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## ***In vivo* Assessment of Antidiabetic and Antioxidant Activities of *Blumea balsamifera* in Streptozotocin-diabetic Rats**

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### **ABSTRACT**

*Blumea balsamifera* Linn. (Compositae) commonly known as 'Sambong' is a thorny deciduous tree grown in tropical Asia and a few species in Australia and Africa. In India, its leaves are traditionally used for diabetes mellitus. The present study was aimed to evaluate the antidiabetic and *in vivo* antioxidant property of the leaves of *Blumea balsamifera* in streptozotocin (STZ) induced diabetic rats. Administration of hydro-ethanolic leaves extract of *Blumea balsamifera* (HEBB) in doses of 300 and 600 mg kg<sup>-1</sup> to the Streptozotocin (STZ) induced diabetic rats showed significant reduction in blood glucose compared to diabetic control rats. Glibenclamide (5 mg kg<sup>-1</sup> b.wt.; p.o.) was used as reference drug. Both the doses of HEBB treated diabetic rats showed a significant alteration in elevated lipid profile level along with serum marker enzyme. Antioxidant potential of HEBB was evaluated by measuring Glutathione (GSH) and Catalase (CAT) levels. Results obtained showed significant increase in GSH and CAT when compared to diabetic control group. This could explain the basis for use of *Blumea balsamifera* (L.) extract to manage diabetic mellitus.

**Key words:** *Blumea balsamifera*, streptozotocin, serum enzyme, antioxidant and diabetes mellitus

### **INTRODUCTION**

Diabetes mellitus is a metabolic state with persistent hyperglycemia which arises due to inadequate response to endogenous insulin or lack of insulin secretion. It is a major endocrine disorder, affecting approximately 5% of the world's population. Thirst, hunger, emaciation and weakness which are the dominant symptoms in diabetic patients might eventually lead to coma (Oberley, 1988). The beta cells of pancreas maintain glucose homeostasis by regulating optimum insulin release. Although the aetiology of diabetes is still obscure, various environmental factors, viral infections or multiple gene defects might be the underlying cause for the abnormal functioning of the pancreatic beta cells (Maritim *et al.*, 2003; Rotheri, 2007). Diabetes mellitus is generally categorised into type 1 and 2. In type 1 diabetes mellitus there is lack or absence of insulin secretion due to autoimmune destruction of the pancreatic beta cells generally mediated by the T cells. Type 2 diabetes mellitus which is rather more complex and prevalent than type 1 is caused mainly due to abnormal beta cell functioning mediated by insulin resistance (Rotheri, 2007). Insulin resistance is an important precipitating factor for diabetic condition and is generally caused

by varying factors viz., obesity, aging etc. The complications of diabetes are the probable outcome of hyperglycemia. Therefore strict glycaemic control can reduce the further complications of the disorder in both type 1 and 2 diabetes mellitus. Though the exact mechanism of glucose mediated toxicity is yet not clear, hyperglycemia is responsible for the complications to a greater extent (Betteridge and Betteridge, 2000). India is having the world's largest number of diabetic patients followed by China. According to World Diabetes Foundation, there exist about 285 million diabetic patients approximately in the entire world till 2010. By 2030 the world diabetic population is expected to toll near about 438 million, encompassing 7.8% of the total adult population. Every year 5% of the population worldwide dies of diabetes (WHO, 2010).

Diabetes mellitus causes derangement of carbohydrate, protein and lipid metabolism which eventually leads to a number of secondary complications. Diabetes is a metabolic state characterised by hyperglycemia. The increased blood glucose level which is primarily responsible for the generation of free radicals further leads to oxidative stress. Therefore, optimising the abnormal blood glucose level can alleviate the complications associated with the disorder. Apart from the primary treatment of the disease, minimising the oxidative stress through antioxidants might be an effective way for reducing the long term complications of the disorder (Giugliano *et al.*, 1996). Prevention is better than cure and despite the advances in medical science diabetes has no cure but can only be controlled. Diabetes has been the most serious and common epidemic worldwide with increasing number of patients every year. People with diabetes mellitus usually develop a resistance to endogenous insulin. In other cases impaired insulin secretion is responsible for causing the disorder. Insulin resistance and impaired insulin secretion are the essential elements in the pathogenesis of type 2 diabetes and the disease results from a combination of the two and impaired beta-cell function. Patients diagnosed with diabetes generally have a body weight above the normal. Persons at high risk for glucose intolerance and diabetes are generally characterised by the metabolic syndrome which includes insulin resistance, upper-body obesity, hypertension, elevated triglycerides and low levels of high-density lipoprotein (Polonsky, 2012).

