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In Vivo Assessment of Antihyperglycemic and Antioxidant Activity from Oil of Seeds of *Brassica Nigra* in Streptozotocin Induced Diabetic Rats

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ABSTRACT

Purpose: This study was made to investigate the antihyperglycemic and antioxidant potential of oil of seeds of *Brassica nigra* (BNO) in streptozotocin -nicotinamide (STZ) induced type 2 diabetic rats. ***Methods:*** BNO was orally administered to diabetic rats to study its effect in both acute and chronic antihyperglycemic study. The body weight, oral glucose tolerance test and biochemical parameters viz. glucose level, insulin level, liver glycogen content, glycosylated hemoglobin and antioxidant parameters were estimated for all treated groups and compared against diabetic control group. ***Results:*** Administration of BNO at a dose 500 mg/kg and 1000 mg/kg body weight p.o. to STZ diabetic rats showed reduction in blood glucose level from 335 mg/dl to 280 mg/dl at 4th h and from 330 mg/dl to 265 mg/dl respectively which was found significant ($p<0.01$) as compared with diabetic control. BNO (500 mg/kg and 1000 mg/kg) and glibenclamide (0.6 mg/kg) in respective groups of diabetic animals administered for 28 days reduced the blood glucose level in streptozotocin-nicotinamide induced diabetic rats. There was significant increase in body weight, liver glycogen content, plasma insulin level and decrease in glycosylated hemoglobin in test groups as compared to control group. *In vivo* antioxidant studies on STZ-nicotinamide induced diabetic rat's revealed decreased malondialdehyde (MDA) and increased reduced glutathione (GSH). ***Conclusion:*** Thus the results showed that the oil of seeds of *Brassica nigra* has significant antihyperglycemic and antioxidant activity.

Introduction

Now a day herbal remedies have become the popular source of medicines due to lesser adverse reactions and various other reasons. There are thousands of plants used from last years for the treatment of various diseases, species of the genus Brassica is one of them among the important medicinal plants used in various systems of medicine.[1] The genus Brassica contains over 150 species that are cultivated worldwide as oil seed crops or vegetables. *Brassica nigra* (black mustard) is a winter annual herb (family Brassicaceae). Like other mustards, black mustard grows profusely and produces allelopathic chemicals that prevent germination of native plants. Brassica nigra is an annual growing to 1.2 m (4ft) by 0.6 m (2ft in). It is hardy to zone 7 and is not frost tender. It is in flower from Jun to August, and the seeds ripen from July to September. The flowers are hermaphrodite (have both male and female organs) and are pollinated by Bees, flies. The plant is self-fertile.[2] The plant prefers light (sandy), medium (loamy) and heavy (clay) soils and requires well-drained soil. The plant prefers acid, neutral and basic (alkaline) soils and can grow in very acid soils. It can grow in semi-shade (light woodland) or no shade. It requires moist soil. The plant can tolerate maritime exposure.[3]

Diabetes is growing with a high speed in India and has become a capital of the world which is affecting the all age group of people.[4] There were an estimated 40 million persons with diabetes in India in 2007 and this number is predicted to rise to almost 70 million people by 2025 according to Diabetes Atlas published by the International Diabetes Federation (IDF). The country with the largest number of diabetic people will be India by 2030. Due to these sheer numbers, the economic burden due to diabetes in India is amongst the highest in the world.[5] Diabetes is of mainly three type's viz., Type I, type II, and Gestational. Type II diabetes is the most common type, accounting for 90–95% of all diabetic cases. So the main concern for management of

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this type of diabetes is very essential. Some studies have suggested that essential oils may be useful in the treatment of type II diabetes mellitus and various oils have been used as therapeutic agents for years without any significant adverse health effects.[6]

The oil has been widely used in the food industries from centuries. As long as we know, the effect of oil on the blood profiles in diabetic models has not been studied. In light of these findings, we carried out this study for the evaluation of antihyperglycemic, and antioxidant potential of oil of seeds of *Brassica nigra*.

Materials and Methods

Drugs and chemicals

The drugs and chemicals used in the study were glibenclamide (Torrent Pharmaceutical, Ahmadabad), streptozotocin, heparin (SRL, India), EDTA (Hi-media Lab. Pvt Ltd., Mumbai, India), Ellman's reagent (5,5'-dithiobis-(2-nitro-benzoic acid); DTNB), sodium sulphate, methanol, pyridine, anthrone, thiourea, benzoic acid, sodium chloride (SD Fine Chem Ltd., Mumbai, India). All the chemicals used in the study were of analytical grade.

