peroxidase (GPx). In addition to these enzymes, glutathione-S-transferase (GST) provides glutathione (GSH) and help to neutralize toxic electrophiles. There is evidence to show the role of free radicals in diabetes and studies indicate that tissue injury in diabetes may be due to free radicals (Wohaieb and Godin 1987; Kakkar et al. 1995). Diabetes is becoming pandemic and despite the recent surge in new drugs to treat and prevent the condition, its prevalence continues to soar (Tiwari and Madhusudana Rao 2002).

Thus, the present study was undertaken to assess the antiperoxidative and antioxidant effect of *Scoparia dulcis* in streptozotocin-induced diabetic rats.

Materials and Methods

Animals

Male albino Wistar rats, body weighing 180–200 g bred in Central Animal House (Rajah Muthiah Medical College, Annamalai University, India) were used in this study. The animals were fed on a pellet diet (Hindustan Lever Ltd., Mumbai, India) and water *ad libitum*. The animals used in the present study were maintained in accordance with the guidelines of the National Institute of Nutrition, Indian Council

of Medical Research (Hyderabad, India) and approved by the Ethical Committee (Vide No. 73, 2001) of Annamalai University.

Drugs and chemicals

All the drugs and biochemicals used in this experiment were purchased from Sigma Chemical Company Inc. (St. Louis, MO, USA). The chemicals were of analytical grade.

Plant material

Scoparia dulcis L. plants were collected from Neyveli (Cuddalore District, Tamil Nadu, India). The plant was identified and authenticated at the Herbarium of Botany Directorate in Annamalai University. A voucher specimen (No. 3412) was deposited in the Botany Deartment of Annamalai University.

Preparation of Scoparia dulcis plant extract (SPEt)

Aqueous and chloroform extracts

500 g of *Scoparia dulcis* fresh whole plants were extracted with 1.5 l of water/chloroform by the method of continuous hot extraction. The filtrate was evaporated to constant weight on a rotavapor. The residual extract was dissolved in sterile water and used in the investigation (Jain 1968).

Ethanol extract

500 g of fresh plant of *Scoparia dulcis* were chopped into small pieces soaked overnight in 1.5 l of 95 % ethanol. This suspension was filtered and the residue was resuspended in an equal volume of 95 % ethanol for 48 h and filtered again. The two filtrates were pooled and the solvents were evaporated in a rotavapor at 40–50 ℃ under reduced pressure and lyophilized. A greenish-black powdered material was obtained (20–30 g). It was stored at 0–4 ℃ until used. When needed, the residual extract was suspended in distilled water and used in the study (Hossain et al. 1992).

Induction of experimental diabetes

A freshly prepared solution of streptozotocin (45 mg/kg) in 0.1 mol/l citrate buffer, pH 4.5 was injected intraperitoneally in a volume of 1 ml/kg (Siddique et al. 1987). 48 h after streptozotocin administration, rats with moderate diabetes having glycosuria and hyperglycemia (i.e. with blood glucose of 200–300 mg/dl) were taken for the experiment.

Experimental design

In the experiment, a total of 72 rats (66 diabetic surviving rats, 6 normal rats) were used. The rats were divided into 12 groups of 6 rats each. Three doses of aqueous, ethanolic and chloroform extracts (50, 100 and 200 mg/kg body weight *per* day) and glibenclamide (600 µg/kg) were tested. All doses were started 48 h after streptozotocin injection. Blood samples were drawn at weekly intervals till

the end of study (i.e., 3 weeks). At the end of 3 weeks, all the rats were killed by decapitation under pentobarbitone sodium (60 mg/kg) anaesthesia. Blood was collected in tubes containing potassium oxalate and sodium fluoride solution for the estimation of blood glucose and plasma was separated for assay of insulin. Liver and kidney were dissected out, washed in ice cold saline, patted dry and weighed.

Biochemical analysis

Determination of blood glucose and plasma insulin

Fasting blood glucose was estimated by O-toluidine method (Sasaki et al. 1972). Plasma insulin was estimated using enzyme-linked immunosorbent assay kit (Boehringer Mannheim, Germany).

