

## Antidiabetic and hypolipidemic effects of mahanimbine (carbazole alkaloid) from *murraya koenigii* (rutaceae) leaves

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### Abstract

*Murraya koenigii* leaves (Rutaceae) are used traditionally in Indian Ayurvedic system to treat diabetes. The purpose of the study is to investigate the effect of mahanimbine (carbazole alkaloid from *Murraya koenigii* leaves) on blood glucose and serum lipid profiles on streptozotocin-induced diabetic rats. Diabetes was induced in adult male Wistar rats by intra-peritoneal injection of streptozotocin (45mg/kg). Mahanimbine (50 and 100mg/kg) were administrated as a single dose per week to the diabetic rats for 30 days. The control group received 0.3% w/v sodium carboxy methyl cellulose for the same duration. Fasting blood sugar and serum lipid profiles were measured in the diabetic and non-diabetic rats. In addition, *in vitro* alpha amylase and alpha glucosidase inhibitory effects of mahanimbine were performed. **Results:** In the diabetic rats, the elevated fasting blood sugar, triglycerides, low density lipoprotein, very low density lipoprotein levels were reduced and high density lipoprotein level was increased by mahanimbine at a dose of 50 and 100mg/kg (i.p). In addition, mahanimbine showed appreciable alpha amylase inhibitory effect and weak alpha glucosidase inhibitory effects when compared with acarbose. **Conclusions:** The present study indicated that mahanimbine possess anti-hyperglycemic and anti-lipidemic effects. Thus results suggesting mahanimbine has beneficial effect in the management of diabetes associated with abnormal lipid profile and related cardiovascular complications.

**Keywords:** Streptozotocin; Hypoglycemic; Hypolipidemic; Mahanimbine

### Introduction

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion or insulin action, or both [1]. Broad research on diabetes leads to a number of synthetic oral hypoglycemic agents like biguanides, sulphonylureas and thiozolidinediones being used to treat diabetes. But all have side effects associated with their uses [2]. On other hand, traditional medicinal

plants with their various biological constituents have been used effectively by the communities since long time to treat diabetes. Several natural products such as alkaloids, flavonoids, terpenoids, saponins, polysaccharides and glycosides are isolated from medicinal plants and are being reported to possess anti-diabetic activities [3]. In addition, herbal drugs are extensively used to treat various diseases due to

their effectiveness, minimal side effects and relatively low cost [4]. Therefore, it is important to isolate the lead molecules from traditional anti-diabetic plants.

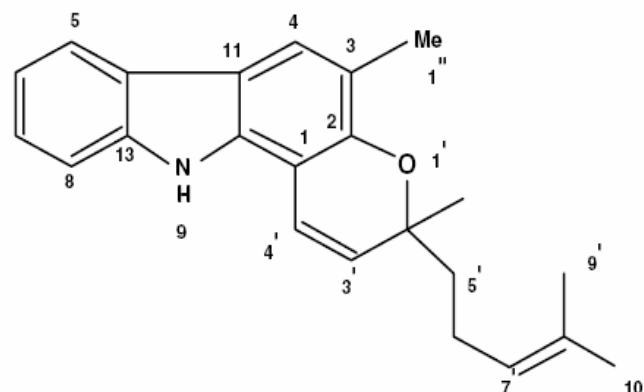
*Murraya koenigii* (Rutaceae) commonly known as “Curry Patta” (Hindi) is widely used as a spice and condiment in India and other tropical countries. Various parts of *Murraya koenigii* have been used in traditional or folk medicine for the treatment of rheumatism, traumatic injury and snake bite and it has been reported to have antioxidant, anti-diabetic and anti-dysenteric activities [5,6]. Mahanimbine is a carbazole alkaloid and present in leaves, stem bark and root of *Murraya koenigii*. Most of the carbazole alkaloids have been isolated from taxonomically related plants of the genus *Murraya*, *Glycosmic* and *Clausena* from the family Rutaceae [7]. The *Murraya* species has richest source of carbazole alkaloids. Further, Carbazole alkaloids has been reported for their various pharmacological activities such as anti-tumor, anti-viral, anti-inflammatory, anti-convulsant, diuretic and anti-oxidant activities [8]. Therefore, the present study was undertaken to evaluate anti-diabetic and anti-hyperlipidemic effects of mahanimbine (carbazole alkaloid) in streptozotocin-induced diabetic rats.