Anti diabetic studies on various plants have shown that majority of these plants contains some active constituents with potential anti diabetic property. Despite the isolation of more than 150 phytoconstituents, till date none of the constituents have been found to alleviate or cure diabetes. On the basis of claimed traditional use, a plant named *Blumea balsamifera* was selected for the present study. *Blumea balsamifera* have been traditionally used for its diverse therapeutic application. The plant has the potential to treat various gastrointestinal disorders like diarrhoea, dysentery, flatulence and dyspepsia. Besides, the roots are used as appetizer. In India the leaves are made into a decoction and used for the treatment of gas distension and intestinal colic. Hemorrhoids can be treated locally by the application of fresh leaves in a paste form. (Nadkarni and Nadkarni, 1976). Along with other phyto-chemical constituents terpenes, tannins and flavonoids, namely dihydroquercetin-7, 4'-dimethyl ether (DQDE), blumeatin (BL), quercetin (QN), 5, 7, 3', 5'-tetrahydroxyflavanone (THFE) and dihydroquercetin-4'-methyl ether (DQME) (Ali *et al.*, 2005) are present in the leaves of the plant.

The present study was undertaken to evaluate the effect of hydro-ethanolic *Blumea balsamifera* (HEBB) leaves extract on the blood glucose level in normoglycemic, glucose-hyperglycemic and streptozotocin induced diabetic rats. Meanwhile, in diabetics, insulin is not produced or is insufficiently produced causing hyperglycemia which together with biochemical alterations of glucose and lipid metabolism leads to increased generation of free radicals (Rajasekaran *et al.*, 2006). Hence, the effect of *Blumea balsamifera* extract on the levels of non-protein sulfhydryl groups, i.e., reduced glutathione and catalase were also determined.

## **MATERIALS AND METHODS**

**Drugs and chemicals:** Streptozotocin (STZ) was purchased from Sigma Chemical Co., USA. Standard drug, Glibenclamide was obtained from Yarrow chem. products, Mumbai, India. All other reagents used were of analytical grade.

**Plant materials:** The leaves of *Blumea balsamifera* were collected in the month of October 2011 from Tripura. The plant species was identified and authenticated by the Botanical Survey of India, Agartala, Tripura. The collected leaves were washed under running tap water, cut into small pieces of 2-3 cm and shade dried for 3-4 weeks. The shade dried plant material was powdered using a dry grinder to get the coarse powder. The powder was stored in air tight container for further use.

**Preparation of extract:** Dried powdered plant leaves (85 g) were extracted with hydro-ethanolic solvent (70% ethanol and 30% water) using soxhlet apparatus for 72 h. The resulting hydro-ethanolic extract was concentrated under reduced pressure in rotary evaporator. The yield of the extract was found to be 14.24 g. The final extract was stored in the refrigerator at 4°C and used for the pharmacological studies.

**Preliminary phytochemical test:** Phytochemical properties of hydro-ethanolic residue of *Blumea balsamifera* were tested using various reagent: Mayer and Dragendorff's reagent for alkaloids (Harborne, 1998);  $\text{FeCl}_3$  for tannins; frothing test for saponins; Magnesium chip and HCl test for flavonoids (Mojab *et al.*, 2003); NaCl and Fehling's solution A and B for glycosides; diethyl ether, sulphuric acid and acetic anhydride for steroids; ether-chloroform and NaOH for anthraquinones and  $\text{FeCl}_3$  and  $\text{K}_3\text{Fe}(\text{CN})_6$  for phenols and poly phenols.

**Animals:** Male Wistar-albino rats (140-160 g) were used for the present studies. The animals were maintained under standard laboratory conditions in polypropylene cages and provided food and water *ad libitum*. The animals were acclimatized for a period of 16 days prior to performing the experiments. The animal study was permitted by the Institutional Animal Ethics Committee (Himalayan Pharmacy Institute/2011/60/IAEC/0099).