Estimation of LPO

LPO in tissues were estimated colorimetrically by TBARS and HPX by the method of Nehius and Samuelson (1968) and Jiang et al. (1992), respectively. In brief, 0.1 ml of tissue homogenate (Tris-HCl buffer, pH 7.5) was treated with 2 ml of (1 : 1 : 1 ratio) TBA-TCA-HCl reagent (TBA 37%, TCA 15% and 0.25 N HCl) and placed in water bath for 15 min, cooled and centrifuged at room temperature for 10 min at 1,000 rpm. The absorbance of clear supernatant was measured against reference blank at 535 nm and expressed as mmol/100 g tissue.

HPX were expressed as mmol/100 g tissue. 0.1 ml of tissue homogenate was treated with 0.9 ml of fox reagent (88 mg butylated hydroxytoluene, 7.6 mg xylenol orange and 9.8 mg ammonium ion sulphate were added to 90 ml of methanol and 10 ml 250 mmol/l sulphuric acid) and incubated at 37 ℃ for 30 min. The colour developed was read colorimetrically at 560 nm.

Determination of CAT and SOD

CAT was assayed colorimetrically at 620 nm and expressed as μmoles of hydrogen peroxide (H_2O_2) consumed/min/mg protein as described by Sinha (1972). The reaction mixture (1.5 ml vol.) contained 1.0 ml of 0.01 mol/l phosphate buffer (pH 7.0), 0.1 ml of tissue homogenate and 0.4 ml of 2 mol/l H_2O_2. The reaction was stopped by the addition of 2.0 ml of dichromate-acetic acid reagent (5% potassium dichromate and glacial acetic acid were mixed in 1 : 3 ratio).

SOD was assayed utilizing the technique of Kakkar et al. (1984). A single unit of enzyme was expressed as 50% inhibition of nitroblue tetrazolium reduction/min/mg protein.

Determination of GPx and reduced GSH

GPx activity was measured by the method described by Rotruck et al. (1984). Brifely, reaction mixture contained 0.2 ml of 0.4 mol/l phosphate buffer (pH 7.0), 0.1 ml of 10 mmol/l sodium azide, 0.2 ml of tissue homogenate (homogenised in 0.4 mol/l, phosphate buffer pH 7.0), 0.2 ml GSH, 0.1 ml of 0.2 mmol/l H_2O_2. The contents were incubated at 37 ℃ for 10 min. The reaction was arrested by 0.4 ml of 10% TCA, and centrifuged. Supernatant was assayed for GSH content by using

Ellmans reagent (19.8 mg of 5,5'-dithiobisnitro benzoic acid in 100 ml of 0.1 %
sodium nitrate).

GSH was determined by the method of Ellman (1959). 1.0 ml of supernatant
was treated with 0.5 ml of Ellmans reagent and 3.0 ml of phosphate buffer (0.2
mol/l, pH 8.0). The absorbance was read at 412 nm. GPx activity was expressed
as μg of GSH consumed/min/mg protein and reduced GSH as mg/100 g of tissue.

Determination of GST

The GST activity was determined spectrophotometrically by the method of Habig
et al. (1974). The reaction mixture (3 ml) contained 1.0 ml of 100 mmol/l phosphate
buffer (pH 6.5), 0.1 ml of 30 mmol/l 1-chloro-2,4-dinitrobenzene (CDNB) and 1.7
ml of double distilled water. After pre-incubating the reaction mixture at 37 ℃ for
5 min, the reaction was started by the addition of 0.1 ml of tissue homogenate and
0.1 ml of GSH as substrate. The absorbance was followed for 5 min at 340 nm.
Reaction mixture without the enzyme was used as blank. The activity of GST was
expressed as mmoles of GSH-CDNB conjugate formed/min/mg protein using an
extinction coefficient of 9.6 $(\text{mmol/l})^{-1}$.

