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Antioxidant potential of *Coriandrum sativum* L. seed extract

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The seeds of *C. sativum* are used as a traditional drug for the treatment of diabetes. The antioxidant and free-radical-scavenging property of seeds *in vitro* was studied and also investigated whether the administration of seeds curtails oxidative stress in the kidney of streptozotocin-induced diabetic rats. Incorporation of seed powder in the diet led to marked lowering of blood glucose and a rise in the levels of insulin in diabetic rats. A parallel beneficial effect was observed on oxidant –antioxidant balance in the kidney. Addition of coriander seed powder not only inhibited the process of peroxidative damage but also significantly reactivated the antioxidant enzymes and antioxidant levels in diabetic rats. The total polyphenolic content of the seeds was found to be 12.2 gallic acid equivalents (GAE)/g while total flavanoid content was found to be 12.6 quercetin equivalents/g. The seeds also showed scavenging activity against superoxides and hydroxyl radicals in a concentration -dependent manner. Maximum free radical-scavenging action and free radical reducing power of coriander seed extract was observed at a concentration of 50 µg GAE. Islet histology structures showed degeneration of pancreatic islets in diabetic rats which was also reduced in diabetic rats treated with seed powder. These results show that *C. sativum* seeds not only possess antihyperglycemic properties but antioxidative properties also. Increased dietary intake of coriander seeds decrease the oxidative burden in diabetes mellitus.

Keywords: Antioxidant level, *Coriandrum sativum.* L, Diabetes, Oxidative stress, Pancreatic β cells

Diabetes is a group of metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, or action or both. The World Health Organisation (WHO) predicts that 300 million people world-wide will have diabetes mellitus by the year 2025[1]. It is also predicted that more than 57 million Indians would suffer from diabetes by the year 2025[2].

The increasing prevalence of the disease and significant morbidity associated with diabetic complications has created an upsurge of interest to test the therapeutic potential of traditionally reputed Indian medicinal plants for the antidiabetic activity[3], through their free radical-scavenging activity[4]. Spice therapy has become a major approach for the treatment and control of diabetes[5]. *Coriandrum sativum* Linn [Umbelliferae (Apiaceae)] is an annual herb and is commonly known as coriander in English, *Dhaniyaa* in Hindi, *Dhanya* in Sanskrit and *Kotthamalli* in Tamil. The seeds of coriander are one of the most important spices in the world and are regularly used by the Indian kitchen. In addition to its culinary value, coriander is known for its wide range of healing properties. It is generally used in gastrointestinal complaints such as anorexia, dyspepsia, flatulence, diarrhea, griping pain and vomiting[6] and as an antiedemic, antiseptic and emmenagogue[7]. The traditional claim of its antidiabetic activity has been validated in streptozotocin (STZ)-diabetic mice[8], and in high fat diet rats[9].

Significant organ damage occurs during the progression of diabetes and kidney is the most affected organ, since the entry of glucose in this tissue is not regulated by insulin. Diabetes is associated with overproduction of reactive oxygen species (ROS) and diminution of antioxidants[10]. ROS mediate activation of signal transduction cascades and transcription factors leading to expression of specific genes that produce tissue damage and ultimately to diabetic complications.

Reports on the antiradical activity of coriander seeds *in vitro* are sparse[11,12]. This prompted us to investigate the effect of coriander seeds on the oxidant-antioxidant system in diabetic rat kidney and to carryout a systematic analysis of its free

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radical-scavenging activity *in vitro*. The study may help in identifying a potential therapeutic lead compound for diabetic nephropathy (DN) since oxidative damage is one of the major factors that contribute to DN.

Materials and Methods

Chemicals—Streptozotocin (STZ) was purchased from Sigma-Aldrich, St Louis, MO, USA. The kits for glucose and insulin assays were purchased from Qualigen Diagnostics, Mumbai, India and Boeringer, Manheim, Germany respectively. BSA was purchased from Merck Pvt Ltd, Mumbai, India. All other chemicals and solvents used were of analytical grade and were purchased from Sisco Research Laboratories (SRL) Mumbai, India.

