Journal of Applied Pharmaceutical Science Vol. 4 (12), pp. 065-071, December, 2014
Available online at http://www.japsonline.com
DOI: 10.7324/JAPS.2014.41212
ISSN 2231-3354

Phytochemical screening and antihyperglycemic activity of *Heliotropium indicum* whole plant in Streptozotocin induced diabetic rats

Subhan Ali Mohammad[1], Shaik Abdul Nabi[1], Saritha Marella[1], Krishna Tilak Thandaiah[1], Malaka Venkateshwarulu Jyothi Kumar [2], Chippada Appa Rao[1]

[1] Department of Biochemistry, Sri Venkateswara University, Tirupati-517502, India.
[2] Department of Biotechnology, Sri Venkateswara University, Tirupati-517502, India.

ARTICLE INFO

Article history:
Received on: 30/09/2014
Revised on: 13/10/2014
Accepted on: 04/11/2014
Available online: 29/12/2014

Key words:
Heliotropium indicum, Antihyperglycemic activity, phytochemical screening, Methanol active fraction, Oral glucose tolerance test, Streptozotocin.

ABSTRACT

Present study was designed to screen phytochemical constituents and antihyperglycemic activity of *Heliotropium indicum* (HI) in Streptozotocin (STZ) induced diabetic rats. *Heliotropium indicum* (Boraginaceae) whole plant is used as traditional medicine for a number of ailments including diabetes. The whole plant was collected, shade dried and extracted with different solvents in the increasing order of polarity. When different solvent extracts of HI each at a dose of 500 mg/kg bw were given to diabetic rats, the methanol and aqueous extracts produced significant ($P<0.0001$) antidiabetic activity. Phytochemical screening of various solvent extracts of HI whole plant revealed the presence of alkaloids, steroids, triterpenes, saponins and tannins. When methanol active fraction of *Heliotropium indicum* (MAFHI) was checked for its antidiabetic activity, the fraction at dose of 750 mg/kg bw produced marked antihyperglycemic activity. The antihyperglycemic activity was also exhibited during oral glucose tolerance test (OGTT) with the same dosage of MAFHI.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disease caused by an absolute or relative lack of insulin and or reduced insulin activity, which results in hyperglycemia and abnormalities in carbohydrate, protein and fat metabolism. Though different types of oral hypoglycemic agents are available along with insulin for the treatment of diabetes mellitus, there is a growing interest in herbal remedies due to the side effects associated with these therapeutic agents (Kameswara *et al.*, 2000). The investigation of antidiabetic agents of plant origin which are used in traditional medicine is thus of great importance. *Heliotropium indicum* (Boraginaceae), commonly known as 'Indian heliotrope' is widely distributed in the south Eastern Ghats (Rayalaseema region, Andhra Pradesh, India) and some parts of Africa and Bangladesh. It is locally called as Nagadanti or Telukondi. It is a coarse foetid herb, up to 2 feet high, hairy stem, white flowers with green calyx. *Heliotropium indicum* has been used in different traditional and folklore systems of medicine for curing various diseases. *Heliotropium indicum* was reported to possess anti-bacterial activity (Das P.K., 2011), antitumor activity (Kugelman *et al*., 1976), anti-inflammatory activity (Srinivas *et al*., 2000), anti tuberculosis activity (Machinan *et al*., 2005), anti proliferative activity (Moongkarndi *et al*., 2004), gastro protective activity (Adelaja *et al.*, 2008), Wound healing activity (Reddy *et al*., 2002), antihyperglycemic (Aqheel *et al*., 2013) and immuno stimulant activities (Ashoka *et al.*, 2009). In India and Bangladesh, it is used in traditional medicine to treat diabetes mellitus (Okvirk *et al.*, 2013; Devi *et al*., 2011). The methanolic extract of root of *Heliotropium indicum* was reported to have significant anti-hyperglycemic activity in Streptozotocin and alloxan induced diabetic rats (Aqheel *et al*., 2013). The other species of this family, *Heliotropium Zeylanicum* was reported to possess antidiabetic, antioxidant and antihyperlipidemic activities in STZ induced diabetic rats (Murugesh *et al.*, 2006).

* *Corresponding Author*
Email: chippadar@yahoo.com

But there are no further reports on the antihyperglycemic activity of *Heliotropium indicum*. Hence the present study was undertaken to evaluate the antihyperglycemic activity of *Heliotropium indicum* whole plant in STZ induced diabetic rats.

MATERIALS AND METHODS

Collection of plant material

The whole plant *Heliotropium indicum* was collected from Tirumala hills and identified by the Botanist, Department of Botany, S.V. University, Tirupati. A voucher specimen (Herbarium Accession No: 812) was deposited in the herbarium, Department of Botany, S.V. University, Tirupati. These *Heliotropium indicum* were shade dried and powdered.