**Determination of acute toxicity ( $\text{LD}_{50}$ ):** Acute oral toxicity study was performed as per Organization for Economic Cooperation and Development (OECD, 2000). After the oral administration of HEBB, animals were observed individually at least once during the first 30 min and periodically during the first 24 h, with special attention given during the first 4 h and daily thereafter, for a total of 14 days.

**Effect of HEBB on oral glucose tolerance test:** Fasted rats were divided into four groups of five rats each. Group 1 which served as control received distilled water. Group 2 served as glucose treated. Group 3 and 4 received HEBB, respectively at doses of 300 and 600  $\text{mg kg}^{-1}$  b.wt. as a fine aqueous suspension orally. Except control group, all groups were challenged with glucose (2  $\text{g kg}^{-1}$  b.wt.) orally 30 min after administration of drug. Blood samples were collected from the tail vein just prior to glucose administration and at 30, 60 and 120 min after the glucose loading. Blood glucose levels were measured using a Glucometer (Bayer Contour Blood glucose meter, Mishawaka, USA) and glucose test strips (Shirwaikar *et al.*, 2006; Barik *et al.*, 2008).

**Induction of experimental diabetes mellitus and treatment schedule:** Experimental diabetes was induced by single intraperitoneal injection of 60 mg kg<sup>-1</sup> of streptozotocin (STZ), freshly dissolved in cold citrate buffer (0.1 M), pH 4.5. The rats were maintained on 5% glucose solution for next 24 h to prevent hypoglycemia. After 72 h, Fasting Blood Glucose (FBG) levels were measured and only those animals showing blood glucose level = 250 mg dL<sup>-1</sup> were considered for further studies. The day on which hyperglycemia had been confirmed was designated as day 0.

The animals were divided into six groups of six rats in each group. The animals of group 1 and 2 served as normal and diabetic control and those in group 3 and 4 received HEBB (300 and 600 mg kg<sup>-1</sup> b.wt.; p.o.). The rats in group V received glibenclamide (5 mg kg<sup>-1</sup> b.wt.; p.o.) and the animals in the normal group and diabetic control group were administered with vehicle only.

**Determination of hypoglycemic activity:** The extract was administered consecutively for 15 days. Blood glucose levels of each animal were determined at days 0, 5, 10 and 15, respectively after the administration of the test samples. For the estimation of blood glucose, blood samples were collected from the tail vein using a Glucometer (Bayer Contour Blood glucose meter, Mishawaka, USA) and glucose test strips.

**Estimation of serum biochemical parameters and antioxidant status:** Blood was collected from overnight fasted rats by cardiac puncture for the biochemical estimations. Plasma lipid profiles such as triglycerides (TG), total cholesterol (TC), High-Density Lipoprotein (HDL) and Low-Density Lipoprotein (LDL) levels were determined by enzymatic methods using commercial kits obtained from Span Diagnostics, India. Other serum biochemical parameters viz., glycosylated haemoglobin (HbA<sub>1c</sub>), AST: Aspartate amino transferase and ALT: Alanine transaminase was also determined in the same manner.

For measurement of tissue GSH and CAT levels, the animals were sacrificed and the liver of each animal were removed. For the enzymatic assays, 1 g of liver of each animal was taken, homogenized in 10 mL of 0.15 M tris buffer (pH 7.4) and centrifuged at 3000 rpm at 4°C for 30 min. Supernatant was collected and used for the assays.