Isolation of oil

The dried seeds of *Brassica nigra* were purchased from Oil and seed section of Chaudhary Charan Singh Haryana Agriculture University, Hisar, India. The seeds were crushed and oil was extracted with the help of Clevenger apparatus. The percentage yield of light yellow colored oil was found to be 30%.

Experimental animals

Healthy albino wistar rats (150-250 g) were procured from Disease Free Small Animal House, Lala Lajpat Rai University of Veterinary & Animal Sciences, Hisar (Haryana). The rats were housed in (Polycarbonate cage size: 29×22×14 cm) under laboratory standard conditions (25±3 °C:35-60% humidity) with alternating light and dark cycle of 12 h each and were feed fed with a standard rat pellet diet (Hindustan Lever Ltd, Mumbai, India) and water *ad libitum*. The experimental protocol was approved by Institutional Animals Ethics Committee (IAEC) and animal care was taken as per the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Govt. of India (Registration No. 0436).

Induction of Diabetes

Type II diabetes mellitus (NIDDM) was induced in overnight fasted animals by a single intraperitoneal injection of 50 mg/kg STZ in 0.1 M citrate buffer (pH-4.5) in a volume of 1 ml/kg body weight 15 minute after the i.p. administration of 110 mg/kg nicotinamide. Diabetes was developed and stabilized over a period of 7 days. Diabetes was confirmed by the elevated blood glucose levels determined at 72 h and on 7th day after injection. Only rats confirmed with permanent NIDDM (Glucose level above 250 mg/dl) were used in the study. Blood was collected by intraocular route.[7]

Acute toxicity studies

Healthy adult albino wistar rats, starved overnight were divided in to six groups (n=6) and were orally fed with the oil of *Brassica nigra* in the increasing dose of 100, 200, 500, 1000, 2000, 5000 mg/kg body weight**.** The rats were observed continuously for 4 h for behavioral changes and after 24 and 72 h for any lethality.

Oral Glucose Tolerance Test

In this test 2 g/kg of body weight of glucose was administered to the animals and then the blood samples were collected at the time interval of 30, 60, 90, 120 min and 24 h and glucose level was estimated.

Experimental design

Rats were divided into the following groups comprising six rats in each group after the induction and confirmation of diabetes.

a) Acute antihyperglycemic model

In the acute antihyperglycemic models the study was carried out for 4 hours to check whether the plant have some effect or not.

Group 1 Normal group
Group 2 Diabetic control group
Group 3 Test group administered glibenclamide (0.6 mg/kg p.o)
Group 4 Test group administered orally 500 mg/kg of BNO
Group 5 Test group administered orally 1000 mg/kg of BNO

b) Chronic antihyperglycemic model

In the chronic antihyperglycemic models the study was carried out for 28 days to study the various parameters of the diabetes to confirm the antihyperglycemic activity of BNO in streptozotocin induced diabetes in rats.

Group 1 Normal rats
Group 2 Diabetic control
Group 3 Diabetic animals were administered glibenclamide (0.6 mg/kg p.o)
Group 4 Diabetic animal were administered orally 500 mg/kg of BNO
Group 5 Diabetic animal were administered orally 1000 mg/kg of BNO

Sample collection

The 24h fasted animals were sacrificed by cervical decapitation on 28th day of treatment. Trunk blood was collected in heparinized tubes and the plasma was obtained by centrifugation at 5000 rpm for 5 min. for the determination of biochemical parameters; glucose, insulin, cholesterol etc.

Estimation of plasma glucose and cholesterol

Plasma cholesterol and glucose level were measured by commercial supplied biological kit Erba Glucose Kit (GOD-POD Method) and Erba Cholesterol Kit (CHOD-PAP Method) respectively using Chem 5 Plus-V_2 Auto-analyser (Erba Mannhein Germany) in plasma

sample prepared as above. Glucose and cholesterol values were calculated as mg/dl blood sample.

Estimation of glycosylated hemoglobin (Hb1Ac)

Glycosylated hemoglobin was measured using commercial supplied biological kit (Erba Diagnostic) in plasma sample prepared as above using Chem 5 Plus-V_2 Auto-analyser (Erba Mannhein Germany). Values are expressed as the percent of total hemoglobin.