Preparation of different solvent extracts

The plant powder of *Heliotropium indicum* was extracted in to the solvents of increasing order of polarity. Hexane, ethyl acetate and methanol extracts were prepared by successive solvent extraction of *Heliotropium indicum* powder in soxhlet apparatus at 68°C-70°C. The filtrates obtained were distilled and concentrated under reduced pressure at low temperature (40°C to 45°C) in the Buchi rotavapor R-200 and finally freeze dried. The yields of the hexane, ethyl acetate and methanol extracts were 18%, 29% and 31% (w/w) respectively. All the extracts were stored at 0°C in airtight containers until needed for further studies.

Preparation of aqueous extract

To prepare aqueous extract the *Heliotropium indicum* plant powder (200 g) was soaked in distilled water in a glass jar for 2 days at room temperature and the solvent was filtered. This was repeated three to four times until the filtrate gave no colouration. The filtrate was distilled, concentrated under reduced pressure in the Buchi rotavapor R-200 and finally freeze dried. The yield of the extract was 24% (w/w). The extract was preserved in a refrigerator till further use.

Preliminary phytochemical analysis

The different solvent extracts of *Heliotropium indicum* were screened for the presence of various phytochemical constituents using standard conventional protocols (Harborne, J.B., 1998).

Preparation of methanol active fraction of *Heliotropium indicum* (MAFHI)

Methanol active fraction of *Heliotropium indicum* (MAFHI) was prepared by a general acid-base extraction method reported earlier (Houghton and Raman., 1998). Further it was screened for the presence of various phytochemical constituents (Harborne, 1998).

Experimental animals

Male albino wistar rats aged 3–4 months with body weights approximately 180–200 g procured from Venkateswara Enterprises, Bangalore, were kept at 25 ± 5^{0}C in a well ventilated animal house under 12 h light and dark cycle. The animals were fed with standard pellet diet (supplied by Venkateswara Enterprises, Bangalore) ad libitum and had free access to water. The experimental protocol was subjected to the scrutiny of the Institutional Animal Ethics Committee and was cleared by the same before beginning of the experiment (No. 27/2012-2013/ (i)/a/CPCSEA/IAEC/SVU/CAR-MSA).

Induction of diabetes

Diabetes was induced in male wistar albino rats aged 4 months (body weight ~180–200 g) by intraperitoneal administration of STZ (Sigma, Detroit, USA) (single dose of 50 mg/kg bw) dissolved in freshly prepared 0.01 M citrate buffer pH 4.5. After 72 h rats with marked hyperglycemia (fasting blood glucose ≥ 250 mg/dL) were selected and used for the study.

EXPERIMENTAL DESIGN

Evaluation of antihyperglycemic activity of different solvent extracts of *Heliotropium indicum* (HI) in STZ induced diabetic rats

The animals were divided in to seven groups of six animals each as given below.

Group 1: Normal control + Distilled water,

Group 2: Diabetic control + Distilled water,

Group 3: Diabetic rats + 500 mg hexane extract of HI/kg bw,

Group 4: Diabetic rats + 500 mg ethyl acetate extract of HI/kg bw,

Group 5: Diabetic rats + 500 mg methanol extract of HI/kg bw,

Group 6: Diabetic rats + 500 mg aqueous extract of HI/kg bw,

Group 7: Diabetic rats + 20mg glibenclamide/kg bw.

After an overnight fast the group 1 and group 2 rats received only distilled water. Whereas group 3, group 4, group 5 and group 6 diabetic rats received hexane, ethyl acetate, methanol and aqueous extracts each at a dosage of 500 mg/kg bw respectively by gastric intubation using a force feeding needle. Group 7 rats received 20mg glibenclamide/kg bw as a reference drug. Blood samples were collected for the measurement of blood glucose from the tail vein at 0, 1, 2, 3, 4, 5 and 6 hours after feeding the extract/glibenclamide, and blood glucose levels were measured by using glucose oxidase-peroxidase reactive strips and a glucometer (Accu-chek, Roche Diagnostics, USA).

Evaluation of antihyperglycemic activity of methanol active fraction of *Heliotropium indicum* (MAFHI) in STZ induced diabetic rats

The animals were divided in to seven groups of six animals each as given below.