## Materials and methods

### Plant materials

*Murraya koenigii* leaves (Rutaceae) were collected from the locality of IIT Kharagpur campus, West Bengal, India in the month of September and October 2007. The leaves were inspected to be healthy and botanically identified and authenticated by M. Senthilkumar, Plant Biotechnologist, Prathyusha Institute of Technology and Management, Chennai. The herbarium *Murraya koenigii* leaves was deposited in the Prathyusha Institute of Technology and Management (PITAM) against voucher no. PITAM/CH/00009/2007. *Murraya koenigii* leaves after collection were dried at room temperature (27-30°C) for 25-30 days. After complete drying (inspection), the dried materials

were grounded into fine powder using a domestic electric grinder (Product: GX 21, Bajaj appliances, Mumbai, India) and used for extraction.



**Figure 1: Structure of Mahanimbine**

### Extraction and isolation

The dried plant powder of *Murraya koenigii* leaves were extracted with petroleum ether (60-80°C) in a Soxhlet apparatus for 72 h. at room temperature. The total extract was concentrated under reduced pressure and kept at room temperature. A greenish solid (3.6%) was separated out. This was dissolved in petroleum ether (60-80°C) and chromatographed using silica gel (60-120 mesh) column and eluted successively with petroleum ether and chloroform mixture. The fractions obtained with 50% petroleum ether (60-80°C) in chloroform afforded compound-I (mahanimbine). The compound-I was subjected to preparative TLC gave pure mahanimbine (0.4%).

### General experiments procedure

Melting point was determined in open capillary tube in SUNBIM melting point apparatus. HPTLC (CAMAG, Switzerland) analysis was performed using silica gel 60 F254 TLC plate. Mahanimbine was spotted (10µl) on a silica gel 60 F254 (Merck, Darmstadt, Germany) TLC plate. The plate was air dried and then developed using the solvent system petroleum ether and chloroform (7:3) in a CAMAG- twin-trough glass

chamber previously saturated with mobile phase vapor for 20 min. After developing the plate, it was dried at 105°C for 15 min and then it was scanned using Scanner 3 (CAMAG, Switzerland) at 254nm using WinCATS 4 software. Confirmative test for mahanimbine (carbazole alkaloid) showed purple colour spot by spraying 10% sulphuric acid on the TLC plate [9]. IR spectrum was recorded on Thermo Nicolet Nexus 870 FT-IR Spectrophotometer using potassium bromide pellet. Mass spectrum was recorded on Electro-Spray Ionization Mass Spectroscopy (Waters, UK). <sup>1</sup>H NMR (200MHZ) and <sup>13</sup>C NMR (50MHZ) spectra were recorded in CDCl<sub>3</sub> in a Bruker 200 NMR spectrometer using Topspin software.

### Animals

Adult male Wistar Rats (weighing 150-200 g) were used for the investigation. Before the starting of the experiment, the animals were acclimatized to the laboratory conditions for a period of 2 weeks. They were maintained at an ambient temperature (25 ± 2 °C) and relative humidity (40-60%), with 12/12 h of light/dark cycle. The animals were maintained on balance diet and water *ad libitum*. Institutional Animal Ethical Committee (IAEC) approved the study and all the experiments were carried out by following the guidelines of CPCSEA, India.

### Induction of diabetes and blood sample collection

A freshly prepared solution of streptozotocin (45mg/kg) in 0.1M citrate buffer pH 4.5 was injected intra-peritoneally in overnight fasted rats. After 3 days, blood was collected in vials from the tail vein of overnight fasting rats as selected under guidance of a vet using the aseptic conditions and disposable kits. FBS level of blood was checked regularly up to the stable hyperglycemia stage, usually one week after streptozotocin injection. Animals with marked hyperglycemia (FBS 250 mg/dl) were selected for the study [10].