Estimation of liver glycogen content

Liver glycogen estimation was done by the method as described by Seifter *et al* (1950).[8] Immediately after excision from the animal, 1 g of the liver was dropped into a previously weighed test tube containing 3 ml of 30% potassium hydroxide solution. The weight of the liver sample was determined. The tissue was then digested by heating the tube for 20 min in boiling water bath, and following this the digest was cooled, transferred quantitatively to a 50 ml volumetric flask, and diluted to the mark with water. The contents of the flask were then thoroughly mixed and a measured portion was then further diluted with water in a second volumetric flask so as to yield a solution of glycogen of 3-30 µg/ml. Five ml aliquots of the final dilution were then pipette into Evelyn tube and the determination with anthrone was carried out. The amount of glycogen in the aliquot used was then calculated using the following equation:

µg of glycogen in aliquot = 100 U/ 1.11S

U is the optical density of unknown solution. S is the optical density of the 100 µg glucose and 1.11 is the factor determined by Morris in 1948 for the conversion of the glucose to the glycogen.

In vivo antioxidant activity

Estimation of MDA level

Malondialdehyde (MDA), an index of free radical generation/lipid peroxidation, was determined as described by Okhawa *et al* 1979.[9] Briefly, the reaction mixture consisted of 0.2 ml of 8.1% sodium lauryl sulphate, 1.5 ml of 20% acetic acid (pH 3.5) and 1.5 ml of 0.8% aqueous solution of thiobarbituric acid added to 0.2 ml of blood plasma. The mixture was made up to 4.0 ml with distilled water and heated at 95 $^{\circ}$C for 60 min. After cooling the contents under running tap water, 5.0 ml of n-butanol and pyridine (15:1 v/v) and 1.0 ml of distilled water was added. The contents were centrifuged at about 3000 rpm for 10 min. The organic layer was separated out and its absorbance was measured at 532 nm using double beam UV-Visible spectrophotometer (Systronics 2203, Bangalore, India) against a blank. MDA values were calculated using the extinction coefficient of MDA-thiobarbituric acid complex 1.56×10^5 l/mol×cm and expressed as nmol/ml.

Estimation of reduced glutathione level

The tissue sample (liver 200 mg) was homogenized in 8.0 mL of 0.02M EDTA in an ice bath. The homogenates were kept in the ice bath until used. Aliquots of 5.0 mL of the homogenates were mixed in 15.0 mL test tubes with 4.0mL distilled water and 1.0mL of 50 % trichloroacetic acid (TCA). The tubes were centrifuged for 15 min at approximately 3000 rpm, 2.0 mL of supernatant was mixed with 4.0 ml of 0.4M Tris buffer pH 8.9, 0.1mL Ellman's reagent [5,5-dithiobis-(2-nitro-benzoic acid)] (DTNB) added and the sample shaken. The absorbance was read within 5 min of the addition of DTNB at 412 nm against a reagent blank with no homogenate. Results are expressed as µmol GSH/g tissue.

Statistical analysis

The data for various biochemical parameters were evaluated by use of one-way ANOVA, followed by Dunnett's t-test using the software Sigma-Stat 3. In all the tests, the criterion for statistical significance was $p<0.05$.

Results

Acute toxicity study

The oral administration of graded dose of BNO to the rats in our acute toxicity study was found to be non lethal up to the dose of 5000 mg/kg body weight.

Oral glucose tolerance test

The effect of BNO on plasma glucose level after glucose loading of 2 g/kg body weight orally to the STZ diabetic rats is expressed in the Table 1. The blood glucose level rises to a maximum in 60 min after glucose loading. The oil (500 mg/kg and 1000 mg/kg body weight) treated groups showed a significant decrease in level of glucose as compared to control group. The oil treated group showed a marked fall in glucose level in 90 min to 120 min interval (Table 1).

Table 1. Effect of *Brassica nigra* oil in oral glucose tolerance test (OGTT).

