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Research Article

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Anti-hyperglycaemic effect of Brahmi (*Bacopa monnieri* L.) in streptozotocin-induced diabetic rats: A study involving antioxidant, biochemical and haematological parameters

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ABSTRACT

Brahmi was evaluated for its antioxidant and anti-diabetic potential in streptozotocin-induced diabetic rats and also the effect of diabetes on routine haematological parameters were determined. Streptozotocin-induced diabetic rats were treated with Brahmi (500 mg/kg b.w./day) for 30 days. The activities of catalase and superoxide dismutase were reduced significantly ($P < 0.05$) while the levels of lipid peroxidation, blood glucose and glycated haemoglobin were found to be significantly ($P < 0.05$) elevated in the diabetic rats. Significant ($P < 0.05$) reduction of haemoglobin levels, total white blood cell count and platelet count were observed in diabetic rats. These were normalized on treatment with Brahmi (500 mg/kg b.w.) and were comparable with that of the glibenclamide (600 µg/kg b.w./day) treated rats. Present study shows that Brahmi possesses significant anti-hyperglycaemic and antioxidant effects in streptozotocin-induced diabetic rats.

Keywords: diabetes, Brahmi, antioxidant, antidiabetic

INTRODUCTION

The incidence of diabetes mellitus has been increasing in both developing and developed countries affecting about 10% population currently[1]. Type II diabetes mellitus is characterized by insulin insufficiency along with insulin resistance resulting in impaired glucose metabolism. This eventually leads to chronic hyperglycaemia, dyslipidaemia, obesity and hypertension[2,3]. The incidence of chronic diabetic complications such as diabetic nephropathy, polyneuropathy, retinopathy and cardiovascular disorders has increased among the diabetic population, demanding the need for agents that help in adequate glycaemic control. Though this can be achieved by treatment with oral anti-hyperglycaemic agents, their long term use has adverse effects and hence the demand for natural agents with anti-diabetic activity has increased in recent years. Brahmi (*Bacopa monnieri* L.) has been historically used in the treatment of various conditions that present with oxidative stress-induced damage. This makes it a candidate in the management of hyperglycaemia-induced oxidative stress that underlies diabetic complications.

Brahmi (*Bacopa monnieri* L.) has antioxidant properties and has been used in traditional Indian ayurvedic medicine to treat epilepsy, anxiety, insomnia, hysteria and also to improve memory and enhance cognitive functions[4,5]. Recently, many studies have been carried out to explore the other significant medicinal properties of this herb especially in conditions like hypertension, Parkinson's and gastric ulcer[6-8]. The leaf extract of Brahmi was shown to lower endogenous oxidative stress in pre-pubertal mice brain[9]. Brahmi has showed anti-inflammatory effects in carrageenan-induced paw oedema in mice and rat models and was also shown to modulate antioxidant responses in the brain and kidneys of diabetic rats[10,11]. Present study was aimed to evaluate anti-diabetic and antioxidant potential of Brahmi in streptozotocin (STZ)-induced diabetes in female Wistar albino rats and also to determine its effect on haematological parameters in experimental diabetes.

EXPERIMENTAL SECTION

2.1 Chemicals and reagents:

Streptozotocin was purchased from Sigma Aldrich, India and Brahmi powder was purchased from Indian Medical Practitioners Co-operative Stores and Society (IMCOPS), Mylapore, Chennai, India. Glibenclamide was purchased from Aventis Pharma Ltd., Goa, India. All the other chemicals and reagents used were of analytical grade and purchased from licensed manufacturers.

2.2 Animal experiment

Twenty four female Wistar albino rats weighing about 151.67±1.25 g were obtained from the Animal house, VIT University, Vellore, Tamilnadu, India. The animals were housed four per cage and maintained in a light and temperature controlled room. Standard pelleted rat feed obtained from Hindustan Lever Ltd., and water was provided *ad libitum*. The experimental protocol (IAEC/VIT/VIII/8) was approved by the Institutional Animal Ethical Committee, VIT University, Tamilnadu, India. The experimental rats were divided into four groups of six each and treated as follows: Group I (normal control): 0.5 ml of 0.1 M citrate buffer (i.p.) alone; Group II (diabetic control): STZ (55 mg/kg b.w.) in 0.1 M citrate buffer (i.p.); Group III: STZ (55 mg/kg b.w.) + Brahmi (500 mg/kg b.w.); Group IV: STZ (55 mg/kg b.w.) + Glibenclamide (600 µg/kg b.w.). The fasting blood glucose of experimental animals was measured before the induction of diabetes. They were then fasted overnight after which diabetes was induced in groups II, III and IV by a single intra-peritoneal injection of freshly prepared solution of streptozotocin (55 mg/kg body weight) in 0.5 ml of 0.1 M cold citrate buffer (pH 4.5). The animals were allowed to drink 5% glucose solution overnight to overcome drug induced hypoglycaemia. Group III and IV were treated orally with Brahmi (500 mg/kg b.w.) and glibenclamide (600 µg/kg b.w.) respectively until day 30.The animals were sacrificed by over dose of ether anaesthesia and blood collected from the trunk at the end of experiment.