### Experimental Design

**Group I** - Normal control

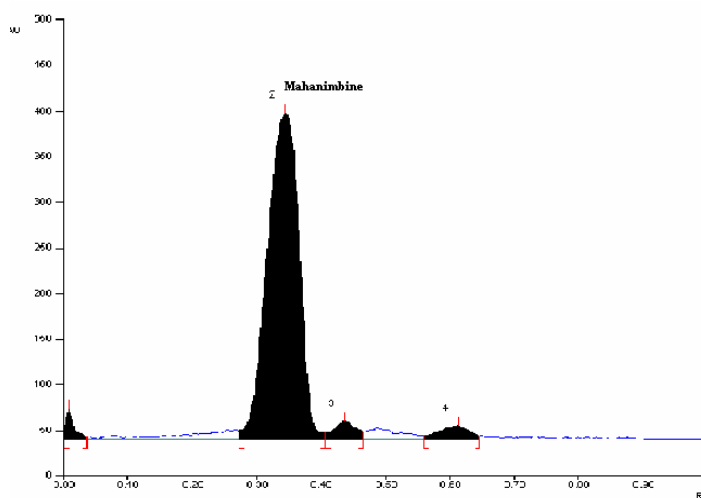
**Group II** - Diabetic control

**Group III** - Diabetic +50 mg/kg (i.p) mahanimbine

**Group IV** - Diabetic +100 mg/kg (i.p) mahanimbine

**Group V** - Diabetic + 0.5 mg/kg (i.p) glibenclamide

The experiment was carried on five groups (I, II, III, IV and V) of six rats each. Group-I served as normal control. Group-II served as diabetic control. Group III received 50 mg/kg (i.p) of Mahanimbine. Group IV received 100 mg/kg (i.p) of Mahanimbine. Group V received 0.5 mg/kg (i.p) of Glibenclamide and served as positive control. The pure mahanimbine was suspended in 0.3% w/v sodium carboxy methyl cellulose (Sodium CMC) as a vehicle and injected intra-peritoneally into rats once a week at a dose of 50 mg/kg and 100 mg/kg body weight, for 30 days. The blood samples were collected from each rat by retro-orbital venepuncture. Biochemical parameters were estimated at the beginning and after 30 days of experiment.

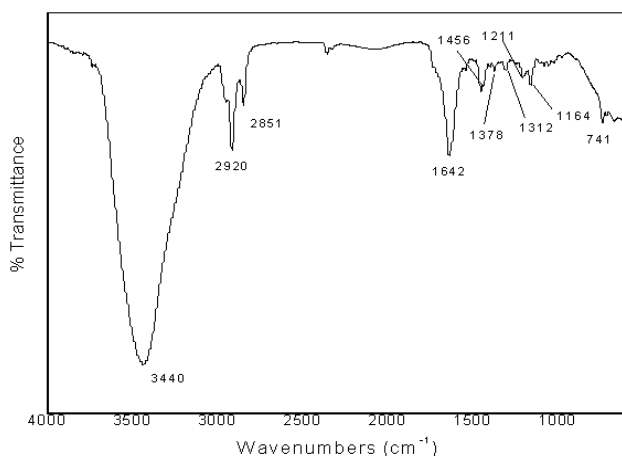


**Figure 2: HPTLC analysis of Mahanimbine**

### Biochemical parameters

Biochemical parameters notably fasting blood sugar (FBS), total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), very low-

density lipoprotein (VLDL) levels and high-density lipoprotein (HDL) level in blood serum were measured spectrophotometrically (Semi-Autoanalyzer, Microlab 300, Merck) by using diagnostic kits and reagents obtained from Merck, India.