Estimation of protein

Protein was determined by the method of Lowry et al. (1951) using bovine serum
albumin as standard, at 660 nm.

Statistical analysis

The data for various biochemical parameters were analysed using ANOVA and the
group means were compared by Duncans multiple range test (DMRT). Values were
considered statistically significant when $p < 0.05$ (Duncan 1957).

Results

In all groups prior to streptozotocin administration, the basal levels of blood glu-
cose of the rats were not significantly different. However, 48 h after streptozotocin
administration, blood glucose levels were significantly higher in rats selected for
the study. In contrast, non-diabetic controls remained persistently euglycaemic
throughout the course of the study.

Table 1 shows the effect of treatment with extracts on blood glucose levels.
In all the SPEt-treated groups (all doses) a significant antihyperglycaemic ($p <$
0.01) effect was evident from first week onwards the decrease in blood sugar being
maximum on completion of the third week (66.5 %, $p < 0.001$) in the group receiving
200 mg/kg/day of aqueous SPEt. On the other hand, ethanolic- and chloroform
extracts-treated groups showed an antihyperglycaemic effect much later (i.e. on
completion of the third week) in groups receiving 200 mg/kg *per* day (60.5 and
56.3 %, respectively). On the basis of these studies, doses of 200 mg/kg *per* day of
aqueous, SPEt was selected for further evaluation.

Table 1. Effect of 3-week treatment with various doses of aqueous, ethanolic and chloroform *Scoparia dulcis* plant extract (SPEt) on glucose in normal and experimental rats

Groups	Day 0	48 h after STZ injection	1 week	2 weeks	3 weeks
				after treatment	
			Blood glucose (mg/dl)		
Normal	80.0 ± 3.0	84.1 ± 5.1	82.1 ± 5.9	81.0 ± 6.0	81.4 ± 5.9
Diabetic control	82.0 ± 4.9	265.0 ± 19.4**	280.0 ± 12.9**	286.0 ± 12.9**	298.0 ± 15.7**
Diabetic + SPEt-Aq-50	79. ± 3.3	255.0 ± 16.2	235.0 ± 13.8* (6.3)	209.1 ± 11.4** (16.6)	185.0 ± 9.7** (26.4)
Diabetic + SPEt-Aq-100	84.0 ± 6.9	247.1 ± 13.7	211.0 ± 12.1* (14.6)	162.0 ± 13.2** (34.5)	113.0 ± 7.3** (54.3)
Diabetic + SPEt-Aq-200	77.2 ± 4.0	256.3 ± 16.6	190.0 ± 12.9** (25.8)	129.0 ± 12.1** (49.7)	86.0 ± 6.5** (66.5)
Diabetic + SPEt-Alc-50	79.0 ± 4.3	246.0 ± 13.2	236.3 ± 10.2* (3.7)	218.0 ± 9.7* (11.2)	190.0 ± 6.5** (22.6)
Diabetic + SPEt-Alc-100	82.0 ± 4.7	253.0 ± 14.1	214.0 ± 11.4* (15.4)	173.0 ± 8.6** (31.6)	131.1 ± 5.1** (48.1)
Diabetic + SPEt-Alc-200	77.3 ± 4.2	259.0 ± 18.8	199.1 ± 13.0** (23.0)	138.0 ± 6.1** (46.7)	102.1 ± 6.8** (60.5)
Diabetic + SPEt-Chloro-50	80.0 ± 3.2	248.0 ± 14.0	238.0 ± 11.1* (4.0)	224.1 ± 6.7* (9.6)	206.0 ± 6.5** (17.0)
Diabetic + SPEt-Chloro-100	79.0 ± 4.5	241.3 ± 14.5	218.0 ± 9.3* (10.8)	180.4 ± 9.8** (25.2)	143.0 ± 9.2** (40.7)
Diabetic + SPEt-Chloro-200	82.2 ± 6.0	252.0 ± 13.0	203.0 ± 13.0** (19.4)	152.0 ± 13.3** (39.7)	110.0 ± 7.0** (56.3)
Diabetic + glibenclamide (600 μg/kg)	77.4 ± 4.4	246.0 ± 13.9	219.2 ± 7.0* (10.7)	192.0 ± 10.8** (21.9)	118.2 ± 4.4** (51.8)