Group 1: Normal control+ distilled water,

Group 2: Diabetic control+ distilled water,

Group 3: Diabetic rats+ MAFHI (250 mg/kg bw),
Group 4: Diabetic rats+ MAFHI (500 mg/kg bw),
Group 5: Diabetic rats+ MAFHI (750 mg/kg bw),
Group 6: Diabetic rats+ MAFHI (1000 mg/kg bw),
Group 7: Diabetic rats+ Glibenclamide (20mg/kg bw) a standard oral antidiabetic drug. After an overnight fast, the MAFHI suspended in distilled water was fed by gastric intubation, using a force feeding needle. Group 1 and group 2 rats were fed distilled water alone. Blood samples were collected for the measurement of blood glucose from the tail vein at 0, 1, 2, 3, 4, 5 and 6 hours after feeding the fraction.

The results were compared with those of the 7th group of rats which were treated with 20 mg glibenclamide/kg bw. Blood glucose levels were measured by using glucose oxidase-peroxidase reactive strips and a glucometer (Accu-chek, Roche Diagnostics, USA).

Effect of MAFHI on fasting blood glucose levels (mg/dL) of normal rats

The animals were divided in to two groups of six animals each and received the following treatments. Group 1: Normal control +distilled water, Group 2: Normal rats + MAFHI (750 mg/kg bw). Blood samples were collected for the measurement of blood glucose from the tail vein at 0, 1, 2, 3, 4, 5 and 6 hours after feeding the fraction, and blood glucose levels were measured by using glucose oxidase-peroxidase reactive strips and a glucometer (Accu-chek, Roche Diagnostics, USA).

Effect of MAFHI on oral glucose tolerance of diabetic rats

Three groups of diabetic rats each group containing six rats were used for this study. Group1: Diabetic rats + distilled water, Group 2: Diabetic rats + 20 mg glibenclamide/kg bw, Group 3: Diabetic rats + 750 mg MAFHI / kg bw. The oral glucose tolerance test (Bonner wier, 1988) was performed in overnight fasted diabetic rats. Glucose (2 g/ Kg bw) was administered orally to all the three groups of rats using a force feeding needle at 0 minute. After 30 minutes of oral glucose administration, the group 2 and group 3 diabetic rats received glibenclamide (20 mg/kg bw) and MAFHI (750 mg/kg bw) respectively. Blood samples were collected from tail vein at 0, 30, 60, 90, 120, 150 and 180 min for estimation of blood glucose using dextrostix with Basic One Touch Accu-chek Glucometer (Glucose oxidase peroxidase method). A comparison was made between the MAFHI and antidiabetic drug glibenclamide, with respect to their antihyperglycemic activities.

Effect of MAFHI on oral glucose tolerance of normal rats

Three groups of normal rats each group containing six rats were used for this study.

Group 1: Normal Control+ distilled water,
Group 2: Normal rats+750 mg MAFHI/kg bw,
Group 3: Normal rats +20mg glibenclamide/kg bw. After overnight fast group 2 and group 3 were fed with MAFHI and glibenclamide respectively and normal untreated rats (Group 1) were fed with distilled water. Thereafter, following 30 min of post fraction and drug administration all groups of animals were fed with glucose (2g/kg bw). Blood samples were collected from tail vein prior to dosing and then at 30, 60, 90, 120, 150 and 180 min after glucose administration for estimation of blood glucose using dextrostix with Basic One Touch Accu-chek Glucometer (Glucose oxidase peroxidase method) (Shirwaikar and Rajendran, 2006; Aslan *et al.,* 2007).

Acute toxicity studies

Acute toxicity of MAFHI was evaluated in healthy wistar male albino rats, according to the guidelines set by Organization for Economic Cooperation and Development (OECD) (Bala *et al.,* 2010). The healthy male rats were randomly divided into two groups of six rats each.

The animals were fasted overnight, provided only water after which methanol active fraction of *Heliotropium indicum* was administered to the groups orally at a dose level of 2000, 3000 mg/kg bw respectively by gastric intubation. The animals were observed continuously for 24 hours for toxic symptoms such as behavioural changes, locomotion, convulsions and mortality.

RESULTS

Preliminary phytochemical screening

Preliminary phytochemical analysis revealed the presence of steroids, alkaloids, triterpenes, saponins and tannins in *Heliotropium indicum* whole plant. Phytochemical constituents of different solvent extracts of *Heliotropium indicum* are given in **Table 1.**

Table. 1: Phytochemical constituents of different solvent extracts of *Heliotropium indicum.*

S.NO	Phytochemicals	Hexane	Ethyl acetate	Methanol	Water	MAFHI
1	Steroids	–	–	+	+	+
2	Terpenoids	–	–	–	–	–
3	Triterpenes	–	+	+	+	+ +
4	Saponins	–	+	+ +	+ +	+ +
5	Alkaloids	–	+	+	+ +	+ +
6	Carbohydrates	–	–	–	–	–
7	Flavonoids	–	–	–	–	–
8	Tannins	–	–	+	+	+
9	Glycosides	–	–	–	–	–

++, major; +, minor; –, no phytochemical.