**Figure 3: FTIR spectrum of Mahanimbine**

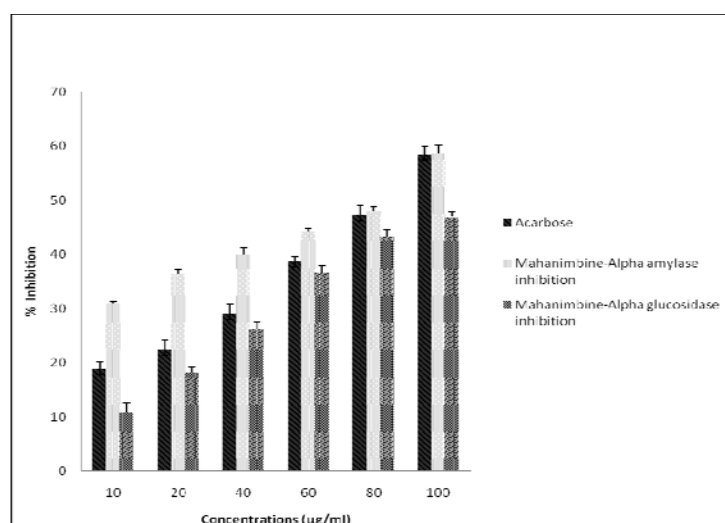
#### ***In vitro* alpha amylase inhibitory assay**

The assay was carried out following the standard protocol with slight modifications [11]. Starch azure (2 mg) was suspended in a tube containing 0.2ml of 0.5 M Tris-Hcl buffer (pH 6.9) containing 0.01 M calcium chloride (substrate). The tube was boiled for 5 min and then pre-incubated at 37° C for 5 min. Mahanimbine (1mg) was dissolved in 1ml of 0.1% of dimethyl sulfoxide in order to obtain concentrations of 10, 20, 40, 60, 80 and 100 µg/ml. Then 0.2 ml of mahanimbine of a particular concentration was put in the tube containing the substrate solution. 0.1 ml of porcine pancreatic amylase in Tris-Hcl buffer (2units/ml) was added to the tube containing the mahanimbine and substrate solution. The process was carried out at 37° C for 10 min. The reaction was stopped by adding 0.5 ml of 50% acetic acid in each tube. The reaction mixture was then centrifuged (Eppendorf -5804 R) at 3000 rpm for 5 min at 4° C. The absorbance of resulting supernatant was measured at 595nm using spectrophotometer (Perkin Elmer Lambda 25 UV-VIS). The concentration of the

mahanimbine required to inhibit 50% of alpha amylase activity under the conditions was defined as the IC<sub>50</sub> value. The experiments were repeated thrice with the same protocol. The α-amylase inhibitory activity was calculated as follows:

$$\text{The } \alpha\text{-amylase inhibitory activity} = \frac{(\text{Ac}+) - (\text{Ac}-) - (\text{As}-\text{Ab})}{(\text{Ac}+) - (\text{Ac}-)} \times 100$$

Where, Ac+, Ac-, As, Ab are defined as the absorbance of 100% enzyme activity (only solvent with enzyme), 0% enzyme activity (only solvent without enzyme), a test sample (with enzyme) and a blank (a test sample without enzyme) respectively.



**Figure 4: Alpha amylase and alpha glucosidase inhibitory effects of mahanimbine**

#### ***In vitro* alpha glucosidase inhibitory assay**

The assay was performed with standard protocol [12]. Alpha glucosidase (2U/ml) was premixed with 20 µl of mahanimbine at various concentrations (10, 20, 40, 60, 80 and 100 µg/ml) and incubated for 5 min at 37°C. 1mM par-nitrophenyl gluco-pyanoside (20 µl) in 50mM of phosphate buffer (pH 6.8) was added to initiate the reaction. The mixture was further incubated at 37°C for 20 min. The reaction was terminated by addition of 50µl of 1M sodium carbonate and the final volume was made up to 150µl. Alpha glucosidase activity was determined spectrophotometrically at 405nm on a Biorad microplate reader by measuring the quantity of

para-nitrophenol released from pNPG. The assay was performed in triplicate. The concentration of mahanimbine required to inhibit 50% of alpha glucosidase activity under the conditions was defined as the IC<sub>50</sub> value. The experiments were repeated thrice with same protocol.