Animals—Adult male Wistar rats of age 7-8 weeks weighing approximately 180-200 g were used for the present study. The animals were maintained under controlled conditions with 12:12 h L:D cycle at 22º±3ºC and 30-70% RH. The animals used in the present study were maintained in accordance with the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) and approved by the Institutional Animal Ethical Committee (IAEC), Rajah Muthiah Medical College, Annamalainagar [Reg No: 160/1999/ CPCSEA vide No.562]. Animals received a standard pellet diet (Karnataka State Agro Corporation, Agro Feeds Division, Bangalore, India) and water *ad libitum*.

Plant material—Coriander seeds obtained from commercial source, Chidambaram, Tamilnadu, India were finely powdered. The seeds were authenticated by Dr. Venkatesalu, Reader in Botany, Annamalai University. A voucher specimen of the plant (No. 201) has been deposited in the herbarium at the department of Botany, Annamalai University.

In vivo studies

Induction and assessment of diabetes mellitus—The rats were rendered diabetic by a single ip injection of STZ (45 mg/kg body weight) dissolved in 0.1*M* citrate buffer *p*H 4.5. Two days after STZ treatment, fasting blood samples were collected. Rats having blood glucose levels higher than 250 mg/dl were identified as diabetic. The dosage of seed powder was fixed on the basis of study by Chithra and Leelamma[13].

Experimental groups—After acclimatization for 7 days, the animals were divided into following 4 groups of 6 each**:**

Group I:(CON) control animals received 0.5 ml saline (ip).
Group II:(DIA) rats administered STZ by (45mg/kg; ip) dissolved in 0.1*M* citrate buffer *p*H 4.5.
Group III:(DIA +COR) diabetic rats treated with seed powder (10g/100g feed)
Group IV:(CON+COR) control animals treated with seed powder (10g/100g feed)

At the end of 45 days, the animals were anesthetized by ketamine hydrochloride (35 mg/kg, ip) and killed by cervical decapitation. Blood was collected from the jugular vein using heparin as the anticoagulant. Glucose, plasma insulin and glycated hemoglobin[14] (% of total hemoglobin) were assayed.

After sacrifice, kidney tissue was removed, cleaned, and processed for biochemical measurements. Tissue homogenate was prepared with 0.1 *M* Tris-HCl buffer *p*H 7.4.

Preparation of plasma and hemolysate—The blood samples were centrifuged at 1000 *g* for 20 min. The clear plasma was separated by a Pasteur pipette. The red blood cells (RBCs) were washed thrice with ice cold saline. From this, 0.5 ml of RBC was pipetted out and lysed in 4.5 ml 0.05 *M* Tris HCl buffer, *p*H 7.4 to prepare the hemolysate. This was used for further biochemical analysis.

Assay of oxidative stress parameters—Oxidative stress was assessed by quantification of thiobarbituric acid reactive substances (TBARS)[15], lipid hydroperoxides (LHP)[16], and the level of protein carbonyl (PC)[17]. Levels of nonenzymic antioxidants vitamin C[18] and E[19] and GSH[20] were quantified and the activities of enzymic antioxidants such as superoxide dismutase (SOD)[21], catalase (CAT)[22], glutathione peroxidase (GPx)[23] and glutathione-s-transferase (GST)[24] estimated.

In vitro studies

Preparation of plant material—For *in vitro* studies, a decoction was prepared from the seeds as per Gray and Flatt[25]. The seeds were ground into a fine powder. Powdered material (1 g) was boiled for 30 min in 40 ml cold distilled water and then

cooled. This suspension was filtered using Whatman no. 1 paper and the volume was made up to 40 ml with distilled water. This decoction has been referred to as CSEt.

Estimation of total phenolic and flavanoid content—The total phenolic content of CSEt was determined[26]with gallic acid (GA) as the standard and was expressed as gallic acid equivalents (GAE)/g. The flavanoid contents were measured by the aluminium chloride colorimetric assay[27]. Aliquot of extract or standard (quercetin) was added to the tube containing 4 ml distilled water and 0.3 ml of 5 % sodium nitrate. After 5 min, 0.3 ml of 10 % aluminium chloride was added followed by the addition of 2 ml 1*M* NaOH. The total volume was made upto 10 ml with distilled water. The colour developed was read at 510 nm. The flavanoid content was expressed in quercetin equivalents/g.

