Research Article

BIOCHEMICAL EVALUATION OF ANTIDIABETIC, ANTILIPIDEMIC AND ANTIOXIDANT NATURE OF *CASSIA AURICULATA* SEEDS STUDIED IN ALLOXAN-INDUCED EXPERIMENTAL DIABETES IN RATS

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ABSTRACT

Cassia auriculata Linn. a member of genus Cassia belongs to family *Caesalpiniaceae* is commonly known as Tanner's cassia. Various parts of the plant have been reported to possess a number of therapeutic activities to manage several diseases. The flowers and seeds are reported to be useful in the treatment of diabetes. Hence, the present study was designed to evaluate the hypoglycemic, hypolipidemic and antioxidant properties of *Cassia auriculata* seed extract in alloxan-induced experimental diabetic rats. The effects of oral administration of *Cassia auriculata* seed extract (400 mg/kg b.w.) on the levels of biochemical parameters were determined in experimental groups of rats. The altered levels of biochemical parameters in the diabetic rats were significantly reverted back to near basal values by the administration of *Cassia auriculata* seed extract for 30 days. The levels of lipid peroxides in the plasma and pancreatic tissues of diabetic rats were elevated significantly and were normalized by the administration of *Cassia auriculata* seed extract. The activities of pancreatic enzymic antioxidants and the levels of plasma non-enzymic antioxidants were markedly declined in the diabetic rats. Upon treatment with *Cassia auriculata* seed extract to diabetic rats, these decreased levels were elevated to near normal values. The altered levels of lipid profile were reverted back to near normalcy upon the extract treatment. The results of the study indicate that *Cassia auriculata* seed extract possesses antilipidemic, antioxidant effects in addition to antidiabetic activity. The results are comparable with glyclazide, an oral standard hypoglycemic drug. The phytochemicals present in the *Cassia auriculata* seed extract may account for the observed pharmacological properties.

Keywords: *Cassia auriculata*, antidiabetic, antilipidemic, antioxidant nature.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder resulting from insulin deficiency and action. It is characterized by hyperglycemia, altered metabolism of carbohydrates, proteins and lipids[1]. The disease is associated with the development of secondary complications as neuropathy, renal failure, vision loss, macrovascular diseases and amputations[2]. Treatment with oral hypoglycemic agents is often associated with side effects related to pharmacokinetic properties, secondary failure rates, hypoglycemia, gastrointestinal disturbances, skin reactions, hematological disorders, and rise in hepatic enzyme levels[3]. Hence, the focus has been shifted to treat various ailments through plant-derived drugs due to their safety, efficacy, cultural acceptability and lesser side effects.

The medicinal value of plants lies in some chemical substances that produce a definite physiological action on the human body. The most important of these bioactive compounds of plants are alkaloids, flavonoids, tannins and phenolic compounds[4]. The WHO considers phytotherapy in its health programs suggested basic procedures for validation of drugs from plants origin in developing countries.

Cassia auriculata Linn a member of genus Cassia belonging to family caesalpiniaceae is commonly known as Tanner's cassia[5]. The plant is also known as Avaram in Tamil language or Avartaki in vernacular. The various parts of plant have been reported to possess a number of therapeutic activities to manage disease states like leprosy, asthma, gout, rheumatism[6] and diabetes[7]. It is also used as antipyretic, antiulcer and in the treatment of skin infections[8]. The plant has been reported to possess hepatoprotective[9], antiperoxidative and antihyper glycemic activity[10] and microbicidal activity[11].

In the absence of systemic studies in the literature, the present study was aimed to evaluate the hypoglycemic, hypolipidemic and antioxidant properties of *Cassia auriculata* seeds in alloxan induced experimental diabetes in rats.

MATERIALS AND METHODS

Plant material

The seeds of *Cassia auriculata* were procured and authenticated by a qualified taxonomist. A voucher specimen was deposited at the herbarium, University of Madras, Chennai.

Preparation of Plant extract

The *Cassia auriculata* seeds were dried at room temperature and powdered in an electrical grinder, which is then stored in an airtight container at 5°C until further use. The seed powder was delipidated with Petroleum Ether (60 - 80°C) for overnight. It was filtered and Soxhalation extracted the residue with 95% Ethanol. Ethanol was evaporated in a rotary evaporator at 40 - 50°C under reduced pressure.