**Estimation of reduced glutathione (GSH) level:** Non-enzymatic antioxidant i.e., reduced glutathione (GSH) was estimated spectrophotometrically by determination of DTNB (dithiobis-2-nitrobenzoic acid) reduced by SH-groups, expressed as µg mg<sup>-1</sup> wet tissue (Ellman, 1959). To 0.1 mL of different tissue samples, 2.4 mL (0.02 M) of EDTA solution was added and kept on ice bath for 10 min. Then 2 mL of distilled water and 0.5 mL of 50% (w/v) trichloro acetic acid were added. This mixture was kept on ice for 10-15 min and then centrifuged at 3000×g for 15 min. To 1 mL of supernatant, 2.0 mL of Tris buffer (0.4 M) was added. Then 0.05 mL of DTNB solution and 0.01 M DTNB in methanol was added and vortexed thoroughly. Optical density was read within 2-3 min after the addition of DTNB at 412 nm in spectrophotometer against a reagent blank. A standard graph was drawn using different concentration of a standard GSH solution (1 mg mL<sup>-1</sup>). With the help of the standard graph, GSH contents in the liver homogenates of the experimental animals were calculated.

**Estimation of catalase (CAT) activity:** Catalase activity was measured based on the ability of the enzyme to break down H<sub>2</sub>O<sub>2</sub>. Catalase (CAT) was assayed and expressed as moles of

decomposed/min/mg of tissue. Catalase activity was measured based on the ability of the enzyme to break down  $H_2O_2$ . Catalase (CAT) was assayed and expressed as moles of  $H_2O_2$  decomposed/min/mg of tissue. The reaction mixture was composed of 20 mM  $H_2O_2$ , 100  $\mu$ L homogenate and phosphate buffer (500 mM, pH-7.0). The disappearance of peroxide was continuously recorded from the absorbance at 240 nm for the specific period of time. One unit CAT activity is the amount of enzyme that liberates half the peroxide oxygen from  $H_2O_2$  solution of any concentration in 100 sec at 25°C which is determined by CAT activity expression (Aebi *et al.*, 1974).

**Statistical analysis:** All the results are expressed as average $\pm$ SEM. Data was statistically evaluated by one-way analysis of variance (ANOVA) followed by Dunnett's test using Instat software (version 4. 0). The  $p < 0.05$  was considered to be statistically significant.

## RESULTS

**Phytochemistry:** Presence of flavonoids, tannins and polyphenols were confirmed by performing phytochemical tests.

**Determination of acute toxicity ( $LD_{50}$ ):** An attempt was made to determine  $LD_{50}$  of 70% hydro-ethanolic extract of *Blumea balsamifera*. At the end of the treatment period there was no lethality or toxic reaction at the dose of 3000 mg  $kg^{-1}$ , for which it was considered as the cut off dose. Therefore, 1/10th and 1/5th of the above HEBB dose i.e., (300 mg  $kg^{-1}$ ) and (600 mg  $kg^{-1}$ ), respectively were the doses considered for the study i.e., for screening of anti-diabetic property and related estimation of biochemical parameters.

**Glucose tolerance:** The effects of HEBB in doses (300 and 600 mg  $kg^{-1}$ ) on glucose tolerance test are shown in Fig. 1. Animals that were subjected to oral glucose tolerance test showed a reduction in mean blood glucose level after 30 min of glucose load compared to glucose treated group. At 30 min the blood glucose level reached the maximum in both the extract treated groups. There was almost no change in the blood sugar level of the control group (without glucose load) at different time intervals throughout the glucose tolerance experiment.

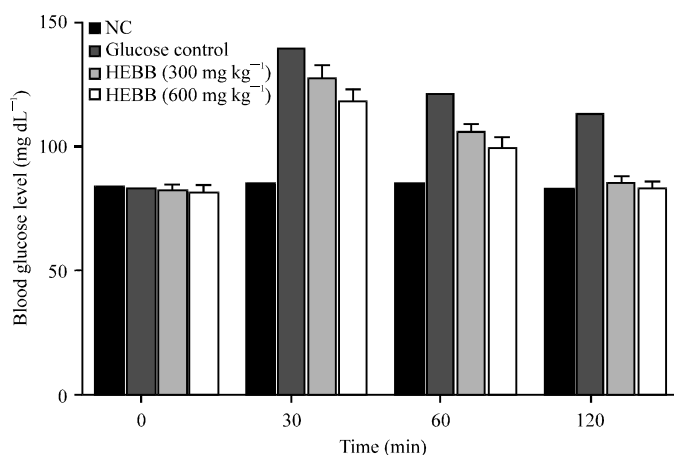


Fig. 1: Oral glucose tolerance test of HEBB extract, NC: Normal Control, HEBB: Hydro-ethanolic *Blumea balsamifera* extract