Hydroxyl radical scavenging assay—The hydroxyl radical scavenging activity of the extract was evaluated by the method of Halliwell *et al*.[28]. The incubation mixture in a total volume of 1 ml contained 0.1 ml of buffer, varying concentrations of CSEt (10, 20, 30, 40 and 50 µg GAE), 0.2 ml of ferric chloride, 0.1 ml of ascorbic acid, 0.1 ml of EDTA , 0.1 ml of H_2O_2 and 0.2 ml of 2-deoxribose. The contents were mixed thoroughly and incubated at room temperature for 60 min and then added 1 ml of TBA (1g in 100 ml 0.05 *N* NaOH) and 1 ml of TCA. All the tubes were kept in a boiling water bath for 30 min. GA was used as a positive control for comparison. The absorbance of the supernatant was read in a spectrophotometer at 535 nm with reagent blank containing water in place of CSEt. Decreased absorbance of the reaction mixture indicated increased hydroxyl radical scavenging activity. The percentage scavenging was calculated using the formula given below:

$$\text{Scavenging } (\%) = \frac{\text{control OD} - \text{test OD}}{\text{control OD}} \times 100$$

Superoxide anion scavenging activity—Superoxide anion scavenging activity was determined by the method of Nishimiki *et al*[29]. The assay was based on NADH-PMS-NBT colour reaction. The reaction mixture in a final volume of 2.5 ml contained, 1 ml of NBT(100 µmol NBT in 100 m*M* phosphate buffer, *p*H 7.4), 1 ml of NADH solution (468 µmol in 100 m*M* phosphate buffer, *p*H 7.4) and varying volumes of CSEt (10, 20, 30, 40 and 50 µg) were added and mixed well. The reaction was started by the addition of 100 µl of PMS (60 µmol/100 m*M* phosphate buffer, *p*H 7.4). The reaction mixture was incubated at 30°C for 15 min after which the absorbance was measured at 560 nm. Blank contained all the solutions and water in place of CSEt. GA was used as standard for comparison. Decreased absorbance of the reaction mixture indicated increased superoxide anion scavenging activity. The percentage scavenging was calculated as per the formula given above.

Reducing powe—The reducing power of CSEt was determined as per Oyiazu[30]. Substances, which have reduction potential react with potassium ferricyanide (Fe^{3+}) to form potassium ferrocyanide (Fe^{2+}), which then reacts with ferric chloride to form ferric-ferrous complex that has an absorption maximum at 700 nm. Varying volumes of (0.1-0.5 ml) of CSEt containing 10, 20, 30, 40 and 50 µg GAE were taken in the test tubes, mixed with 2.5 ml of phosphate buffer (0.2 *M*, *p*H 6.6) and 2.5 ml of potassium ferricyanide (1% w/v). The mixture was incubated at 50ºC for 20 min. Later 1.5 ml of TCA was added and centrifuged at 3000 *g* for 10 min. Supernatant (0.5 ml) from all the tubes was mixed with 1 ml of distilled water and 0.5 ml of $FeCl_3$ (0.1 w/v). The absorbance was measured at 700 nm in a spectrometer. Blank contained the same with water in the place of CSEt. Increased absorbance of the reaction mixture indicated increasing reducing power. GA was used as positive control for comparison.

DPPH•(2,2'-diphenyl-b-picrylhydrazyl) radical radical scavenging assay—The DPPH is a stable free radical, which has been widely accepted as a tool for estimating the free radical-scavenging activities of antioxidants. The free radical-scavenging activity of CSEt against DPPH• was determined[31]. Reaction mixture in a total volume of 3 ml contained 1 ml of 100 µM DPPH• in methanol, equal volumes of CSEt containing 10, 20, 30, 40 and 50 µg GAE and 1 ml of phosphate buffer *p*H 7.4. The tubes were incubated for 10 min at 37º C in dark. The absorbance was measured at 517 nm. Blank was carried out to determine the absorbance of DPPH• in absence of the extract. The percentage of free radical scavenging was calculated as per the formula mentioned above.