Preliminary phytochemical screening

The ethanolic extract of *Cassia auriculata* seeds were subjected to preliminary phytochemical screening of various plant constituents[12,13].

Experimental animals

Male albino wistar rats (150-180 g) were purchased from TANUVAS, Madavaram, Chennai. The rats were housed in polypropylene cages lined with husk and kept in Animal house, Department of Biochemistry. It was renewed every alternate days. The rats were fed with commercial pellated rats chow (Lipton Ltd., Bangalore, India) and had free access to water. The experimental rats were maintained in a controlled environment (12:12 hours light/dark cycle) and temperature (30 ± 2°C). The experiments were designed and conducted in accordance with the ethical norms approved by Ministry of Social Justices and Empowerment, Government of India and Institutional Animal Ethics Committee Guidelines for the investigation of experimental pain in conscious rats. The rats were acclimatized for one week before starting the experiments.

Experimental design

The rats were grouped into 4 groups, comprising of 6 rats in each group as follows:

Group I : Control rats (Water and food *ad libitum*)

Group II : Alloxan induced diabetic Rats

Group III: Diabetic rats treated with *Cassia auriculata* seed extract (400 mg/Kg Body weight/day) in aqueous solution orally for 30 days.

Group IV: Diabetic rats treated with glyclazide (5mg/KgBody weight/day) in aqueous solution orally for 30 days.

During the experimental period, body weight and blood glucose levels of all the rats were determined at regular intervals. At the end of the experimental period, the rats were fasted over night, anaesthetized, and sacrificed by cervical decapitation. The blood was collected with and without anticoagulant for plasma and serum separation respectively.

Preparation of tissue homogenate

The pancreatic tissues were excised, rinsed in ice- cold saline. Known amount of the tissues were homogenized in Tris–HCl buffer (100 mM, pH 7.4) at 4°C, in a Potter–Elvehjem homogenizer with a Teflon pestle at 600 rpm for 3 min. The homogenate was then centrifuged at 12,000-×g for 30 min at 4°C. The supernatant was collected as tissue homogenate, which was used to assay various parameters.

Blood glucose level was estimated by the method of glucose oxidase/peroxidase as described by Trinde[14] and urea by Natelson *et al.*[15] Plasma was separated and used for insulin assay using ELISA kit for rats. Levels of hemoglobin and glycosylated hemoglobin were estimated according to methods of Drabkin and Austin[16] and Nayak and Pattabiraman[17], respectively. Plasma was used for protein assay[18] and serum for determination of creatinine[19] and uric acid[20].

The pancreatic tissue homogenate was then centrifuged at 5000g to remove cellular debris and supernatant was used for the determination of lipid peroxides and enzymatic antioxidants. Lipid peroxides were determined using thiobarbituric acid reactive substances by the method of Ohkawa *et al*.[21] Levels of vitamin C, vitamin E, ceruloplasmin and glutathione (GSH) were determined by the methods of Omaye *et al*,[22] Desai[23], Ravin[24], Sedlak and Lindsay[25], respectively. Enzymatic antioxidants such as superoxide dismutase[26], catalase[27], glutathione peroxidase[28] in pancreatic supernatant.

Oral Glucose Tolerance Test (OGTT)

At the end of the experimental period, a fasting blood sample was collected from all the groups of rats to perform oral glucose tolerance test, rats were fasted for 12 h before the test and 2 g/kg glucose solution was administered orally. Blood samples were taken by severing the tip of the tail 1 h before and at 30, 60, 90 and 120 minutes after glucose administration. Blood glucose was determined using ortho toluidine reagent.

Lipid profile

Plasma was used for the estimation of lipid profile. Cholesterol content was estimated by the method of Parekh and Jung[29]. Triglyceride was estimated by the method of Rice[30]. HDL Cholesterol fraction was separated by the precipitation techniques of Burstein and Scholnick[31] and the cholesterol content was determined by method of Parekh and Jung[29].

RESULTS

The preliminary results of the study revealed that *Cassia auriculata* seed extract at the dose of 400 mg/Kg body weight significantly normalize the elevated blood glucose level, body weight and restored biochemical parameters towards near normalcy.