Effects of different solvent extracts of HI on the blood glucose levels of diabetic rats

The effect of different solvent extracts of *Heliotropium indicum* on the fasting blood glucose levels of diabetic rats is shown in **Table 2.**

The diabetic rats treated with aqueous extract at a dosage of 500 mg/ kg bw showed significant (47%) reduction in blood glucose levels. No reduction of blood glucose levels was observed in diabetic rats treated with hexane and ethyl acetate extracts at the same dosage. Whereas the methanol extract has produced 31.5% fall in the FBG level of the diabetic rats.

Table 2: Effect of different solvent extracts of HI on fasting blood glucose levels of STZ induced diabetic rats. Values are given as mean ± S.D.

GROUPS	Fasting Blood Glucose (mg/dl) levels after treatment with different solvent extracts of HI						
	0h	1h	2h	3h	4h	5h	6h
1	82.66±4	83.66±5	81.16±2	82±3	79.1±2	79.5±3	80.66±3
2	303.33±19†	305.16±20	307.66±19	309±19	310.66±18	314.16±18	316.66±16
3	311±19†	308.66±19	306.33±19	304.66±19	303.33±21	300.5±19	294.33±21
4	354.71±12†	349.71±13	348.28±13	345±13	342±14	339.85±14	332.28±14
5	385.66±19†	362.33±19	335.66±15*	325.16±15*	312.33±14**	295.5±14**	264.16±11**(31.5%)
6	334±19†	316.83±17	306.5±15	263.5±11.6**	246.66±13**	227.66±11**	177.66±15**(47%)
7	328±24†	299±10	271.3±6*	249±5**	228.5±5**	202.8±5**	193.66±7**(40%)

† P <0.0001 compared with the initial level of blood glucose (0h) of normal rats.
** P<0.0001 compared with the initial level of blood glucose (0h) in the respective group.
* P<0.001 compared with the initial level of blood glucose (0h) in the respective group.
Numbers in parenthesis indicate the percentage of fall in 0h blood glucose.

Table 3: Effect of different doses of MAFHI on fasting blood glucose levels of STZ induced diabetic rats.

GROUP	Fasting Blood Glucose (mg/dL) levels after treatment with different doses of MAFHI						
	0h	1h	2h	3h	4h	5h	6h
1	81.83±2.8	79.66±4.6	81.33±3.5	78.5±3.6	77.33±4.5	82±4.5	78.66±5.7
2	280.16±15†	284.5±10	289.66±6.7	291.5±7.6	287.16±13	292.33±8.0	293.16±7.2
3	344±27 †	322.33±30	305±27	292.66±22	284.83±20	280.33±19*	268.16±21*(22%)
4	402.33±42†	358±41	329.83±38	290±26*	265±42*	234.66±50**	212.83±34**(47.1%)
5	384.66±43†	342.16±31*	281.83±20**	244±24**	198.16±19**	177±18**	153.16±17**(60%)
6	358.16±17†	272.3±9**	208.3±14**	199±11**	184.5± 6.5**	178.13±5**	156.8±12**(56.2%)
7	331.83±14†	304.33±16	278.5±10**	265±12**	236±11**	212.5±13**	201.5±8**(39.2%)

All values are expressed as mean ± S.D from six rats in each group.
† P <0.0001 compared with the initial level of blood glucose (0h) of normal rats.
** P<0.0001 compared with the initial level of blood glucose (0h) in the respective group.
* P<0.001 compared with the initial level of blood glucose (0h) in the respective group.
Numbers in parenthesis indicate the percentage of fall in 0h blood glucose.

Table 4: Effect of MAFHI on fasting blood glucose levels of normal rats.

GROUP	Fasting Blood Glucose (mg/dL) levels after treatment with MAFHI						
	0h	1h	2h	3h	4h	5h	6h
1	86.8± 3.7	83.6± 5.4	88.0± 4.5	91.8± 3.7	86.3± 6.3	89.0 ± 3.8	86.8± 6.9
2	79.5±3.8	88.33±4.2	82.66±5.0	84.2±4.5	86.13±3.5	81.66±3.9	82.33±4.5

All values are expressed as mean ± S.D from six rats in each group.