Islet histology—A portion of pancreas was fixed in 2% formalin for 24 h, dried and embedded in paraffin. Sections (3-5 µm thick) were stained with

hematoxylin and eosin for granulated beta-cells and examined under light microscopy.

Statistical analysis—The results of animal experiments are given as mean±SE. Data within groups were analyzed using one way analysis of variance (ANOVA) followed by DMRT. For *in vitro* studies the results given are the average of 5 determinations and were analyzed using Student's "*t*" test for unpaired comparison. A value of $P<0.05$ was considered statistically significant.

Results and Discussion

Spices have been recognized to possess medicinal properties and their use in traditional systems of medicine has been on record for a long time[32]. Coriander seeds are one such spice used traditionally to treat diabetes. STZ-treated rats were found to be hyperglycemic with a corresponding hypoinsulinaemia (Table 1). STZ is a deoxy-s [(methyl-nitrosoamino) carbonyl)-amino]-D gluco pyranose molecule that produces selective toxic effects on β cells that induces diabetes mellitus[33]. The amount of coriander powder consumed by each rat was calculated from the food intake and the average consumption was 1.2±0.5 g/day/rat. Treatment with coriander seeds produced significant decrease in blood glucose level (44%), and significant increase in plasma insulin level (40%) and reduction in glycated hemoglobin (58%) as compared to untreated diabetic rats. The antidiabetic potential of the seeds have been reported earlier[8,9] and the insulin-releasing and insulin–like activities by Gray and Flatt[25].

Elevation of lipid peroxides and TBARS is attributed to the enhanced production of ROS. In the present study, excessive formation of TBARS, LHP and PC (Table 2) the indices of lipid peroxidation was observed. Coriander seed powder supplementation significantly abrogated LHP levels suggesting the potent antioxidant activity of seed components such as linalool, limoene, quercetin, rutin, sitosterol cineole, p-hydroxy benzoic acid and many other compounds including tannins[34]. Elevated levels of lipid peroxidation in plasma and tissue is one of the characteristic features of chronic diabetes[35] and hence inhibition of free radical generation and oxidative damage could be considered as an important strategy in the management of diabetes. Lipid peroxides are a conglomeration of extremely reactive products of fatty acid peroxidation which is a common process in all oxygen-consuming cells and have been shown to bring about deleterious effects on the other cellular constituents like proteins and DNA. The rise in the lipid peroxide levels could also be attributed to the toxic effects of STZ on the kidney. Hyperglycemia induces glucose autooxidation, protein glycation and subsequent oxidative degradation of glycated proteins leading to disproportionate increase in ROS formation[36]. ROS potentially damage the

Table 1 — The Levels of fasting blood glucose ,plasma insulin and glycated hemoglobin in control and diabetic animals
[Values are means ± SD from each group]

Groups	Fasting blood glucose (mg/dl)	Plasma insulin (μU/ml)	Glycated Hb (% total Hb)
CON	92.87 ± 7.32	12.18 ± 0.55	2.31± 0.18
DIA	280.62 ± 8.59[a]	3.89 ± 0.38[a]	4.58±0.35[a]
DIA+COR	124.12 ± 7.22[b]	9.82 ± 1.17[b]	2.68±0.13[b]
CON+COR	94.24 ± 7.86	12.02 ± 0.99	2.58±0.14

P: <0.05
[a]significant as compared to control rats. [b]significant as compared to streptozotocin treated rats
CON, control rats; DIA, streptozotocin –treated rats; DIA +COR, streptozotocin induced rats treated with coriander seed powder; CON+COR, control rats treated with coriander seed powder

Table 2—Activities of LHP, TBARS and PC in plasma and kidney of control and experimental animals
[Values are means ± SD from each group]

Groups	LHP		TBARS		PC
	Plasma (μ mol/L)	Kidney (μmol /mg protein)	Plasma (μ mol/L)	Kidney (μmol /mg protein)	Kidney (μmol /mg protein)
CON	0.92 ±0.07	1.72 ± 0.13	2.80 ±0.21	1.66 ± 0.13	1.90 ± 0.14
DIA	1.31 ± 0.10[a]	2.38 ± 0.18[a]	5.28 ± 0.40[a]	2.76 ± 0.21[a]	2.29 ± 0.17[a]
DIA+COR	1.02 ±0.08[b]	1.76 ± 0.14[b]	2.98 ± 0.23[b]	1.72 ± 0.80[b]	1.97 ± 0.15[b]
CON+COR	0.95 ± 0.07	1.71 ± 0.13	2.82 ± 0.21	1.64 ± 0.12	1.88 ± 0.14