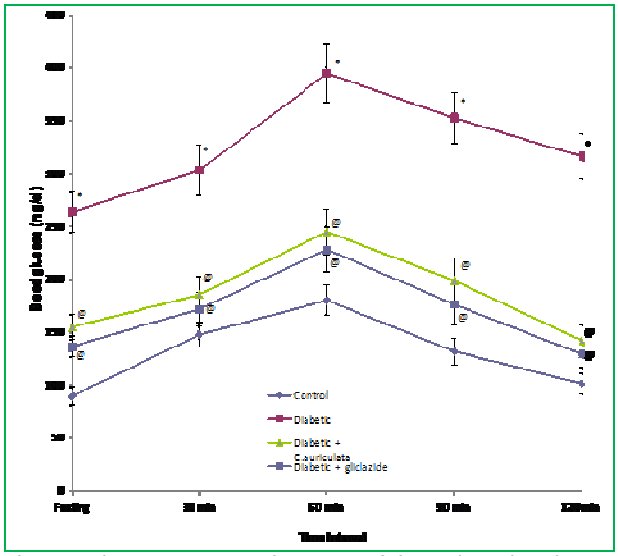
Table 1 shows the qualitative analysis of phytochemical in the ethanolic extract of *Cassia auriculata* seeds. Phytochemical evaluation indicated the presence of alkaloids, flavonoids, proteins, carbohydrates, saponins, tannins, glycosides and phenols.

Fig 1 shows the changes in the levels of blood glucose, after oral administration of glucose (3g/Kg) in normal control and experimental group of rats. The data of OGTT revealed that the blood glucose value in normal control rat reach peak at 60 minutes after the oral glucose load and gradually reverted back to near normal levels after 120 minutes. In diabetic control rats, the peak increase in blood glucose concentration was observed after 60 minutes and remained high over the next 60 minutes. Treated group showed definite lower peak blood glucose values, 60 minutes after glucose load also gives lower values almost at the end of 120 minutes.

Table 1: Phytochemical screening of the ethanolic extract of *Cassia auriculata* seeds

Phytoconstituents	Inference
Alkaloids	+
Flavonoids	+
Carbohydrates	+
Glycosides	-
Saponins	-
Tannins	+
Phytosterol	+
Triterpenoids	-
Proteins	-
Aminoacids	+
Anthraquinones	+
Phenols	+

Figure 1: Effect of *Cassia auriculata* seed extract on (GTT) in normal and alloxan induced diabetic rats



Values are given as mean ± SD for groups of six rats in each. Values are statistically significant at $p < 0.05$. Statistical significance was compared within the groups as follows: *compared with control, @ compared with diabetic rats.

Table 2: Effect of *C.auriculata* extract on the levels of biochemical parameters in the experimental groups of rats

Groups	Glucose (mg/dl)	Insulin (µU/ml)	Hemoglobin (g/dl)	Glycosylated hemoglobin (%)	Urine sugar
Control	98.79 ± 11.35	15.88 ± 2.85	15.85 ± 1.46	6.67 ± 1.52	Nil
Diabetic	297.78 ± 21.46*	6.74 ± 1.12*	11.18 ± 1.67*	14.68 ± 2.39*	+++
Diabetic + *C.auriculata* extract	147.22 ± 13.54@	11.51 ± 1.45@	13.45 ± 2.39@	7.82 ± 1.94@	Nil
Diabetic + gliclazide	126.12 ± 15.57@	12.54 ± 1.78@	13.90 ± 2.04@	7.59 ± 2.03@	Nil

Values are given as mean ± SD for groups of six rats in each. Values are statistically significant at $p < 0.05$. Statistical significance was compared within the groups as follows: *compared with control, @ compared with diabetic rats. +++ indicates more than 2% sugar.