Treatment	Dose	Mean blood glucose concentration (mg/dl) ± S.E.M				
		0 min.	30 min.	60 min.	90 min.	120 min.
Normal	----	80±2.6	87 ±2.8	90 ± 3.8	86 ± 2.5	83 ± 2.7
Diabetic control	----	290 ± 4.6	390 ±5.3	413.2 ± 4.3	360 ± 2.7	331 ± 2.8
BNO	500 mg/kg	250 ± 3.0	287 ±3.7	329 ± 3.0	301 ± 4.6**	277 ± 3.9**
BNO	1000 mg/kg	272 ± 4.6	295 ± 4.5	356 ± 4.1	284 ± 3.4**	242 ± 3.3**

Values are presented as mean ± S.E.M.; n = 6 in each group. One way ANOVA followed by *Dunnett's* test **p < 0.01 vs. diabetic control; BNO: Oil of seed of *Brassica nigra*

Effect of BNO on STZ diabetic rats in acute study

Administration of BNO at a dose 500 mg/kg body weight p.o. to STZ diabetic rats showed reduction in blood glucose level from 335 mg/dl to 280 mg/dl at 4th h. When the dose was increased as 1000 mg/kg then the blood glucose level decreased from 330 mg/dl to 265 mg/dl which was found significant ($p< 0.01$) when compared with diabetic control (Table 2).

Table 2. Effect of *Brassica nigra* oil in STZ induced diabetic rats in acute antihyperglycemic study.

Treatment	Dose	Mean blood glucose concentration (mg/dl) ± S.E.M)				
		0 h	1/2 h	1h	2h	4h
Normal	--	76 ± 4.2	80 ± 3.2	77 ± 2.5	82 ± 4.1	79 ± 5.3
Control	--	340.5 ±10.2	342 ± 11.3	346 ± 7.6	341.0 ± 6.7	332.0 ± 7.2
BNO	500 mg/kg p.o	335 ±5.7	332.1± 5.4	310 ± 4.5**	303 ± 3.4**	280 ± 3.6**
BNO	1000 mg/kg p.o	330 ±1.8	315 ± 1.8*	297 ± 3.3**	275 ± 3.4**	265 ± 5.5**

Values are presented as mean ± S.E.M.; n=6 in each group. One way ANOVA followed by *Dunnett's* test *p<0.05; **p<0.01 vs. diabetic control; BNO: Oil of seed of *Brassica nigra*

Effect of BNO on STZ diabetic rats in chronic study

In chronic study administration of BNO at the dose of 500 mg/kg body weight to STZ diabetic rats for 28 days showed a fall in plasma glucose level from 335 mg/dl to 190 mg/dl on 28th day when compared to 0 day value. BNO at the dose of 1000 mg/kg body weight showed a significant ($p<0.01$) fall in plasma glucose level from 330 mg/dl to 160 mg/dl on 28th day (Table 3).

Table 3. Effect of *Brassica nigra* oil in STZ induced diabetic rats in chronic antihyperglycemic study.

Treatment	Dose	Mean blood glucose concentration (mg/dl) ± S.E.M				
		0th Day	7th Day	14th Day	21st Day	28th
Normal	--	80 ± 4.2	79 ± 3.2	82 ± 2.5	85.5 ± 4.1	78 ± 2.1
Control	--	380 ±7.3	379 ±7.6	384 ±6.7	416 ±7.2	410 ± 5.4
BNO	500 mg/kg p.o	335 ±10.4	298 ±9.5**	276 ±6.2**	240 ±6.9**	190 ± 7.2**
BNO	1000 mg/kg p.o	330 ±5.2	280 ± 6.9**	202 ± 5.8**	180 ±4.4**	160 ± 5.8**

Values are presented as mean ± S.E.M.; n = 6 in each group. One way ANOVA followed by *Dunnett's* test **p < 0.01 vs. diabetic control; BNO: Oil of seed of *Brassica nigra*

Effect of BNO on body weight

An increase in the body weight of normal rats was observed whereas the weight of diabetic control rats decrease from day 1 to day 28. BNO at the dose of 500 mg/kg and 1000mg/kg body weight respectively groups when administered to diabetic rats showed a significant change in body weight and it was increase as compared to the diabetic control group. ($p<0.01$) (Table 4).

Table 4. Effect of *Brassica nigra* oil on body weight in diabetic rats.