P <0.05; [a]significant as compared to control rats; [b]significant as compared to streptozotocin treated rats.
CON, control rat; DIA, streptozotocin –treated rats: DIA+COR, streptozotocin induced rats treated with coriander seed powde;. CON+COR, control rats treated with coriander seed powder.LHP-lipid hydroperoxide; TBARS- thiobarbutric acid reactive substances; PC- protein carbonyl;

biomolecules and activate the stress-signaling pathways that are implicated in the initiation and development of diabetic complications.

The effects of coriander seeds on the activities of SOD, CAT, GPx and GST and levels of non-enzymic antioxidants such as vitamins C and vitamin E and GSH are presented in Tables 3 and 4 respectively. Associated with changes in lipid peroxidation, the diabetic kidney showed decreased levels of antioxidants viz SOD, CAT, GST, GPx, Vit C, Vit E and GSH. Under hyperglycemic conditions SOD may undergo glycation at specific lysine residues causing inactivation[37]. ROS are known to attack proteins and Datta *et al*.[38] found that CAT and GPx are susceptible for free radical attack. The reduction in GSH and vitamins C and E could be attributed to increased utilization in an attempt to counteract the oxidative stress. These results are in affirmation with earlier studies in tissues of diabetic animals[39,40]. Antioxidants are very important in scavenging ROS and the removal of the toxic intermediates. A decrease in the activity of these cellular antioxidants can lead to an excess availability of O_2 and H_2O_2 in biological systems, which in turn generate $OH^{\bullet}$ resulting in initiation and propagation of lipid peroxidation.

Administration of coriander seed powder resulted in a significant increase in activities of these enzymes in kidney of diabetic rats. Chithra and Leelamma[13] observed that rats fed high fat diet supplemented with coriander seeds increased the antioxidant levels in Sprague-Dawley female rats. The excess availability of antioxidants upon coriander seed supplementation facilitates to enrich the antioxidant content, which could prevent the lipid peroxidation and protect against toxic effects of free radicals. H_2O_2-induced oxidative stress in human lymphocytes was suppressed by the polyphenolic compounds from coriander[41]. The antioxidant properties of coriander seeds could be directly linked to both scavenging activity against ROS and elevation of antioxidant

Table 3—Activities of SOD, CAT, GPx and GST in haemolysate and kidney of control

[Values are means ± SD from each group]

Groups	SOD		CAT		GPx		GST	
	Haemolysate (μmol/min/mg Hb)	Kidney (μmol/min/mg protein)	Haemolysate (μmol/min/mg Hb)	Kidney (μmol/min/mg protein)	Haemolysate (μmol/min/mg Hb)	Kidney (μmol/min/mg protein)	Haemolysate (μmol/min/mg Hb)	Kidney (μmol/min/ mg protein)
CON	3.04 ± 0.23	4.01 ± 0.31	170.47 ± 13.05	58.99 ± 4.80	9.14 ± 0.70	5.98 ± 6.46	6.28± 0.48	5.80 ± 0.44
DIA	2.34 ± 0.18[a]	2.74 ± 0.21[a]	140.04 ±10.71[a]	44.89 ± 3.43[a]	6.68 ± 0.51[a]	4.67 ± 0.35[a]	4.72 ± 0.36[a]	4.22 ± 0.35[a]
DIA+COR	2.98 ± 0.28[b]	3.94 ± 0.22[b]	168.67 ±10.31[b]	54.67 ± 3.13[b]	8.48 ± 0.65[b]	5.89 ± 0.45[b]	5.98 ± 0.46[b]	5.68 ± 0.43[b]
CON+COR	3.08 ± 0.23	4.03 ± 0.31	174.07 ± 13.32	59.23 ± 4.53	9.18 ± 0.70	6.00 ± 0.46	6.30 ± 0.48	5.82 ± 0.44

P: <0.05; [a]significant as compared to control rats; [b]significant as compared to streptozotocin treated rats
CON, control rats; DIA, streptozotocin –treated rats; DIA +COR, streptozotocin induced rats treated with coriander seed powder; CON+COR, control rats treated with coriander seed powder.