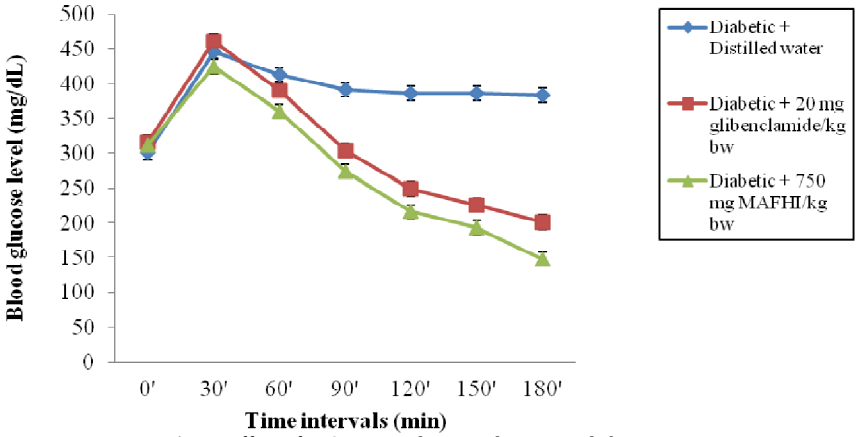

Fig. 1: Effect of MAFHI on glucose tolerance in diabetic rats.

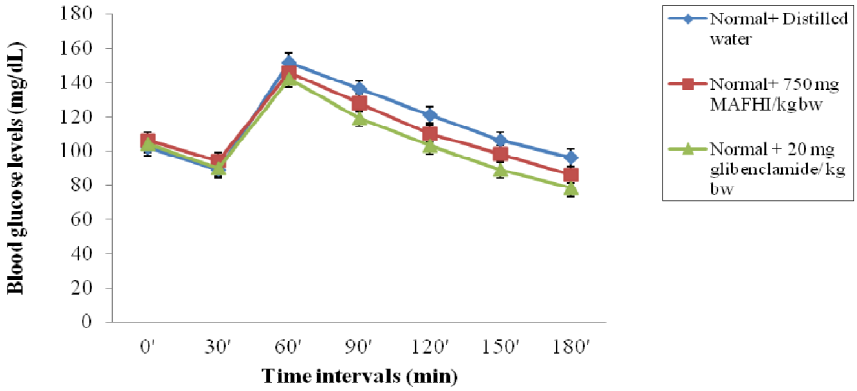

Fig. 2: Effect of MAFHI on glucose tolerance in normal rats.

Effect of MAFHI on fasting blood glucose levels (mg/dL) of STZ induced diabetic rats and normal rats

The effect of different doses of methanol active fraction of *Heliotropium indicum* (MAFHI) on the fasting blood glucose levels of diabetic rats is given in **Table 3**. The fasting blood glucose levels of diabetic untreated rats (Group 2) were significantly higher than the fasting blood glucose levels of normal untreated rats (Group 1). A significant (60%) decrease in fasting blood glucose levels was observed in diabetic rats treated with MAFHI at the dosage of 750 mg/kg bw. Whereas the doses 250 and 500 mg/kg bw produced a fall of 22% and 47% respectively in the FBG levels. However, further increase (1000 mg/kg bw) in the dose of MAFHI did not increase the hypoglycemic response. The hypoglycemic effect of MAFHI was compared with that of glibenclamide (20mg/kg bw) a standard drug. The effect of MAFHI was much higher than that of glibenclamide which has produced only 39% fall in the blood glucose levels. The treatment with MAFHI at a dosage of 750 mg/kg bw in normal rats did not show any hypoglycemic activity. The results are depicted in Table4.

Effect of MAFHI on oral glucose tolerance in STZ induced diabetic rats

After 30 minutes of oral glucose administration (2g/kg bw), the administration of 750 mg MAFHI/kg bw or 20 mg glibenclamide/kg bw has significantly improved the glucose tolerance in the diabetic rats. In the diabetic untreated rats the glucose levels remained higher without much change even at 180 min after glucose load. Oral administration of MAFHI (750 mg/kg bw) and glibenclamide (20 mg/kg bw) for group 3 and group 2 diabetic rats respectively, resulted in a significant fall in blood glucose levels from 30 minutes onwards and continued up to 180 minutes. The effect of MAFHI was much higher when compared to that of glibenclamide. The results are depicted in **Fig. 1.**

Effect of MAFHI on oral glucose tolerance in normal rats

The blood glucose levels of all groups of animals were measured from 0 min to 180 minutes after glucose load. In all the groups the blood glucose levels were raised after 30 min of glucose administration but after that there was a significant decrease in the blood glucose levels of group 2 and group 3 when compared to those in group 1. But there was no hypoglycemia in any group of rats. The results are depicted in **Fig. 2.**

Acute toxicity study

The various observations showed the normal behavior of the treated rats. No toxic effects were observed even at the dose of 3000 mg MAFHI/kg bw. There were no lethal effects in any of the groups, indicating that MAFHI is non toxic.