Sr. No.	Treatment	Dose	Initial Body Weight (g)	Final Body Weight (g)	Change in weight
1.	Normal	--	220 ± 1.1	240 ± 1.5	+20
2.	Diabetic Control	--	215 ± 1.8	194 ± 2.0	-21[a]
3.	BNO	500 mg/kg p.o	225 ± 2.2	226 ± 1.0	+1
4.	BNO	1000 mg/kg p.o	230 ± 1.3	240 ± 1.4	+10**

Values are presented as mean ± S.E.M.; n = 6 in each group. One way ANOVA followed by *Dunnett's* test [a] p<0.01 vs. normal; **p<0.01 vs. diabetic control; BNO: Oil of seed of *Brassica nigra*

Effect of BNO on insulin level

Table 5 shows the level of plasma insulin in the control and experimental groups of rats. Diabetic rats showed a significant decrease in plasma insulin compared with normal rats. Following dose of oral administration of BNO, plasma insulin level increased when compared to control rats (Table 5).

Effect of BNO on glycosylated hemoglobin (HbA1c)

The effect of BNO on HbA1c in STZ diabetic rats is shown in the Table 5. The level of glycosylated hemoglobin significantly increased ($p<0.01$) in diabetic rats as compared to normal control group. The diabetic rats when treated with BNO for 28 days showed a

significant ($p<0.01$) decreased level of glycosylated Hb as compared to untreated diabetic group. The fall in glycosylated hemoglobin level was found to be dose dependent (Table 5).

Table 5. Effect of *Brassica nigra* oil on glycosylated hemoglobin (HbA1c), hepatic glycogen and insulin in the study.

Treatment	Dose	HbA1c (% of Hb)	Hepatic glycogen (mg/g wt of tissue)	Insulin (micro U/ml)
Normal	--	6 ± 1.4	74 ± 6.6	14 ± 2.1
Diabetic Control	--	11.3 ± 2.4[a]	27 ± 4.5[a]	7.9 ± 1.1[a]
BNO	500 mg/kg	9.5 ± 2.1	45 ± 2.6*	9.8 ± 2.0
BNO	1000 mg/kg	7.8 ± 2.5**	62 ± 4.6**	11.7 ± 2.5*

Values are presented as mean ± S.E.M; n = 6 in each group. One way ANOVA followed by Dunnett's test [a]p<0.01 vs. normal; *p<0.05; **p<0.01 vs. diabetic control; BNO: Oil of seed of *Brassica nigra*

Effect of BNO on hepatic glycogen

The hepatic glycogen content in diabetic rats decreased sharply as compared to control animal (Table 5). After chronic administration of BNO to diabetic rats, a significant increased ($p<0.01$) liver glycogen content as compared to diabetic control group was observed.

Effect of BNO on Lipid profile

Table 6 shows the level of lipids in normal and tested animals. There was a significant decrease in the level of HDL-cholesterol and a significant increase in the levels of total cholesterol and triglycerides in diabetic rats when compared to normal rats. The administration of BNO reverse the level of lipids significantly ($p<0.05$ and $p<0.01$).

Table 6. Effect of *Brassica nigra* oil on Lipid profile.

Treatment	Dose	Cholesterol (mg/dl)	Triglyceride (mg/dl)	HDL (mg/dl)
Normal	--	85 ± 1.5	16 ± 2.5	66 ± 1.9
Diabetic Control	--	232 ± 2.4[a]	43 ± 3.1[a]	37.4 ± 1.2[a]
BNO	500 mg/kg	171 ± 3.6**	30 ± 1.6**	44 ± 2.1
BNO	1000 mg/kg	109 ± 2.5**	20 ± 1.3**	49 ± 1.3*

Values are presented as mean ± S.E.M; n = 6 in each group. One way ANOVA followed by Dunnett's test [a] p<0.01 vs. normal; *p<0.05; **p<0.01 vs. diabetic control; BNO: Oil of seed of *Brassica nigra*

Effect of BNO on in vivo antioxidant parameters

The data depicted in Table 7 show the effect of oil on plasma malondialdehyde and reduced glutathione level. Plasma MDA level was found to be significantly higher in STZ diabetic rats compared to normal rats. The oil at dose 1000 mg/kg body weight p.o significantly reduced the level of MDA in diabetic rats. Plasma GSH level was found to be significantly lowered in STZ diabetic rats as compared to normal rats. The chronic administration of BNO at 1000 mg/kg body weight significantly increased the level of glutathione in diabetic rats.

Table 7. Effect of *Brassica nigra* oil on antioxidant parameters (MDA and GSH).