Table 3: Effect of *C. auriculata* seed extract on the levels of protein, urea, creatinine and uric acid in experimental groups of rats

Groups	Protein (g/dl)	Urea (mg/dl)	Creatinine (mg/dl)	Uric acid (mg/dl)
Control	8.02 ± 1.05	23.91 ± 3.05	1.06 ± 0.10	2.57 ± 0.82
Diabetic	5.36 ± 0.72*	46.62 ± 3.98*	2.22 ± 0.22*	5.16 ± 1.38*
Diabetic + *C.auriculata* extract	6.75 ± 0.78@	33.19 ± 3.42@	1.31 ± 0.10@	3.24 ± 0.86@
Diabetic + gliclazide	7.22 ± 0.85@	31.82 ± 3.08@	1.30 ± 0.09@	2.76 ± 1.04@

Values are given as mean ± SD for groups of six rats in each. Values are statistically significant at $p < 0.05$. Statistical significance was compared within the groups as follows: *compared with control, @ compared with diabetic rats.

Table 4: Effect of *C.auriculata* extract on the level of TBARS in plasma and pancreas experimental groups of rats

Groups	TBARS	
	Plasma	Pancreas
Control	4.27 ± 0.95	40.14 ± 3.95
Diabetic	8.02 ± 1.51*	79.26 ± 8.44*
Diabetic + *C.auriculata* extract	5.39 ± 1.06@	59.29 ± 6.71@
Diabetic + gliclazide	5.14 ± 1.01@	54.99 ± 7.33@

Units: mM/100 g in tissues; nM/ml in plasma. Values are given as mean ± SD for groups of six rats in each. Values are statistically significant at $p < 0.05$. Statistical significance was compared within the groups as follows: *compared with control, @compared with diabetic rats.

Table 5: Effect of *C. auriculata* seed extract on the levels of non enzymatic antioxidants in plasma of experimental groups of rats

Groups	Vitamin C	Vitamin E	Ceruloplasmin	GSH
Control	1.50 ± 0.16	0.68 ± 0.08	12.30 ± 1.52	31.84 ± 3.99
Diabetic	0.51 ± 0.08*	0.33 ± 0.03*	5.03 ± 0.90*	15.99 ± 2.25*
Diabetic + *C.auriculata* extract	0.97 ± 0.13@	0.56 ± 0.08@	9.85 ± 1.36@	21.86 ± 2.97@
Diabetic + gliclazide	1.01 ± 0.13@	0.60 ± 0.06@	10.41 ± 1.78@	24.15 ± 3.06@

Units: mg/dl. Values are given as mean ± SD for groups of six rats in each. Values are statistically significant at $p < 0.05$. Statistical significance was compared within the groups as follows: *compared with control, @ compared with diabetic rats.

Table 6: Effect of *C.auriculata* seed extract on the activity of SOD, Catalase and GPx, in pancreas of experimental groups of rats

Groups	SOD	Catalase	GPx
Control	5.36 ± 1.25	15.82 ± 2.19	6.26 ± 1.01
Diabetic	1.49 ± 0.31*	6.13 ± 1.40*	3.09 ± 0.31*
Diabetic + *C.auriculata* extract	3.71 ± 0.82[@]	12.85 ± 1.99[@]	4.96 ± 0.63[@]
Diabetic + gliclazide	3.98 ± 0.87[@]	13.06 ± 1.95[@]	5.39 ± 0.89[@]

Activity is expressed as: 50% of inhibition of epinephrine autoxidation/min for SOD; µM of hydrogen peroxide decomposed/min/mg of protein for catalase; µM of glutathione oxidized/min/mg of protein for GPx. Values are given as mean ± SD for groups of six rats in each. Values are statistically significant at $p < 0.05$. Statistical significance was compared within the groups as follows: *compared with control, [@] compared with diabetic rats.

Table 7: Effect of *C. auriculata* seed extract on the levels of lipid profile in the plasma of experimental groups of rats

Groups	Total cholesterol	Triglycerides	LDL	HDL
Control	85.71 ± 11.54	61.89 ± 10.03	46.31 ± 5.32	28.69 ± 2.18
Diabetic	166.12 ± 18.95*	149.87 ± 16.67*	123.35 ± 8.51*	13.54 ± 1.32*
Diabetic + *C.auriculata* extract	107.57 ± 14.78[@]	90.04 ± 9.85[@]	69.72 ± 6.42[@]	20.13 ± 1.78[@]
Diabetic + gliclazide	96.38 ± 11.92[@]	84.66 ± 7.59[@]	61.07 ± 5.89[@]	23. 51 ± 2.04[@]

Units: mg/dl. Values are given as mean ± SD for groups of six rats in each. Values are statistically significant at $p < 0.05$. Statistical significance was compared within the groups as follows: *compared with control, [@]compared with diabetic rats.