DISCUSSION

Diabetes currently is a major health problem for the people of the world. Diabetes is a chronic metabolic disorder of carbohydrate, fat and protein metabolism characterized by elevation of both fasting and post prandial blood glucose levels. The synthetic oral hypoglycemic agents can produce serious side effects (Akhtar and Iqbal., 1991; Holman and Turner., 1991). The increases in number of diabetic patients have motivated scientists to find new methods to cure diabetes (Adeghate E., 1999). STZ is an antibiotic obtained from *Streptomyces achromogenes*. It possesses diabetogenic properties mediated by pancreatic β- cell destruction; hence this compound has been widely used to induce diabetes mellitus in experimental animals (Junod A., 1969). Low dose of STZ was used in the present study resulting in partial destruction of β-cells resembling type 2 diabetes mellitus in humans.

Heliotropium indicum has been in use traditionally for treatment of several diseases. But there are not many studies on antidiabetic activity of *Heliotropium indicum*. In the present study 500 mg aqueous extract of HI/kg bw has shown a maximum fall in blood glucose levels by about 47 % in STZ induced diabetic rats, which is significantly higher than the hypoglycemic effect of 20 mg/kg bw of glibenclamide in the diabetic treated rats. The onset of antihyperglycemic action was observed from 1st hr of the treatment and a steady state increase in the action continued up to 6th hr. The methanol extract also produced significant but less antihyperglycemic activity (a maximum of 31.5%) in comparison with that of aqueous extract. No antihyperglycemic action was observed with hexane and ethyl acetate extracts.

In this study the methanol active fraction of *Heliotropium indicum* at a dose of 750 mg/kg bw produced a significant (60%) fall in the fasting blood glucose levels of diabetic rats, but it has no effect in normal rats. The blood glucose lowering effect of MAFHI is higher than that of the oral hypoglycemic agent, glibenclamide (20 mg/kg bw). The decreased antihyperglycemic activity at dose higher than 750 mg/kg bw could be due to reduced or no effect of the components present in the extracts at higher doses (Prince *et al.*, 1999) and/ or the presence of other antagonistic components in the extract.

The oral glucose tolerance test showed that the MAFHI gave definite blood glucose lowering activity. The onset of anti hyperglycemic action was observed from 30 minutes of the treatment and a steady state increase in the action continued up to 180 minutes in diabetic rats. The MAFHI would have enhanced the glucose utilization, so blood glucose levels were significantly decreased in glucose loaded rats.

Phytochemical analysis of MAFHI revealed the presence of steroids, triterpenes, alkaloids, saponins and tannins in *Heliotropium indicum* whole plant. Triterpenes constitute a large structurally diverse group of natural compounds that possess various biological activities. Many experiments have shown that these compounds have several antidiabetic mechanisms. They can inhibit enzymes involved in glucose metabolism, prevent the development of insulin resistance and normalize plasma glucose and insulin levels (Nazaruk and Borzym-Kluczyk., 2014). These natural compounds, in contrast to synthetic drugs, apart from producing a hypoglycemic effect have also been found to manifest hypolipidemic and anti-obesity activity. Triterpenes are also

promising agents in the prevention of diabetic complications. They have strong antioxidant activity and inhibit the formation of advanced glycation end products, implicated in the pathogenesis of diabetic nephropathy, embryopathy, neuropathy or impaired wound healing. Two triterpenes of *Momardica charantia* were reported to show hypoglycemic effects in the alloxan-injected mice at 400 mg/kg (Harinantenaina *et al.,* 2006). Until now very few clinical studies have been concerned with the application of triterpenes in treating diabetes.

The alkaloids are well known phytoconstituents responsible for anti-inflammatory (Srinivas *et al.,* 2000; Barbosa-Filho *et al.,* 2006; Idowu *et al.,* 2006), antioxidant (Murugesh *et al.,* 2006; Idowu *et al.,* 2006), antidiabetic (Singh *et al.,* 2001; Ponnachan *et al.,* 1993), anticancer (Kugelman *et al.,* 1976; Jagetia and Baliga., 2006), antibacterial (Zhang *et al.,* 2010), analgesic (Shang *et al.,* 2010) and many other activities. Saponins have been reported as plant phytochemical having insulin sensitization and antihyperlipidemic effects in diabetic rats. (Bhavsar *et al.,* 2009; Eu *et al.,* 2010; Lee *et al.,* 2011; Elekofehinti *et al.,* 2013).

CONCLUSION

From the above results it is concluded that the oral administration of MAFHI to STZ induced hyperglycemic rats showed a prominent reduction in blood glucose levels and normalization of blood glucose levels when compared to STZ control rats. *Heliotropium indicum* possesses various phytochemical constituents, which may be responsible for the antihyperglycemic activity in STZ induced diabetic rats. Further work has to be carried out to investigate the active compounds in the methanol active fraction of *Heliotropium indicum*.