Values are given as mean ± S.D. for 6 rats in each group. Values in parentheses indicated the percentage lowering of blood glucose in comparison to basal reading after streptozotocin (STZ) administration at 48 h. Diabetic control was compared with normal. Experimental groups were compared with corresponding values after STZ injection (48 h). * $p < 0.01$, ** $p < 0.001$.

Table 2. Body weight, food and fluid intake in streptozotocin diabetic rats before and after oral treatment with *Scoparia dulcis* plant extract (SPEt) for 3 weeks

Groups	Body weight (g)		Fluid intake (ml/rat per day)		Food intake (g/rat per day)	
	Initial	Final	Before	After	Before	After
Normal	176 ± 10	179 ± 9	77 ± 4.4	74 ± 4.7^a	14 ± 1.3	13 ± 1.1^a
Normal + SPEt-Aq-200	179 ± 3	182 ± 4	78 ± 2.7	75 ± 3.2^a	15 ± 2.9	14 ± 0.6^a
Diabetic control	181 ± 7	$137 \pm 7^{\bullet\bullet\bullet}$	155 ± 7.5	168 ± 6.0^b	42 ± 2.6	59 ± 2.1^b
Diabetic + SPEt-Aq-200	175 ± 5	$187 \pm 7^{***}$	120 ± 5.3	79 ± 5.8^c	24 ± 1.8	22 ± 9.3^c
Diabetic + glibenclamide (600 μg/kg)	210 ± 10	$230 \pm 10^{***}$	126 ± 22.0	92 ± 1.8^d	25 ± 1.5	33 ± 2.0^d

Values are given as mean $\pm$ S.D. from six rats in each group. Values not sharing a common superscript letter differ significantly at $p < 0.05$ (Duncan's multiple range test). Duncan procedure, ranges for the level: 2.95, 3.09, 3.20, 3.22. Diabetic control was compared with normal,
$^{\bullet\bullet\bullet} p < 0.001$. Experimental groups were compared with diabetic control, *** $p < 0.001$.

Table 3. Changes in levels of plasma insulin, tissue thiobarbituric acid reactive substances (TBARS) and hydroperoxides (HPX) in normal and experimental animals

Groups	Normal	Normal + SPEt-Aq-200	Diabetic control	Diabetic + SPEt-Aq-200	Diabetic + glibenclamide (600 μg/kg)
Plasma insulin (μU/ml)	10.3 ± 0.9^a	11.0 ± 0.7^a	4.2 ± 0.04^b	9.2 ± 0.4^c	8.5 ± 0.4^c
TBARS (mmol/100 g tissue)					
Liver	0.7 ± 0.04^a	0.7 ± 0.03^a	1.8 ± 0.07^b	1.1 ± 0.01^c	1.4 ± 0.05^d
Kidney	$1.7 \pm 0.09^{a,c}$	1.6 ± 0.1^a	3.5 ± 0.3^b	1.9 ± 0.2^c	2.3 ± 0.1^d
HPX (mmol/100 g tissue)					
Liver	79.0 ± 3.5^a	77.0 ± 2.4^a	97.8 ± 7.5^b	$82.0 \pm 4.3^{a,c}$	87.6 ± 6.1^c
Kidney	54.6 ± 3.8^a	51.5 ± 4.3^a	75.4 ± 5.8^b	60.8 ± 3.6^c	68.1 ± 4.2^d

Values are given as mean $\pm$ S.D. for 6 rats in each group. Values not sharing a common superscript letter differ significantly at $p < 0.05$ (DMRT). Duncan procedure, ranges for the level: 2.95, 3.09, 3.20, 3.22.