The effect of oral administration of *Cassia auriculata* seed extract on the levels of blood glucose, plasma insulin, hemoglobin, glycosylated hemoglobin and urine sugar in the control and experimental groups of rats were depicted in Table 2. The elevated levels of blood glucose, glycosylated hemoglobin in the diabetic group of rats were reverted to near normal level by the administration of *Cassia auriculata* seed extract. Conversely, the decreased levels of plasma insulin, hemoglobin in diabetic group of rats were elevated by the administration of *Cassia auriculata* seed extract to diabetic rats for 30 days. Urine sugar which is present in the diabetic group of rats was absent in *Cassia auriculata* seed extract as well as gliclazide treated diabetic group of rats. The results are comparable with gliclazide, an oral hypoglycemic drug. Urine sugar present in the diabetic rats was found to be absent in the rats treated with seed extract.

The effect of oral administration of *Cassia auriculata* seed extract on the levels of total protein, urea, uric acid and creatinine are presented in Table 3. The altered levels of these parameters were reverted back to near normalcy upon the treatment with the seed extract.

Table 4 represents the effect of *Cassia auriculata* seed extract on the levels of lipid peroxides in the plasma and pancreas of experimental groups of rats. The levels of lipid peroxides were significantly ($p<0.05$) elevated in the diabetic group of rats. Upon oral administration of *Cassia auriculata* seed extract as well as gliclazide to diabetic group of rats were significantly ($p<0.05$) reverted to normal levels when compared to control group of rats.

The effect of *Cassia auriculata* seed extract on the plasma levels of non-enzymatic antioxidants such as vitamin C, vitamin E, reduced glutathione and ceruloplasmin in experimental groups of rats are shown in table 5. The diminished levels of non-enzymatic antioxidants in the diabetic group of rats were significantly ($p<0.05$) improved to near normal values by the oral administration of *Cassia auriculata* seed extract as well as glyclazide, after 30 days of treatment.

Table 6 depicts the activities of pancreatic enzymatic antioxidants such as superoxide dismutase, catalase, glutathione peroxidase and glutathione-S-transferase in the experimental groups of rats. The decreased activity of enzymatic antioxidants observed in the diabetic group of rats were significantly ($p<0.05$) elevated to near normal levels after treatment with *Cassia auriculata* seed extract as well as gliclazide.

The levels of cholesterol, triglycerides, HDL and LDL in control and experimental groups of rats are shown in Table 7. The levels of cholesterol, triglycerides, LDL and were significantly increased whereas the HDL-cholesterol was significantly decreased in alloxan-induced diabetic rats. Treatment with seed extract as well as gliclazide significantly ameliorated these levels to near normal levels.

DISCUSSION

Alloxan, a β-cytotoxin, induces, "chemical diabetes" through selective destruction of pancreatic beta cells which results in a decrease of insulin secretion[32]. Alloxan also increases the oxidative stress which is the possible mechanism of its diabetogenic action[33].

The medicinal values of plants lie in bioactive phytochemical constituents that produce definite physiological actions on the human body. These bioactive phytochemical constituents in medicinal plants include alkaloids, flavonoids, phenolic compounds, tannins, anthracine derivatives and essential oils[34]. The preliminary phytochemical screening of the *Cassia auriculata* ethanolic seed extract revealed the presence of phenols, alkaloids, flavonoids, tannins, carbohydrates. These chemical compounds were speculated to account for the observed pharmacological effects of the extract.

Diabetes mellitus is characterized by decreased glucose tolerance due to low secretion of insulin or its action. This is manifested by elevated blood glucose levels and glucosuria, which may be accompanied by changes in lipid and protein metabolism. When the diabetic rats were

challenged with an oral glucose load, the blood glucose levels reached a peak at 60 minutes and gradually decreased to pre-glucose load level around 120 minutes, the present study revealed that oral administration of the ethanolic extract of *Cassia auriculata* seed improved the glucose tolerance in alloxan - induced diabetic rats.