REFERENCES

Adeghate E. Effect of subcutaneous pancreatic tissue transplants on Streptozotocin- induced diabetes in rats. II. Endocrine and metabolic functions. Tissue & Cell, 1999; 31(1): 73-83.

Adelaja AA, Ayoola MD, Otulana JO, Akinola OB, Olayiwola AA, Ejiwumi AB. Evaluation of the Histo-Gastroprotective and Antimicrobial Activities of *Heliotropium indicum* Linn (Boraginaceae). Malaysian J. Med. Sci., 2008; 15(3): 22-30

Akhtar, MS, Iqbal, J. Evaluation of the hypoglycemic effect of *Achyranthes aspera* in normal and alloxan diabetic rabbits. Journal of Ethanopharmacology, 1991; 31:49-57.

Aqheel MA, Janardhan M, Durrai vel S. Evaluation of the antihyperglycemic activity of methanolic extract of root of *Heliotropium indicum* in Streptozotocin and alloxan induced diabetic rats. Indian Journal of Research in Pharmacy and Biotechnology, 2013; 1:707-710.

Ashoka M, Shasty CS, Sridevi K, Gopkumar P. Stimulation of Immune Function Activity of the Extract of *Heliotropium indicum* Leaves. Internet J. Pharmacol, 2009; 7: 1.

Aslan M, Orhan DD, Orhan N, Sezik E, Yesilada E. In vivo antidiabetic and antioxidant potential of *Helichrysum plicatum ssp. plicatum capitulums* in Streptozotocin-induced-diabetic rats. Journal of Ethno pharmacology, 2007; 109: 54–59.

Bala A, Kar B, Haldar PK, Mazumder UK, Bera S. Evaluation of anticancer activity of *Cleome gynandra* on Ehrlich's ascites carcinoma treated mice. Journal of Ethno Pharmacology, 2010; 129: 131-134.

Barbosa-Filho JM, Piuvezam MR, Moura MD, Silva MS, Lima KVB, Da Cunha, EVL, Fechine IM, Takemura OS. Anti-inflammatory activity of alkaloids: A twenty-century review. Rev. Bras. Farmacogn. 2006; 16:109-139.

Bhavsar SK, Singh S, Giri S, Jain MR, Santani DD. Effect of saponins from *Helicteres isora* on lipid and glucose metabolism regulating genes expression. Journal of Ethnopharmacology, 2009; 124: 426–433

Bonner-Wier S. Morphological evidence of pancreatic polarity of beta cells within islets of langerhans. Diabetes. 1988; 37: 616-621.

Das PK. Antibacterial activity of leaf extracts of *Heliotropium indicum* Linn. Life sciences Leaflets, 2011; 20: 904-907.

Devi WI, Devi GS, Singh CB. Traditional herbal medicine used for the treatment of diabetes in Manipur, India. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2011; 2 (4): 709-715.

Elekofehinti OO, Kamdem JP, Kade IJ, Rocha JBT, Adanlawo IG. Hypoglycemic, antiperoxidative and antihyperlipidemic effects of saponins from *Solanum anguivi* Lam. fruits in alloxan-induced diabetic rats. South African Journal of Botany, 2013; 88: 56-61.

Eu CH, Lim WY, Ton SH, Kadir KA. Glycyrrhizic acid improved lipoprotein lipase expression, insulin sensitivity, serum lipid and lipid deposition in high-fat diet induced obese rats. Lipids in Health and Disease, 2010; 9: 1–9.

Harborne JB. 1998. Phytochemical methods. A guide to modern techniques of plant analysis, Chapman and Hall, London. pp 60.

Harinantenaina L, Tanaka M, Takaoka S, Oda M, Mogami O, Uchida M, and Asakawa Y. *Momordica charantia* constituents and antidiabetic screening of the isolated major compounds. Chem. Pharm. Bull. (Tokyo), 2006; 54: 1017–1021.

Holman RR, Turner RC. 1991. Oral agents and insulin in the treatment of NIDDM. In pick up, J., Williams, G. (Eds.), Text book of diabetes. Blackwell, Oxford. pp. 407-469.

Houghton PJ, Raman A. 1998. Method of extraction and sample clean up. In: Fractionation of Natural Extracts. Chapman and Hall Publications, London. 22-52.

Idowu TO, Iwalewa EO, Aderogba MA, Akinpelu BA, Ogundaini AO. Antinociceptive, anti-inflammatory and antioxidant activities of eleagnine: An alkaloid isolated from *Chrysophyllum albidum* seed cotyledons. J. Biol. Sci, 2006; 6:1029-1034.