The body weights of SPEt- and glibenclamide-treated groups were increased significantly ($p < 0.001$) on 3rd week compared with diabetic control rats (Table 2). The food intake was significantly lowered in the SPEt-treated groups ($p < 0.001$) when compared with the diabetic control group. Similarly, the water intake was significantly reduced ($p < 0.001$) in SPEt-treated groups.

TBARS and HPX (Table 3) from liver and kidney homogenate were significantly decreased and plasma insulin was significantly increased with SPEt treatment whereas diabetic control rats showed significantly increased levels of LPO products and decreased level of plasma insulin.

For studying the effect of SPEt on antioxidant status, the activities of SOD, CAT, GPx, GST and GSH were measured (Table 4). They presented significant increases in SPEt treatment when compared with diabetic control rats. The extent of increase was higher in groups treated with aqueous SPEt than glibenclamide-treated groups. Treatment with SPEt to normal animals did not show any significant alterations.

Discussion

The use of traditional medicine and medicinal plants in most developing countries, as a normative basis for the maintenance of good health, has been widely observed (Bhattaram et al. 2002). Furthermore, an increasing reliance on the use of medicinal plants in the society has been traced to the extraction and development of several drugs and chemotherapeutics from these plants as well as from traditionally used rural herbal remedy (Bhattaram et al. 2002). This study was therefore

Table 4. Changes in activities of catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione-S-transferase (GST) and reduced glutathione (GSH) in liver and kidney of normal and experimental animals

Groups	Normal	Normal + SPEt-Aq-200	Diabetic control	Diabetic + SPEt-Aq-200	Diabetic + glibenclamide (600 μg/kg)
CAT (mg protein)					
Liver	$73.5 \pm 6.3^{a,b}$	75.3 ± 2.9^{b}	46.3 ± 2.5^{c}	69.2 ± 4.8^{a}	52.0 ± 2.3^{d}
Kidney	34.9 ± 6.5^{a}	35.5 ± 1.9^{a}	17.6 ± 1.4^{b}	28.7 ± 2.7^{c}	24.3 ± 2.4^{d}
SOD (mg protein)					
Liver	6.1 ± 0.6^{a}	6.2 ± 0.5^{a}	3.6 ± 0.3^{b}	5.0 ± 0.6^{c}	4.6 ± 0.4^{c}
Kidney	$14.9 \pm 1.3^{a,b}$	15.2 ± 0.9^{b}	9.6 ± 0.8^{c}	13.7 ± 1.2^{a}	11.9 ± 1.7^{d}
GPx (mg protein)					
Liver	6.1 ± 0.4^{a}	6.4 ± 0.2^{b}	3.2 ± 0.1^{c}	5.7 ± 0.3^{a}	4.1 ± 0.1^{d}
Kidney	4.2 ± 0.2^{a}	4.4 ± 0.2^{a}	2.1 ± 0.1^{b}	4.1 ± 0.2^{a}	3.8 ± 0.2^{c}
GST (mg protein)					
Liver	6.2 ± 0.5^{a}	6.4 ± 0.5^{a}	3.4 ± 0.2^{b}	5.9 ± 0.5^{a}	4.6 ± 0.3^{c}
Kidney	5.0 ± 0.4^{a}	5.3 ± 0.4^{a}	2.1 ± 0.1^{b}	4.8 ± 0.3^{a}	3.6 ± 0.3^{c}
GSH (mg/100 mg tissue)					
Liver	46.7 ± 3.9^{a}	48.1 ± 4.5^{a}	23.2 ± 1.8^{b}	40.0 ± 2.8^{c}	32.7 ± 2.1^{d}
Kidney	34.0 ± 2.3^{a}	36.3 ± 1.3^{b}	19.0 ± 1.5^{c}	30.4 ± 2.6^{d}	23.6 ± 2.0^{e}

Values are given as mean $\pm$ S.D. for 6 rats in each group. Values not sharing a common superscript letter differ significantly at $p < 0.05$ (DMRT). Duncan procedure, ranges for the level: 2.95, 3.09, 3.20, 3.22.

undertaken to assess antioxidant effect of *Scoparia dulcis* in streptozotocin diabetes.