Table 4— Activities of GSH, vitamin C and E in plasma and kidney of control and experimental animals

[Values are means ± SD from each group]

Groups	GSH		Vitamin C		Vitamin E	
	Plasma (μmol/L)	Kidney (μmol /mg protein)	Plasma (μmol/L)	Kidney (μmol/mgprotein)	Plasma (μmol/L)	Kidney (μmol /mg protein)
CON	936.80 ± 71.17	164.15 ± 12.56	164.15 ±12.56	40.99 ± 2.57	24.43 ± 1.87	20.22 ± 1.78
DIA	648.55 ± 49.65[a]	4.64 ± 0.35[a]	102.86 ± 7.87[a]	24.02 ±1.84[a]	15.98 ± 1.23[a]	12.96 ± 0.99[a]
DIA +COR	876.63 ± 58.44[b]	5.38 ± 0.41[b]	156.11 ± 11.95[b]	38.28 ± 3.04[b]	22.28 ± 1.70[b]	18.72 ± 1.63 [b]
CON+COR	937.90 ± 71.80	5.33 ± 0.41	166.38 ± 11.74	41.22 ± 3.21	26.38 ± 2.02	21.02 ± 2.69

P <0.05; [a]significant as compared to control rats; [b]significant as compared to streptozotocin treated rats
CON, control rats; DIA, streptozotocin –treated rats; DIA +COR, streptozotocin induced rats treated with coriander seed powder; CON+COR, control rats treated with coriander seed powder.

make-up. Antioxidants generally decrease the level of oxidation by transferring the hydrogen atoms to the free radical structure[42]. The active components of coriander could act as electron donors, which can react with free radicals to form more stable products and thereby terminate the radical chain reaction. Susceptibility of kidney to oxidative stress during diabetes mellitus is an important factor in the development of DN, since ROS activates the inflammatory pathways that cause glomerular damage. Therefore improvement of antioxidant enzymes by the seed extract could be implicated in the utility of this plant in ameliorating the pathology of DN.

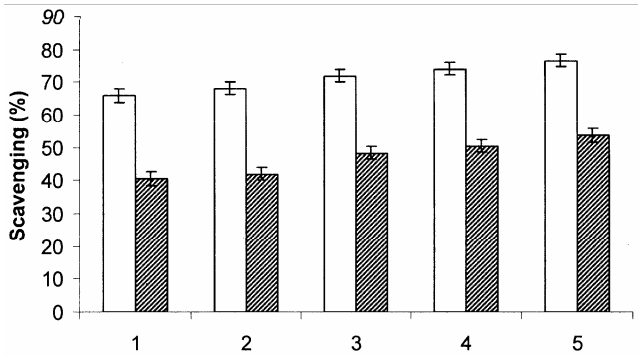

Fig.1— The hydroxyl radical- scavenging action of coriander seed extract (CSEt) and gallic acid (GA).[1= CSEt -10 µg gallic acid equivalents (GAE); GA-10 µg, 2= CSEt -20 µg gallic acid equivalents (GAE); GA-20 µg, 3= CSEt -30 µg gallic acid equivalents (GAE); GA-30 µg, 4= CSEt -40 µg gallic acid equivalents (GAE); GA-40 µg, 5= CSEt -50 µg gallic acid equivalents (GAE); GA-50 µg (□ CSEt ▨ GA) Results are means±SD of 5 measurements. ** significant at $P<0.001$ when compared with CSEt].