The antihyperglycemic activity of *Cassia auriculata* seed extract could be due to its insulinogenic action as increased levels of insulin were found in diabetic rats upon treatment with extract. Therefore, the extract was able to potentiate the release of insulin from pancreatic islets similar to that observed after gliclazide administration. A number of plants have been reported to exhibit glycemic control through insulin releasing stimulator effect[35, 36].

Blood glucose is an index for the diagnosis of diabetes mellitus. Liver functions as a "principal seat" for glucose homeostasis and plays a vital role in the maintenance of blood glucose levels. Alloxan administration induces pronounced increase in the concentrations of blood glucose. Blood glucose levels are maintained mainly by insulin that facilitates the uptake, utilization and storage of glucose. During diabetes, the blood glucose levels are drastically increased which results from reduced glucose utilization by various tissues, which is a typical condition of insulinopenic diabetes. The elevated blood glucose level observed in diabetic rats was almost normalized upon extract treatment which may be due to stimulation of glucose utilization by the peripheral tissues.

Administration of *Cassia auriculata* seed extract to alloxan induced diabetic rats resulted in activation of beta cells and granulation returns to normal insulinogenic effect. Since the percentage fall in plasma glucose level was different in models with varying intensity of hyperglycemia it implies that the anti-hyperglycemic effect of the plant is based on the dose of diabetogenic agent and on the degree of β-cell destruction[37].

Diabetes mellitus is mainly due to insulin deficiency. Insulin deficiency is manifested in a number of biochemical and physiological alterations. Insulin is synthesized from its precursor proinsulin. Proinsulin is cleaved in the secretory granules into equimolar amounts of insulin and c-peptide[38]. The decreased level of the plasma insulin observed in diabetic rats was found to be normalized in the extract treated rats which might be due to the insulinogenic effects of phytoconstituents present in the seeds.

During diabetes, the excess of glucose present in blood reacts with haemoglobin to form glycosylated hemoglobin leads to decreased levels of hemoglobin in diabetic rats[39]. Glycation with proteins represents the excessive levels of glucose in blood, which causes pathophysiological changes in diabetes mellitus. In uncontrolled diabetes, there is an increased glycation of a number of proteins including haemoglobin and alpha crystalline or lens[40]. This glycation alters the structure and function of haemoglobin resulting in Hb desaturation and precipitation of red blood cells as Heing bodies[41].

Protein serves as a source of nutrition for the tissues and its synthesis and regulation determines normal function. Insulin plays a pivotal role in protein synthesis. Diabetes mellitus shows profound changes in circulating aminoacids and hepatic aminoacid uptake[42]. The significant decrease of plasma protein in alloxan-induced diabetic rats could be attributed to suppressed protein synthesis. Urea is a non-protein nitrogenous waste product whose level reflects a normal and continued protein metabolism. Diabetes mellitus is associated with changes in negative nitrogen balance and loss of nitrogen from most organ systems. The increase in synthesis of urea in diabetic rats may be due to the enhanced catabolism of both liver and plasma proteins. There was increased protein catabolism with flow of aminoacids into the liver, which feeds glyconeogenesis during diabetes[43]. Dighe *et al*[44] reported that accelerated proteolysis of uncontrolled diabetes occurs as a result of deranged glucagon mediated regulation of cAMP formation in insulin deficiency. This accounts for the observed decrease in the total protein content in alloxan induced diabetic rats. Oral administration of *Cassia auriculata* seed extract to diabetic rats significantly inhibits proteolysis caused by insulin deficiency and thus increases the level of plasma proteins to near normal levels.

The supraphysiological concentration of glucose in diabetic state causes severe derangement in protein metabolism that result in the development of negative nitrogen balance. This in turn elevates urea and creatinine level[45] (Asayama *et al*., 1994), which act as a biochemical diagnostic marker for assessing renal impairment and drug-induced toxicity. The observed alteration in the levels of blood urea and serum creatinine in group of diabetic rats reverted to near normalcy by treatment with *Cassia auriculata* seed extract, indicating its renal protective nature.