Streptozotocin at a given dose preferentially destroys the pancreatic insulin secreting β-cells, what leaves less active pancreatic cells and results in a diabetes mellitus (Gilman et al. 1990). In the present study, treatment with aqueous, ethanolic and chloroform SPEt showed significant antihyperglycaemic activity. The maximum reduction in glucose levels was seen in groups receiving 200 mg/kg of the three extracts, respectively, and therefore the subsequent work was carried with aqueous extract at 200 mg/kg. This is probably indicative of efficacy of the plant. Moreover, it indirectly indicates that part of the antihyperglycaemic activity of this plant is due to release of insulin from the existing β-cells of pancreas. The possible mechanism of action of extract could be correlated with the reminiscent effect of the hypoglycaemic sulphonylureas, which promote insulin-secreting channels, membrane depolarisation, and stimulation of Ca^{2+} influx, an initial key step in insulin secretion. In this context a number of other plants have also been reported to have

antihyperglycaemic and insulin-release stimulatory effects (Latha and Pari 2003; Venkateswaran et al. 2002).

The involvement of free radicals in diabetes and the role of these toxic species in LPO and the antioxidant defense system have been studied. The results show increased LPO in the tissues of diabetic group. The increase in oxygen free radicals in diabetes could be due to increase in blood glucose levels, which upon auto-oxidation generate free radicals. Streptozotocin has been shown to produce oxygen free radicals (Ivorra et al. 1989). Lipid peroxide mediated tissue damages have been observed in the development of type I and type II diabetes mellitus (Feillet-Coudray et al. 1999). Previous studies have reported that there was an increased LPO in liver and kidney of diabetic rats (Pari and Latha 2002; Venkateswaran and Pari 2002).

Under *in vivo* conditions, GSH acts as an antioxidant and its decrease was reported in diabetes mellitus (Baynes and Thorpe 1999). We have observed a significant decrease in GSH levels in liver and kidney during diabetes. The decrease in GSH levels represents increased utilization due to oxidative stress (Anuradha and Selvam 1993). The depletion of GSH content may also lower the GST activity as GSH is required as a substrate for GST activity (Rathore et al. 2000). Depression in GPx activity was also observed in liver and kidney during diabetes. GPx has been shown to be an important adaptive response to condition of increased peroxidative stress (Matkovics et al. 1982). The increased GSH content in the liver and kidney of the rats treated with SPEt and glibenclamide may be one factor responsible for inhibition of LPO.

SOD and CAT are the two major scavenging enzymes that remove toxic free radicals *in vivo*. Previous studies have reported that the activity of SOD is low in diabetes mellitus (Vucic et al. 1997). Reduced activities of SOD and CAT in liver and kidney have been observed during diabetes and this may result in a number of deleterious effects due to the accumulation of $O_2^{\bullet-}$ and H_2O_2 (Searle and Wilson 1980). Administration of SPEt increased the activity of enzymes and may help to control free radical, as *Scoparia dulcis* has been reported to be rich in flavonoids and diterpenoids, well-known antioxidants (Hayashi et al. 1990, 1991, 1993), which scavenge the free radicals generated during diabetes. Any compound, natural or synthetic, with antioxidant properties, might contribute towards the partial or total alleviation of this damage. Therefore, removing $O_2^{\bullet-}$ and OH^* is probably one of the most effective defenses against diseases (Lin et al. 1995). The result of the SOD and CAT activity suggest that SPEt contains a free radical scavenging activity, which could exert a beneficial action against pathological alterations caused by the presence of $O_2^{\bullet-}$, H_2O_2 and OH^*. This action could involve mechanisms related to scavenging activity.

In conclusion, the present investigation show that SPEt possesses an antidiabetic effect in addition to antioxidant activity, which may be attributed to its protective action on LPO and to the enhancing effect on cellular antioxidant defense contributing to the protection against oxidative damage in streptozotocin diabetes.

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