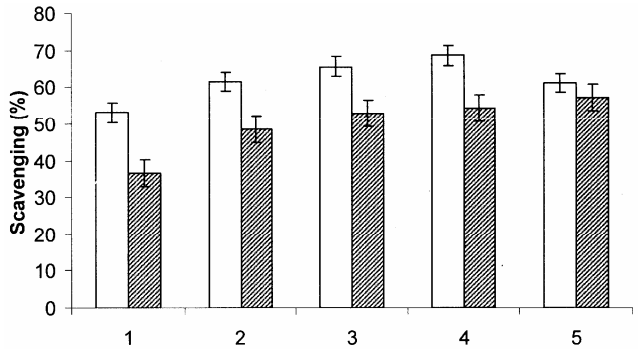

Fig.2— Superoxide anion scavenging effect of coriander seed extract (CSEt) and gallic acid (GA) [Results are means±SD of 5 measurements. ** significant at $P<0.001$ when compared with CSEt. NS-not significant when compared with CSEt. Other details are same as in Fig. 1.]

The total polyphenolic and flavanoid content of CSEt was determined to be 12.2 GAE/g and 12.6 quercetin equivalents/g CSEt respectively. The percentage hydroxyl radical-scavenging activity of CSEt and GA at various concentrations are presented in Fig. 1. The extract showed significant inhibitory activity in a concentration-dependant manner. The maximum inhibition was 70% at 40 µg. The concentration needed for 50% inhibition was 20 µg GAE.

Scavenging of superoxide anion by CSEt was proportional with increasing concentrations of the extract added and was comparable with that of GA (Fig. 2). The scavenging capacity of the CSEt was 52% at 10 µg GAE and 80% at 50 µg GAE. The reduction potential of CSEt at various concentrations is presented in (Fig. 3). There was a concentration-dependent increase in the reducing power of the extract as determined by the colour formation.

Inhibition of $DPPH^{\bullet}$ radical formation was proportional to increasing concentrations of the CSEt (Fig. 4). The inhibition percentage of CSEt was 45% at 10 µg GAE and 75% at 50 µg GAE while GA

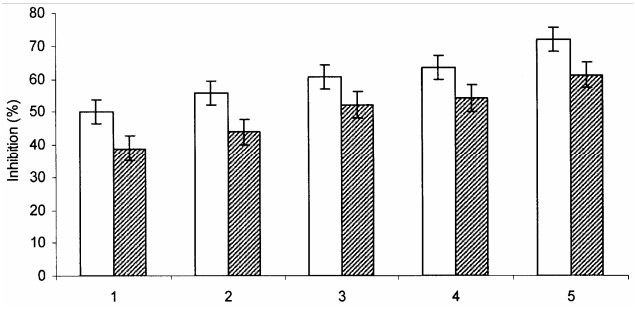

Fig.3—The DPPH scavenging capacity of coriander seed extract (CSEt) and gallic acid (GA)[Results are means±SD of 5 measurements. ** significant at $P<0.001$ when compared with CSEt. Other details are same as in Fig. 1]

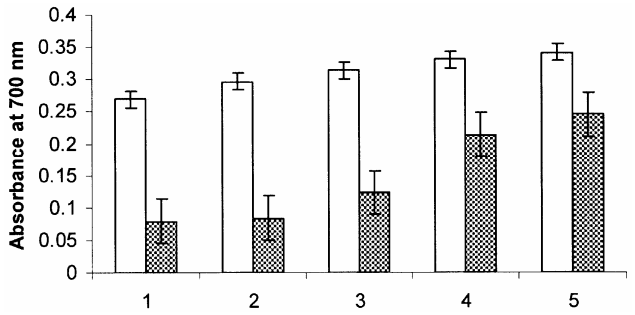

Fig.4—The Reducing power of coriander seed extract(CSEt) and gallic acid(GA) [Results are means±SD of 5 measurements. **significant at $P<0.001$ when compared with CSEt. Other details are same as in Fig. 1]

exhibited the 35% at 20 µg and 68% at 50 µg. CSEt exhibited strong inhibition of all the free radicals and the effect was more pronounced than GA.

The strong scavenging activity of coriander seeds against a spectrum of ROS, may be contributed by cumulative effect of various antioxidant phytochemicals[34]. The seeds were found to be more efficient in scavenging free radicals than GA. The crude oil fraction of coriander seeds is shown to posses strong radical scavenging ability against DPPH[10]. Coriander seeds and leaves scavenged DPPH radical and inhibited and Fe^{2+}-induced peroxidation in porcine brain[43]. The authors suggested that the inclusion of seeds and leaves from coriander in the cuisine would increase the antioxidant content of the food and thus prevent oxidative deterioration of food.