### Statistical analysis

All values were expressed mean  $\pm$  standard deviation. Statistical analysis of *in vivo* results were performed by one-way analysis of variance (ANOVA) followed by Student's t-test.  $P < 0.05$  was considered statistically significant. *In vitro* inhibitory assay statistical difference and linear regression analysis were performed using Graphpad prism 5 statistical software.

### Results

Mahanimbine was isolated from *Murraya koenigii* leaves. Mahanimbine (Figure 1): white solid, C<sub>23</sub>H<sub>25</sub>NO, m.p 87-90°C. In HPTLC analysis indicated the retention factor (R<sub>f</sub>) values of mahanimbine was 0.34 (Figure 2). Confirmative test for mahanimbine showed purple colour spot (carbazole alkaloid). IR (KBr disc): 3440 (N-H), 2920, 1642 (C=C), 1456, 1378, 1312 (C-N), 1211 (C-O), 1164, 741 cm<sup>-1</sup> (Figure 3). In <sup>1</sup>H NMR (CDCl<sub>3</sub>): data showed presence of aromatic methyl group at  $\delta$  2.34, gem dimethyl on a double bond at  $\delta$  1.58 and 1.66. A tertiary methyl adjacent to oxygen at a sharp singlet  $\delta$  1.45 and a triplet at  $\delta$  5.12 (1H). A multiplet at  $\delta$  2.12-2.17 along with gem dimethyl signals showed presence of iso-prenyl side chain. A triplet at  $\delta$  1.77 (2H) and two doublets at  $\delta$  5.67 (1H) and 6.67 (1H) along with tertiary methyl signal, showed presence of a 2, 2 dimethyl chromene ring linked by an iso-prenyl side chain. The signals at  $\delta$  7.38 (d, 1H), 7.17 (t, 1H), 7.30 (t, 1H) and 7.93 (d, 1H) indicated showed presence of other ring protons. The signal at 7.89 showed due to presence of N-H proton. In <sup>13</sup>C NMR (CDCl<sub>3</sub>): data showed signal at  $\delta$ 16.04 due to presence of aromatic methyl signal on C<sub>3</sub>. Signals at  $\delta$  78.19, 128.48, 124.25, 22.78 and 17.57 showed presences of 2, 2 dimethyl chromene rings on C<sub>1</sub> and C<sub>2</sub> in carbazole moiety. Signals at

104.22, 116.67, 118.40 and 123.98 were due to presence of C<sub>1</sub>, C<sub>12</sub>, C<sub>11</sub> and C<sub>3</sub> respectively. The signals at  $\delta$  110.39, 117.56, 119.47, 121.90 and 124.21 showed presence of C<sub>8</sub>, C<sub>6</sub>, C<sub>4</sub>, C<sub>5</sub> and C<sub>7</sub> respectively. The signals  $\delta$  25.64, 25.87, 40.85, 119.28 and 131.64 indicated presence of an iso-prenyl chain attached to one of the gem dimethyl of the 2, 2 dimethyl chromene unit. The remaining twelve signals unequivocally confirmed the presence of carbazole nucleus. ESI-MS (m/z, % intensity): m/z 354 [M-H]<sup>-</sup>.

The body weight was slightly increased in normal control rats compared to initial body weight whereas streptozotocin-induced diabetic rats showed loss of body weight (173.1  $\pm$  0.57g) after 30 days as compared with initially weight of diabetic rats (198.3  $\pm$  0.64g). However, body weight of diabetic rats was restored by treating with glibenclamide (0.5 mg/kg) and mahanimbine (at a dose of 50 mg/kg and 100 mg/kg, i.p) once a week for 30 days (Table 1).