Jagetia GC, Baliga MS. Evaluation of anticancer activity of the alkaloid fraction of *Alstonia scholaris* (Sapthaparna) *in vitro* and *in vivo*. Phytother. Res. 2006; 20: 103–109.

Junod A. Diabetogenic action of Streptozotocin: relationship of dose to metabolic response. J Clin Invest, 1969; 48:2129-2139.

Kameswara BR, Giri R, Kesavulu MM, Apparao CH. Effect of oral administration of bark extracts of *Pterocarpus santalinus* L. on blood glucose level in experimental animals. Journal of Ethanopharmacology, 2000; 74: 69-74.

Kugelman M, Liu WC, Axelrod M, McBride TJ, Rao KV. Indicine-N-oxide: the antitumor principle of *Heliotropium indicum* Lloydia, 1976; 39(2-3): 125-128.

Lee KT, Jung TW, Lee HJ, Kim SG, Shin YS, Whang WK. The antidiabetic effect of genosenoside Rb2 via activation of AMPK. Archives of Pharmaceutical Research, 2011; 34: 1201–1208.

Machinan T, Korth J, Boonsom L, Saisunee L, Stephen G. Composition and antituberculosis activity of the volatile oil of *Heliotropium indicum* Linn. Growing in Phitsanulok, Thailand Flavour Fragrance J, 2005; 21(2): 265-267.

Moongkarndi P, Kosem N, Luanratana O, Jongsomboonkusol S, Pongpa N. Antiproliferative activity of Thai medicinal plant extracts on human breast adenocarcinoma cell line Fitoterapia, 2004; 75:375-377.

Murugesh K, Veerendra Y, Deepak Kumar D, Pinaki S, Bhim Chandra M, Tapan Kumar M. Antidiabetic, antioxidant and antihyperlipidemic status of *Heliotropium Zeylanicum* extract on Streptozotocin induced diabetic rats. Biol. Pharm. Bull. 2006; 29 (11): 2202-2205.

Nazaruk J, Borzym-Kluczyk, M. The role of triterpenes in the management of diabetes mellitus and its complications. Phytochem Rev. 2014; 10:1007/s11101-014-9369-x.

Okvirk S, Martin K, Shusmita K, Shamim HT, Hauner H. Traditional medicinal plants used for the treatment of diabetes in rural and urban areas of Dhaka, Bangladesh- an ethno botanical survey. Journal of Ethnobiology and Ethno medicine, 2013; 9: 43.

Ponnachan PTC, Paulos CS, Panikkar KR. Hypoglycemic effect of alkaloids preparation from leaves of *Aegle Marmelose*, Amala Research Bulletin, 1993; 13: 37-40

Prince PSM, Menon VP, Gunasekharan G. Hypolipidemic action of *Tinospora cardifolia* roots in alloxan diabetic rats. Journal of Ethanopharmacology, 1999; 64: 53-57.

Reddy JS, Rao PR, Reddy MS. Wound healing effects of *Heliotropium indicum, Plumbago zeylanicum* and *Acalypha indica* in rats. J. Ethnopharmacol, 2002; 79(2): 249-251.

Shang JH, Cai XH, Feng T, Zhao YL, Wang JK, Zhang LY, Yan M, Luo XD. Pharmacological evaluation of *Alstonia scholaris*: Anti-inflammatory and analgesic effects. J. Ethnopharmacol, 2010; 129: 174-181.

Shirwaikar A, Rajendran K. Effect of aqueous bark extract of *Garuga pinnata Roxb*. in streptozotocin–nicotinamide induced type-II diabetes mellitus. Journal of Ethnopharmacology, 2006; 112: 1–6.

Singh SN, Vats P, Suri S, Shyam R, Kumria MML, Ranganathan S, and Sridharan K. Effect of an antidiabetic extract of *Catharanthus roseus* on enzymatic activities in STZ induced diabetic rats. J. Ethanopharmacol, 2001; 76: 269-277.

Srinivas K, Rao MEB, Rao SS. Anti-inflammatory activity of *Heliotropium indicum* Linn and *Leucas aspera spreng* in albino rats. Indian J. Pharmacol, 2000; 32: 37-38.

Zhang FF, Gan LL, Zhou CH. Synthesis, antibacterial and antifungal activities of some carbazole alkaloids. Bioorg Med Chem Lett, 2010; 20: 1881–1884.

How to cite this article:

Subhan Ali Mohammad, Shaik Abdul Nabi, Saritha Marella, Krishna Tilak Thandaiah , Malaka Venkateshwarulu Jyothi Kumar, Chippada Appa Rao. Phytochemical screening and antihyperglycemic activity of *Heliotropium indicum* whole plant in Streptozotocin induced diabetic rats. J App Pharm Sci, 2014; 4 (12): 065-071.