**Fasting blood glucose levels:** The fasting blood glucose levels were determined and the results were expressed in Table 1. Administration of HEBB for 14 days decreased the blood glucose levels in a sustained and dose dependent manner as compared to diabetic control group. In diabetic rats blood glucose levels were reduced from  $219.99 \pm 7.57$ - $165 \pm 5.46$  mg dL<sup>-1</sup> at 300 mg kg<sup>-1</sup> extract treated group whereas 600 mg kg<sup>-1</sup> dose reduced the glucose levels from  $217.98 \pm 5.30$ - $132 \pm 3.75$  mg dL<sup>-1</sup>. The standard oral hypoglycaemic drug, glibenclamide (5 mg kg<sup>-1</sup>) showed more potent anti diabetic activity by reducing glucose level from  $245.06 \pm 6.46$ - $97.52 \pm 3.50$  as compared to diabetic control group.

**Serum biochemical parameters:** The serum lipid profile i.e., HDL, LDL, total cholesterol and triglyceride are demonstrated in Table 2a. The HDL levels were significantly decreased, whereas levels of Total Cholesterol (TC), triglycerides (TG) and LDL were significantly increased in diabetic rats. The animals were treated with HEBB once a day for 14 days. Treatment of diabetic rats with HEBB (300 mg kg<sup>-1</sup> and 600 mg kg<sup>-1</sup>) significantly reduced the elevated lipid levels and increased the HDL levels. LDL levels were decreased significantly (p<0.001) by 34, 43 and 47% in case of HEBB 300 and 600 mg kg<sup>-1</sup> and standard treated groups, respectively. There was about 20.39 and 41.00% reduction in total cholesterol in case of HEBB 300 and 600 mg kg<sup>-1</sup> and standard treated groups, respectively. TG levels also decreased by 13, 23 and 32%, respectively, in case of HEBB 300 and 600 mg kg<sup>-1</sup> and standard treated groups while HDL levels were improved significantly by 50, 60 and 74% in case of HEBB 300 and 600 mg kg<sup>-1</sup> and standard treated groups, respectively.

Table 1: Effect of hydro-ethanolic *Blumea balsamifera* leaves extract treatment on fasting blood glucose of streptozotocin induced diabetic rats

Group	Treatment (mg kg <sup>-1</sup> )	Fasting blood glucose concentration (mg dL <sup>-1</sup> )			
		0 day	5th day	10th day	15th day
1	Vehicle control (VC)	75.66±2.72	83.63±3.62	85.0±3.57	85.33±4.84
2	Diabetic control (DC)	250.06±8.36***	284.70±4.72***	364.5±8.92***	356.8±9.19***
3	HEBB (300)	219.99±7.57**	219.00±5.97***	187.3±4.60***	165.00±5.46***
4	HEBB (600)	217.98±5.30**	206.00±8.48***	184.2±5.60***	132.00±3.75***
5	Glibenclamide (5)	245.06±6.46	234.20±5.78***	142.2±8.66***	97.52±3.50***

Values are expressed as Mean±SEM, (n = 5 in each group), \*\*\*p<0.001 compared to vehicle control group, \*\*p<0.01, \*\*\*p<0.001 compared with diabetic control group

Table 2a: Effect of hydro-ethanolic *Blumea balsamifera* leaves extract treatment on serum lipid profiles of streptozotocin induced diabetic rats

Treatment (mg kg <sup>-1</sup> )	HDL (mg dL <sup>-1</sup> )	LDL (mg dL <sup>-1</sup> )	TC (mg dL <sup>-1</sup> )	TG (mg dL <sup>-1</sup> )
Vehicle control	49.61±2.71	78.16±3.52	95.54±4.62	95.26±4.50
Diabetic control	20.00±1.43***	175.99±4.82***	123.81±5.64**	145.2±2.87***
HEBB (300)	30.01±0.94 <sup>#</sup>	115.10±4.70***	97.85±4.06 <sup>#</sup>	125.4±3.45 <sup>#</sup>
HEBB (600)	32.15±3.46 <sup>#</sup>	100.12±3.45***	75.42±3.00***	111.32±3.52***
Glibenclamide (5)	34.99±3.48 <sup>#</sup>	92.49±2.97***	72.27±4.45***	97.42±3.80***