**Table 1: Body weights of streptozotocin-induced diabetic rats after treatment with Mahanimbine**

Group	Initial body weight	Final body weight
Normal control	195.5 $\pm$ 0.49	203.8 $\pm$ 1.31
Diabetic control	198.3 $\pm$ 0.64	173.1 $\pm$ 0.57*
50 mg/kg mahanimbine	194.2 $\pm$ 0.63	188.3 $\pm$ 0.71*
100 mg/kg mahanimbine	192.1 $\pm$ 0.74	186.2 $\pm$ 0.69*
0.5 mg/kg of glibenclamide	187.0 $\pm$ 0.53	179.1 $\pm$ 0.69*

Values are expressed as mean  $\pm$  S.D. \*  $P < 0.05$ , treated diabetic groups Vs diabetic control group.

Streptozotocin treatment resulted in elevation of fasting blood glucose, triglycerides, total cholesterol, low density lipoprotein and very low density lipoprotein and reduction in high density-lipoprotein levels as compared to the normal control rats as noted at end of the study (Table 2). When diabetic rats treated with mahanimbine (at

a dose of 50mg/kg and 100 mg/kg, i.p) once a week for 30 days showed significant ( $P < 0.05$ ) reduction in fasting blood sugar levels ( $217.0 \pm 0.61$  mg/dl and  $198.0 \pm 0.84$  mg/dl respectively). However, the standard drug glibenclamide (0.5mg/kg, i.p) exhibited potent anti-diabetic activity with maximum reduction of fasting blood sugar level ( $175.4 \pm 0.77$  mg/dl) on 30 days as compared to the diabetic control. There was a

significant ( $P < 0.05$ ) reduction in triglycerides, total cholesterol, low density lipoprotein and very low density lipoprotein levels of diabetic rats treated with mahanimbine (50 and 100mg/kg, i.p) as comparable to diabetic control. However, there was a significant ( $P < 0.05$ ) elevation of HDL level in mahanimbine (50 and 100mg/kg, i.p) treated diabetic rats on 30 days as compared to the diabetic control group.

**Table 2: Effect of Mahanimbine on FBS, TC, TG, HDL, LDL and VLDL in normal and diabetic rats for 30 days**

BBP	Days	Group 1	Group 2	Group 3	Group 4	Group 5
<b>FBS</b>						
(mg/dl)	0	85.3 $\pm$ 1.6	265.0 $\pm$ 1.3	241.1 $\pm$ 0.50	226.2 $\pm$ 0.47	215.1 $\pm$ 1.67
	30	92.2 $\pm$ 1.5	318.0 $\pm$ 0.74#	217.0 $\pm$ 0.61*	198.0 $\pm$ 0.84*	175.4 $\pm$ 0.77*
<b>TC</b>						
(mg/dl)	0	86.1 $\pm$ 1.48	176.2 $\pm$ 0.49	171.3 $\pm$ 0.81	168.1 $\pm$ 0.87	157.3 $\pm$ 0.60
	30	89.0 $\pm$ 0.73	196.4 $\pm$ 0.94#	162.5 $\pm$ 0.78*	151.4 $\pm$ 0.36*	148.7 $\pm$ 0.65*
<b>TG</b>						
(mg/dl)	0	85.4 $\pm$ 0.54	154.5 $\pm$ 0.49	148.4 $\pm$ 0.75	141.3 $\pm$ 0.57	138.5 $\pm$ 0.80
	30	91.0 $\pm$ 0.98	188.7 $\pm$ 0.58#	134.1 $\pm$ 0.67*	117.1 $\pm$ 0.64*	105.1 $\pm$ 0.65*
<b>HDL</b>						
(mg/dl)	0	32.5 $\pm$ 0.80	31.0 $\pm$ 0.61	33.0 $\pm$ 0.77	35.2 $\pm$ 0.75	37.1 $\pm$ 0.71
	30	34.1 $\pm$ 0.80	28.2 $\pm$ 0.57#	36.3 $\pm$ 0.72*	39.4 $\pm$ 0.70*	42.0 $\pm$ 0.64*
<b>LDL</b>						
(mg/dl)	0	45.2 $\pm$ 0.60	120.3 $\pm$ 0.75	115.5 $\pm$ 0.84	107.5 $\pm$ 0.57	98.7 $\pm$ 0.63
	30	47.0 $\pm$ 0.61	132.0 $\pm$ 0.71#	102.1 $\pm$ 0.55*	97.7 $\pm$ 0.53*	87.5 $\pm$ 0.69*
<b>VLDL</b>						
(mg/dl)	0	20.4 $\pm$ 0.71	43.2 $\pm$ 0.66	41.2 $\pm$ 0.71	38.6 $\pm$ 0.65	35.4 $\pm$ 0.74
	30	22.1 $\pm$ 0.75	49.1 $\pm$ 0.69#	33.0 $\pm$ 0.61*	27.1 $\pm$ 0.83 *	21.1 $\pm$ 0.71*