2.3 Biochemical and haematological parameters

The activities of antioxidant enzymes such as catalase (CAT)[12]and superoxide dismutase (SOD)[13]and the levels of lipid peroxidation (LPO)[14]were measured using liver tissue homogenates. The levels of plasma blood glucose were determined by glucose oxidase method using commercial diagnostic kit (Autospan diagnostics, India). The HbA1C levels in whole blood of the control and experimental rats were measured by BIO-RAD D-10 HPLC.

The whole blood samples collected in EDTA-containing vacutainers were analysed for measurement of haematological parameters using Sysmex haematology analyser (XP-300).

RESULTS AND DISCUSSION

The activities of antioxidant enzymes such as CAT and SOD were significantly ($P < 0.05$) reduced in the diabetic control group while treatment with Brahmi showed to improve the activities of these enzymes to near normal levels which was comparable with that of the glibenclamide treated group (Table 1). There was significant ($P < 0.05$) increase in LPO levels in diabetic control rats which was reduced significantly ($P < 0.05$) in Brahmi treated group (Table 1). This was comparable with the glibenclamide treated rats.

Brahmi has been traditionally used in Indian ayurvedic medicine and has been reported to have several medicinal properties and pharmacological effects. The present study is an evidence of the antioxidant and anti-diabetic properties of Brahmi in STZ-induced diabetes in Wistar Albino rats. This herb was shown to increase the activities of antioxidant enzymes (SOD; CAT) and reduce the extent of lipid peroxidation thereby providing protection against damage caused due to reactive oxygen species in diabetes. This could be due to rich source of active components such as bacopaside I, II, III, IV and V, pseudojujubogenin, alkaloids such as brahmine, herpestine, hydrocotyline, and saponins such as monnierin, bacopa saponin A, B, C and D found in Brahmi[15-18]. Triterpenoid saponins are the main active components of Brahmi which contribute to its antioxidant property and other pharmacological effects. Previous studies have demonstrated antioxidative properties of Brahmi and its active components *in vitro* and *in vivo*[9, 18].

The levels of plasma blood glucose were significantly ($P < 0.05$) elevated in the diabetic group while treatment with Brahmi showed to reduce the elevated blood glucose to normal levels (Table 2). There was evidence of elevated ($P < 0.05$) HbA1C levels in diabetic control rats whereas Brahmi treated rats showed normal levels of HbA1C (Table 2). The results were comparable with that of glibenclamide treated group. The anti-diabetic effect of Brahmi is clearly evident from results of the present study. Moreover, the efficacy of Brahmi in maintaining normal levels of glycosylated haemoglobin is indicative of good control over blood glucose levels as this particular parameter reflects diabetes management and prognosis. This effect could be due to the presence of compounds possessing antioxidant property. Presence of flavonoids such as apigenin and luteonin and phytochemicals such as Betulinic

acid, Betulic acid, Wogonin, Oroxindin and Beta-sitosterol could have further added on to the beneficial effects of Brahmi[19]. The anti-diabetic effect of Brahmi had been studied by Tirtha *et al* (2008) in alloxan-induced diabetic rats and the results obtained in our study concur with their findings[20].

The diabetic rats showed significant ($P < 0.05$) reduction in total white blood cell (WBC) count and haemoglobin levels. The mean corpuscular volume of the red blood cells in diabetic rats was also found to be reduced ($P < 0.05$) when compared to that of normal control rats (Table 3). There was significant ($P < 0.05$) reduction of platelet count in the diabetic group. These parameters were found to be significantly ($P < 0.05$) normalised in Brahmi treated group and were comparable with that of standard drug treated group. Anaemia is a common feature in chronic cases of kidney disease. There is significant reduction in the levels of haemoglobin among diabetic patients with chronic kidney complications. Studies have shown that reduced haemoglobin levels adversely affect endothelial functions thereby disturbing vasoregulation[21].