Treatment	Dose	MDA (nmol/dl)	GSH (µmol/g)
Normal	--	2.8 ± 0.2	41.2 ± 2.8
Diabetic Control	--	5.4 ± 0.4[a]	14 ± 1.15[a]
BNO	500 mg/kg	3.7 ± 0.7	20.6 ± 2.6
BNO	1000 mg/kg	3.2 ± 0.2**	32 ± 2.2**

Values are presented as mean ± S.E.M; n = 6 in each group. One way ANOVA followed by Dunnett's test [a]p<0.01 vs. normal; **p<0.01 vs. diabetic control; BNO: Oil of seed of *Brassica nigra*

Discussion

The aim of the study was to evaluate the antidiabetic and antioxidant potential of the BNO in STZ induced diabetic rats. Diabetes mellitus causes a disturbance in the uptake of glucose as well as glucose metabolism. A dose of STZ as low as 50 mg/kg produces an incomplete destruction of pancreatic beta cells even though the rats become permanently diabetic.[10] After treatment with a low dose of STZ many beta cells survive and regeneration is also possible.[11] Hyperglycemia generates abnormally high levels of free radicals by autoxidation of glucose and protein glycation, and oxidative stress has been reported to be a positive factor of cardiovascular complications in STZ-induced diabetes mellitus.[12] Hyperglycemia is associated with the generation of reactive oxygen species (ROS) causing oxidative damage particularly to heart, kidney, eyes, nerves, liver, small and large vessels and gastrointestinal system.[13] The increased levels of plasma glucose in STZ-induced diabetic rats were lowered by BNO administration. The plasma glucose lowering activity was compared with glibenclamide, a standard hypoglycemic drug that stimulates insulin secretion from pancreatic beta cells.[14] From the results of the present study, it appears that

still insulin producing cells are functioning and the stimulation of insulin release could be responsible for most of the metabolic effects. It may be suggested that the mechanism of action of BNO is similar to glibenclamide. The glucose lowering activity of BNO may be related to both pancreatic (enhancement of insulin secretion) and extra pancreatic (peripheral utilization of glucose) mechanism.

An increase in the level of glycosylated hemoglobin (HbA1c) in the diabetic control group of rats is due to the presence of large amount of blood glucose which reacts with hemoglobin to form glycosylated hemoglobin.[15] Oxidative stress increases due to the activation of transcription factors, advanced glycated end products (AGEs), and protein kinase C. If diabetes is persistent for long time, the glycosylated hemoglobin is found to increase.[16] The level of HbA_1C was decreased after the administration of BNO 1000 mg/kg as compared to diabetic control group.

In STZ induced diabetes mellitus, the loss of body weight is caused by increase in muscle wasting and catabolism of fat and proteins.[17] Due to insulin deficiency protein content is decreased in muscular tissue by proteolysis.[18] A decrease in body weight was registered in case of STZ diabetic control group rats while in tested groups the weight loss was reversed. Fatty acid mobilisation from adipose tissue is sensitive to insulin. Insulin's most potent action is the suppression of adipose tissue lipolysis.[19]A rise in plasma insulin concentration of only 5 IU/mL inhibits lipolysis by 50%, whereas a reduction in basal insulin levels result in a marked acceleration of lipolysis.[20] We demonstrated that BNO increased plasma insulin concentrations in diabetic rats. Insulin levels higher than those of the control group may result in inhibition of lipolysis and decreased plasma triglyceride and cholesterol levels. Some studies suggest that the antihyperglycemic action of traditional antidiabetic plant extracts may be due in part to decreased glucose absorption in vivo.[21] This mechanistic explanation may also apply to the actions of BNO in lowering the triglyceride and cholesterol level.

The conversion of glucose to glycogen in the liver cells is dependent on the extracellular glucose concentration and on the availability of insulin which stimulates glycogen synthesis over a wide range of glucose concentration.[16] Diabetes reduces activity of glycogen synthase thereby affecting the glycogen storage and synthesis in rat liver and skeletal muscle.[22] Oral administration of BNO 1000 mg/kg body weight significantly increased hepatic glycogen levels in STZ diabetic rats possibly because of the reactivation of the glycogen synthase system as a result of increased insulin secretion

In conclusion, the present study showed that oral administration of BNO has potential antidiabetic and antioxidant effect in STZ induced diabetic rats. The potent antioxidant activity may be responsible for the antihyperglycemic effects. This investigation reveals the potential of BNO for use as a natural oral agent with antihyperglycemic and antioxidant effects.

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Conflict of Interest

The authors report no conflicts of interest.

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