Values are expressed as mean  $\pm$  S.D. n=6/group. Group-I served as normal control. Group-II served as diabetic control. Group III received 50 mg/kg (i.p) of mahanimbine. Group IV received 100 mg/kg (i.p) of mahanimbine. Group V received 0.5 mg/kg (i.p) of glibenclamide (positive control). BBP-Biochemical parameters, FBS-fasting blood sugar, TC-total cholesterol, TG-triglycerides, LDL-low-density lipoprotein, VLDL-very low-density lipoprotein, HDL-high-density lipoprotein. #  $P < 0.05$ , Group 1 vs. Group 2. \*  $P < 0.05$ , treated diabetic groups vs. diabetic control group.

Mahanimbine showed appreciable alpha amylase inhibitory effects ( $IC_{50}$  value of  $83.72 \pm 1.4\mu\text{g/ml}$ ) and a weak alpha glucosidase ( $IC_{50}$  value of  $99.89 \pm 1.2\mu\text{g/ml}$ ) as compared with acarbose ( $IC_{50}$  value of  $83.33 \pm 1.8\mu\text{g/ml}$ ) (Figure 4).

## Discussion

The present study was designed to explore the effect of mahanimbine (carbazole alkaloid from

*Murraya koenigii* leaves) on blood glucose and serum lipid profiles on streptozotocin-induced diabetic rats. When compared FTIR, ESI-MS,  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra of isolated mahanimbine with the previously reported mahanimbine showed significant similarity [13, 14].

Intra-peritoneal administration of 50mg/kg and 100 mg/kg of mahanimbine once a week for 30 days showed anti-diabetic and hypolipidemic

effects in diabetic rats. Since, lipid abnormalities accompanying with atherosclerosis is the major cause of cardiovascular disease in diabetes. Therefore ideal treatment of diabetes, in addition to glycemic control, should have a favorable effect on lipid profiles. High level of TC and LDL are major coronary risk factors [15]. Further, several studies suggested that TG itself is indendently related to coronary heart disease [16, 17]. The abnormalities in lipid metabolism lead to elevation in the levels of serum lipid and lipoprotein that in turn play an important role in occurrence of premature and severe atherosclerosis, which affects patients with diabetes [18]. Hence, measurements of biochemical parameters are necessary to prevent cardiac complications in diabetes condition.

In the present study, an increase in blood sugar levels in diabetic rats was observed after the induction of diabetes by streptozotocin. This was prevented by treating diabetic rats with mahanimbine (at a dose 50 and 100 mg/kg, i.p) once in a week for 30 days. The standard drug glibenclamide has been used to treat diabetes, which stimulate insulin secretion from pancreatic beta cells, it may be suggested that the mechanism of action of mahanimbine is similar to glibenclamide. Several alkaloids had been reported to possess similar anti-diabetic effects of glibenclamide [19-20]. The possible mechanism by which the mahanimbine decreases blood sugar level may be by potentiating of insulin effect either by increasing the pancreatic secretion of insulin from beta cells of islets of langerhans or by increasing the peripheral glucose uptake. The mahanimbine (at a dose 50 and 100 mg/kg, i.p) treated diabetic rats showed a significant reduction in both fasting blood sugar levels and serum lipid profiles (TC, TG, LDL, and VLDL). There are several studies regarding the biological activity of carbazole alkaloids. Many carbazole alkaloids such as mukonicine, isomurrayazoline, koenoline, isomahanine, murrayanol and mahanimbine were isolated from different parts (leaves, stem bark, seed) of *Murraya Koenigii* [21-25]. Carbazole alkaloid and benzoisofuranone derivative isolated from stem