From the results obtained in the present study, it is evident that Brahmi possesses antioxidant and anti-hyperglycaemic effect in STZ-induced diabetic rats. Identification of the candidate compound present in Brahmi which is responsible for this effect and the specific mechanism involved require further investigation. This would pave way for effective diabetes management and prevention of diabetic complications.

TABLE 1: Effect of brahmi on the antioxidant status of STZ-induced diabetic rats

Parameters	Group I (Normal)	Group II (Diabetic)	Group III (STZ+Brahmi 500 mg/kg b.w.)	Group IV (STZ+glibenclamide 600 µg/kg b.w.)
Catalase	10.26±0.43	6.89±0.29a*	9.86±0.38b*	9.42±0.38a*b*
Superoxide dismutase	208.64±2.02	149.33±1.57a*	197.74±1.96a*b*	195.63±1.97a*b*
Lipid peroxidation	2.07±0.08	4.38±0.14a*	2.98±0.11a*b*	3.12±0.13a*b*

*N=6 animals in each group. The values are expressed as mean ±S.D. Comparisons indicated by lower case letters were made as follows: a – group I vs. group II, III and IV; b – group II vs. group III and IV; c – group III vs. group IV. Statistical analysis was carried out by one way ANOVA followed by Student's Newman – Kuel's test. The symbols represent statistical significance at: *P< 0.05. Units: Catalase- micromoles of H2O2 consumed/min/mg protein; Superoxide dismutase- units/mg protein (1 U= amount of enzyme that inhibit the autoxidation of pyrogallol by 50%); Lipid peroxidation- nmol of MDA formed/mg protein.*

TABLE 2: Effect of brahmi on HBA1C and plasma blood glucose levels in STZ-induced diabetic rats

Parameters	Group I (Normal)	Group II (Diabetic)	Group III (STZ+Brahmi 500 mg/kg b.w.)	Group IV (STZ+glibenclamide 600 µg/kg b.w.)
HbA1C (%Hb)	5.6±0.6	12.86±1.24a*	6.27±0.84b*	6.58±0.8b*
Fasting Blood glucose (mg/dl)	78.34±1.56	263.86±4.16a*	113.21±2.23a*b*	115.42±2.56a*b*

*N=6 animals in each group. The values are expressed as mean ±S.D. Comparisons indicated by lower case letters were made as follows: a – group I vs. group II, III and IV; b – group II vs. group III and IV ; c – group III vs. group IV. Statistical analysis was carried out by one way ANOVA followed by Student's Newman – Kuel's test. The symbols represent statistical significance at: *P< 0.05.*

TABLE 3: Haematological parameters in the control and experimental rats

Parameters	Group I (Normal)	Group II (Diabetic)	Group III (STZ+Brahmi 500 mg/kg b.w.)	Group IV (STZ+ glibenclamide 600 µg/kg b.w.)
WBC (x10^3/ mm^3)	17.04±0.38	12.94±0.24a*	17.8±0.34b*	16.56±0.29a*b*c*
RBC (x10^6/ mm^3)	6.96±0.08	6.05±0.06 a*	7.01±0.08 b*	6.91±0.11 a*b*c*
Hb (g/dl)	14.81±0.81	11.78±0.67a*	14.65±0.81 b*	14.08±0.77 a*b*
PCV (%)	44.38±1.86	35.34±1.59a*	42.02±1.76 a* b*	43.98±0.77 a*b*
MCV (fL)	59.86±2.08	51.62±1.84a*	60.84±2.11 b*	57.16±1.89 a*b*c*
Platelet count (x10^5/mm^3)	6.42±0.08	5.41±0.06a*	5.97±0.07 a*	5.91±0.08 a*b*

*N=6 animals in each group. The values are expressed as mean ±S.D. Comparisons indicated by lower case letters were made as follows: a – group I vs. group II, III and IV; b – group II vs. group III and IV; c – group III vs. group IV. Statistical analysis was carried out by one way ANOVA followed by Student's Newman – Kuel's test. The symbols represent statistical significance at: *P< 0.05.*

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