Under light microscopy (100X magnification), pancreatic sections from control rats and rats treated with seed powder showed normal structure, size, and distribution of both islets and islet cells (Fig. 5a and d). Focal lymphocyte infiltration, hydropic cell degeneration, decreased islet size and cell numbers were observed in STZ-treated rats (Fig. 5b). However, in STZ rats treated with coriander seed powder the extent of degeneration and lymphocyte infiltration was less severe (Fig. 5c). Coriander seed supplementation elicited a significant reduction in fat accumulation and protected against pancreatic cell damage induced by STZ.

The involvement of oxidative stress in the etiology and pathophysiology of hyperglycemia has been reviewed[44]. There may be a biochemical basis that involves ROS-induced activation of stress-sensitive pathways mediated by activated transcription factors and kinases which underlie the development of diabetes and late diabetic complications[45]. Because the prooxidant state is closely linked to the DN, coriander with antioxidant properties may prevent, reverse or delay the onset of pathology. These favorable effects can be attributed to the presence of different types of active principles with single or diverse range of biologic activities that can act individually or synergistically. Charaterization of active constituents is essential to propose the mechanism of action.

In conclusion the results of the present study provide new data indicating that coriander seeds possess beneficial action on kidney and pancreas. The beneficial effect of coriander seeds *in vivo* was verified by normalization of blood glucose and insulin, revival of β cells, regeneration of antioxidant

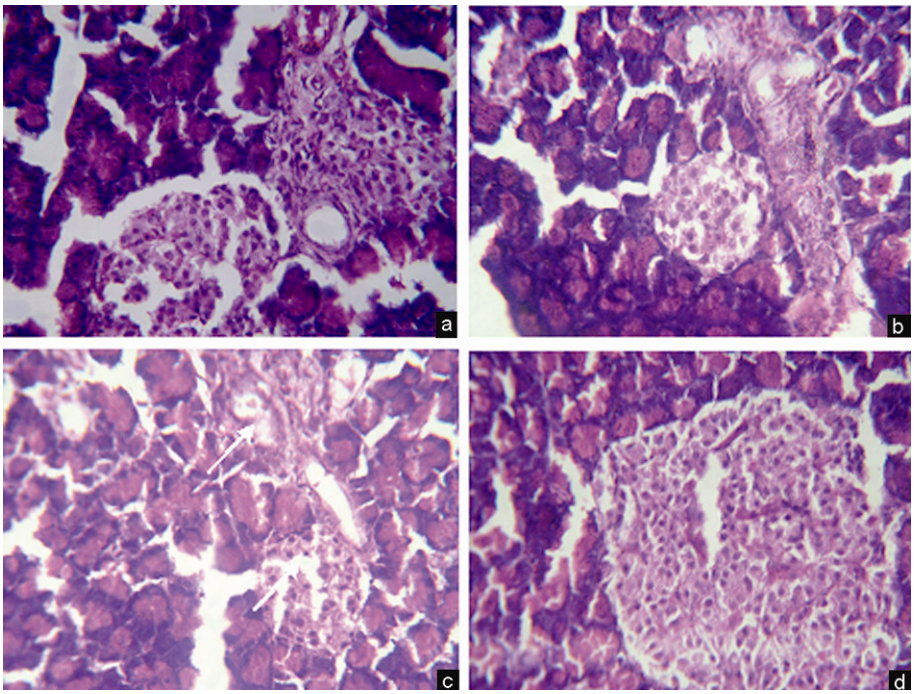

Fig 5 —Histology of pancreas- 5 (a) CON: Normal islet and acinar histology; 5 (b) DIA: Arrrow shows marked reduction in islet celluarity with focal fatty changes; lymphocyte infilteration, and cell degeneration, decreased islet size are seen; 5(c) DIA + COR: Arrow shows that mild increase in cellularity and absence of fatty change; degeneration and fatty changes are reduced; 5(d) CON+COR: Normal pancreatic architecture. [100 X; H& E]

apparatus and amelioration of peroxidative damage. *C. sativum* seeds appear to have a great potential as an adjunct therapy in the treatment of diabetes.

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