Values are expressed as Mean ± SEM; (n = 5 in each group), \*\*p<0.01, \*\*\*p<0.001 compared to vehicle control group, <sup>#</sup>p<0.05, <sup>#</sup>p<0.01, \*\*\*p<0.001 compared to diabetic control group, HDL: High density lipoprotein, LDL: Low density lipoprotein, TC: Total cholesterol and TG: Triglyceride

Table 2b represents the serum levels of AST: Aspartate amino transferase, ALT: Alanine transaminase and HbA<sub>1c</sub>: Glycosylated haemoglobin. There was a significant elevation of glycosylated haemoglobin and serum transaminases in the diabetic control group compared to the normal or vehicle control group. Both the extract treated groups (HEBB 300 and 600 mg kg<sup>-1</sup> b.wt.) restored the elevated levels of glycosylated haemoglobin and transaminases in STZ-diabetic rats which were comparable to glibenclamide. Treatment of diabetic rats with HEBB (300 and 600 mg kg<sup>-1</sup> b.wt.; p.o) reduced the elevated levels of AST and ALT by 13.77, 14.59, 17.88 and 27.21%, respectively. HEBB (600 mg kg<sup>-1</sup> b.wt.) exhibited significant reduction in HbA<sub>1c</sub> to 6.11±0.19 i.e., 45.98% as compared to the diabetic control group and was comparable to glibenclamide (5 mg kg<sup>-1</sup>; p.o).

**Antioxidant status:** The diabetic animals, induced with streptozotocin, exhibited a reduction in the reduced glutathione (GSH) and catalase (CAT). Oral administration of HEBB for 2 weeks increased the liver antioxidant enzymes level compared to diabetic control. The plant extract, HEBB at high dose (600 mg kg<sup>-1</sup>) restored the low antioxidant levels in a more effective way than the lower dose (300 mg kg<sup>-1</sup>). HEBB at doses 300 and 600 mg kg<sup>-1</sup> demonstrated an increase in GSH level. The elevated level was 78.12±4.6 and 83.7±5.6 µg g<sup>-1</sup> of wet liver tissue, respectively. The standard drug, glibenclamide increased the GSH to 86.68±2.5 µg g<sup>-1</sup> of wet liver tissue. The animals treated with HEBB at doses (300 and 600 mg kg<sup>-1</sup>) and standard group, treated with glibenclamide (5 mg kg<sup>-1</sup>) showed an increase in the CAT levels which were expressed as 1.21±0.13, 1.47±0.14 and 1.78±0.15 µM of H<sub>2</sub>O<sub>2</sub> decomposed/min/mg, respectively. The results are depicted in Table 3.

Table 2b: Effect of hydro-ethanolic *Blumea balsamifera* leaves extract treatment on serum biochemical parameters of streptozotocin induced diabetic rats

Treatment (mg kg <sup>-1</sup> )	AST (IU L <sup>-1</sup> )	ALT (IU L <sup>-1</sup> )	HbA <sub>1c</sub> (%)
Vehicle control	91.99±2.83	34.14±2.11	5.06±0.15
Diabetic control	120.6±8.800***	80.61±4.62***	11.31±0.32***
HEBB (300)	104.0±3.060	66.20±3.57*	9.87±0.46**
HEBB (600)	103.0±2.860*	58.68±3.75***	6.11±0.19***
Glibenclamide (5)	99.0±1.060**	40.02±2.05***	5.55±0.30***

Values are expressed as Mean±SEM, (n = 5 in each group), \*\*\*p<0.001 compared to vehicle control group, \*p<0.05, \*\*p<0.01, \*\*\*p<0.001 compared to diabetic control group, AST: Aspartate amino transferase, ALT: Alanine transaminase and HbA<sub>1c</sub>: Glycosylated haemoglobin

Table 3: Effect of hydro-ethanolic *Blumea balsamifera* leaves extract treatment on liver antioxidant enzymes level of streptozotocin induced diabetic rats