Uric acid is the main catabolic product from purine nucleotides by xanthine oxidase enzymatic system. It is a biomarker for the development of diabetic complications. Costa *et al*.[46] (2002) suggested increased uric acid concentration to be a risk factor for cardiovascular diseases. The levels of serum uric acid in diabetes induced rats were found to be increased. *Cassia auriculata* extract treatment for the diabetic rats significantly ameliorated the toxic effects of alloxan as indicated by the restoration of serum uric acid levels.

Diabetes is usually accompanied by increased production of free radicals or impaired antioxidant defenses. Excessive generation of free radicals cause damage to cellular proteins, membrane lipids and nucleic acids and eventually cell death. Decreased plasma insulin in diabetic conditions increases fatty acyl coenzyme A oxidase activity, which initiates β-oxidation of fatty acids, resulting in lipid peroxidation. Increased lipid

peroxidation impairs membrane activity by decreasing membrane fluidity and altering activity of membrane-bound enzymes and receptors. The products of lipid peroxidation are injurious to most cells in the body and are associated with a variety of diseases, such as atherosclerosis and brain damage. The significant increase in levels of TBARS observed in plasma and pancreas of diabetic rats were decreased to near normalcy upon oral administration of *Cassia auriculata* seed extract to diabetic rats which could be a result of improved antioxidant status.

Oxidative stress definitely refers to the situation of an imbalance between the production of Reactive Oxygen Species (ROS) and antioxidant defense. There is emerging evidence that the formation of ROS is a direct consequence of hyperglycemia[47] (Daisuke koya *et al.*, 2003). Antioxidant treatment could be a potential therapeutic procedure for diabetic complications[48] (Brownlee, 2001).

The enzymatic antioxidants such as SOD, catalase, glutathione peroxidase and glutathione-S-transferase are involved in the scavenging of reactive oxygen metabolites that are produced as result of chronic hyperglycemia. Gauthaman *et al.*[49] have reported that the plant *Cassia auriculata* could reduce the oxidative stress by stimulating the activities of the scavenging enzymes like SOD, CAT and GSH and decreasing the lipid peroxidation levels in ischemic reperfused injuries. In diabetic milieu, the activities of all these enzymatic antioxidants are declined notably because of the detonated production of free radicals arise out of chronic hyperglycemia. Oral administration *Cassia auriculata* seed extract caused a significant increase in the levels of non-enzymatic antioxidants such as vitamin C, vitamin E, reduced glutathione and ceruloplasmin and enzymatic antioxidants such as SOD, catalase, glutathione peroxidase and glutathione-S-transferase suggesting that the *Cassia auriculata* seed extract possess free radical scavenging and antioxidant activity.

Hypertriglyceridemia and hypercholesterolemia are lipid associated abnormalities which are characteristic features of diabetes. Accumulation of cholesterol in liver due to elevated plasma free fattyacids has been reported in diabetic rats[50]. The higher concentration of plasma total cholesterol observed in diabetic rats is probably due to mobilization of free fatty acids from the peripheral fat depots[51]. *Cassia auriculata* flower extract have reported to possess antihyperlipidemic in triton induced hyperlipidemic rats[52].

It is well known that dyslipidemia is associated with uncontrolled diabetes mellitus. The plasma levels of TC, LDL-C, and TG increases, while the HDL levels decline, contributing to secondary complications of diabetes[53]. Acute insulin deficiency initially causes and increases in free fatty acid mobilization from adipose tissue. This results in an increased production of LDL-C particle[54]. In the present study, diabetic rats exhibited a significant elevation of TC, TG and LDL-C, while HDL-C as decreased. *Cassia auriculata* administration resulted in lowering the plasma levels of TC, TG and LDL-C with elevation of HDL-C level indicating the hypolipidemic activity of the extract.

CONCLUSION

The results of the present study indicate that the *Cassia auriculata* seed extract posess both hypoglycemic, antidyslipidemic and antioxidant activities. The possible mechanism of the antidiabetic action may be through a stimulation of insulin release from the remnant pancreatic β cells. The observed antidiabetic and antidyslipidemic effects may be due to the synergetic actions of the phytoconstituents present in the seed extract. The result of the present study also provides a scientific rationale for the use of *Cassia auriculata* seeds in the traditional medicine system for the treatment of diabetes mellitus.

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