Treatment (mg kg <sup>-1</sup> )	Antioxidant enzymes level in liver	
	GSH	CAT
Normal control	89.26±4.74	2.09±0.52
Diabetic control	67.78±2.06	1.03±0.14
HEBB (300)	78.12±4.60	1.21±0.13
HEBB (600)	83.70±5.60*	1.47±0.14
Glibenclamide (5)	86.68±2.50*	1.78±0.15

Values are expressed as Mean±SEM, (n = 5 in each group). \*p<0.05, compared to vehicle control group, GSH: Reduced glutathione and CAT: Catalase



## DISCUSSION

Diabetes is a chronic metabolic disorder affecting majority of the population worldwide. Control in diet and effective management which can optimise the blood sugar level and correct hyperglycemia can decrease the risk of developing micro vascular diseases and minimise their complications (Kim *et al.*, 2006). The conventional therapies for diabetes have many short comings like side effect and high rate of secondary failure. Hence there is increase in the trend to use traditional indigenous plants widely available in India for the treatment of diabetes mellitus. Over 150 plant extracts and some of their active principles including flavonoids, tannins, alkaloids etc are used for the treatment of diabetes.

These extracts might enhance glucose utilization since it significantly decreased the blood glucose level in glucose-loaded rats (OGTT). This fact could be attributable for potentiation of the pancreatic secretion of insulin from existing  $\beta$ -cells or its release from bound insulin (Eidi *et al.*, 2005; Kasiviswanath *et al.*, 2005).

Abnormal lipid metabolism altering lipid profile is a common diabetic complication. The elevated lipids are generally responsible for various coronary heart diseases causing for most of the early deaths in diabetes (Tattersall, 2005). Present study showed increase in plasma triglyceride, total cholesterol and LDL with decrease in HDL cholesterol supporting the findings of the other researchers (Tattersall, 2005; Randle *et al.*, 1963). Potential of the extract to decrease cholesterol and triglyceride levels could be helpful in improving lipid metabolism in diabetes which will help to prevent diabetic complications (Sivajyothi *et al.*, 2008).

Streptozotocin (STZ) is having a cytotoxic methyl nitrosourea moiety. Due to its alkylating nature it hampers the oxidation of glucose and inhibits insulin synthesis and its secretion by selectively necrotizing the  $\beta$  cells of pancreas (Szudelski, 2001). STZ induced hyperglycemia leads to free radical generation which thereby leads to DNA damage, protein degradation, lipid peroxidation and eventually damage to various organs of the body like kidney, brain and eyes. These elevated free radicals and depressed antioxidant defence may lead to cell disruption, oxidative damage to the cell membranes and hence increase the susceptibility to lipid peroxidation. Excessive generation of free radicals viz.,  $\cdot O_2^-$ ,  $\cdot OH$  etc., should be checked and this can protect against free radical induced damage (Yazdanparast *et al.*, 2007). In the present study, hydro-ethanolic plant extract reduced the elevated level of liver biochemical parameters (ALT and AST) and improved antioxidant enzymes (GSH and CAT) level in STZ treated diabetic rats.

In diabetes mellitus, due to persistent hyperglycemia, the excess blood glucose reacts with haemoglobin in a non-enzymatic process to form glycosylated haemoglobin. Since the glycation rate is directly proportional to blood glucose concentration, level of glycosylated haemoglobin indicates glycaemic control in the diabetic rats. Estimation of haemoglobin is well established parameter useful in management and prognosis of the disorder (Kesson *et al.*, 1982). In the present study, administration of HEBB significantly reduced the elevated glycosylated haemoglobin levels in STZ diabetic rats.

## CONCLUSION

The present study showed that hydro-ethanolic leaves extract of *Blumea balsamifera* significantly reduced elevated blood glucose level in STZ diabetic rats without showing any hypoglycaemic effect in normal rats. Since STZ effectively destroys pancreatic  $\beta$  cells and causes persistent hyperglycemia, the mechanism of action might involve action other than pancreatic beta

cells insulin release or secretion. The ant diabetic activity could be due to increased utilization of glucose by peripheral tissues, improved sensitivity of target tissues for insulin or it may be due to antioxidant activity.

However, comprehensive research is required to identify the active constituents responsible for this effect.

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