bark of *Murraya koenigii* showed antimicrobial activity [26]. Some of the isolated carbazole alkaloids and their derivative from *Murraya koenigii* leaves showed anti-trichomonal activity [27]. Three carbazole alkaloids (namely, Mahanine, Pyrayafoline-D and Murrayafoline -I) were isolated from *Murraya koenigii* leaves and reported that these alkaloids could be used for treatment of cancer as chemopreventive agents [28]. *Murraya koenigii* leaves extract showed the therapeutic protective nature in diabetes by decreasing oxidative stress and pancreatic beta cell damage [29]. Different doses of curry leaves (5, 10 and 15%) were given to normal rats, mild and moderate diabetic rats for 7 days. The results showed that *Murraya koenigii* could be useful for management of pre-diabetic state or mild diabetes [30]. The carbazole alkaloids (koenimbine and kurryam) were isolated from *Murraya koenigii* seed and oral administration of 50 mg/kg of koenimbine and kurryam exhibited significant ant-diarrhoeal effects in castor oil-induced diarrhoea rats [31].

In this study, treatment with mahanimbine (at a dose 50 and 100 mg/kg, i.p) once a week for 30 days caused significant reduction in fasting blood glucose level of diabetic rats. This is an interesting, as the treatment with dose of 50 and 100 mg/kg mahanimbine will not result in hypoglycemic shock in diabetic rats. Treatment with mahanimbine (at a dose 50 and 100 mg/kg, i.p) for 30 days significantly reduced total cholesterol, triglycerides, low density lipoprotein and very low density lipoprotein associated with significant increase in HDL levels in diabetic rats. Since HDL is responsible for the transportation of cholesterol from peripheral tissues to the liver for metabolism. The weight loss in diabetic rats may be associated with lipid lowering activity of mahanimbine or due to its influence on various lipid regulation systems. Hence, treatment with mahanimbine (at a dose 50mg/kg and 100 mg/kg body weight) in diabetic rats has potential role to prevent formation of atherosclerosis and coronary heart disease. Therefore, our *in vivo* study clearly indicated that intra-peritoneal administration of mahanimbine

(carbazole alkaloid from *Murraya koenigii* leaves) at a dose 50 and 100 mg/kg exhibited anti-diabetic and hypolipidemic effects in streptozotocin-induced diabetic rats.

In addition, one of the therapeutic approaches for Type 2 diabetes is to reduce the post-prandial hyperglycemia. Alpha amylase and alpha glucosidase are the enzymes involved in the metabolism of carbohydrates. Alpha amylase degrades complex dietary carbohydrates to oligosaccharides and disaccharides, which are ultimately converted into monosaccharide by alpha glucosidase. Liberated glucose is then absorbed by the gut and results in postprandial hyperglycemia. Inhibition of alpha amylase and alpha glucosidase limits postprandial glucose levels by delaying the process of carbohydrate hydrolysis and absorption [32]. The plant based alpha amylase and alpha glucosidase inhibitor offers a prospective therapeutic approach for the management of post-prandial hyperglycemia [33]. In the present study, mahanimbine showed appreciable alpha amylase inhibitory effects and a weak alpha glucosidase inhibitory effect as compared with acarbose. Therefore, mahanimbine might be useful in management of postprandial hyperglycemia.

### Conclusion

The present study demonstrated that mahanimbine exhibited anti-diabetic and hypolipidemic effects in streptozotocin-induced diabetic rats. Therefore, mahanimbine could be used as anti-diabetic agent in the management of diabetes associated with abnormalities of lipid profiles.

### Acknowledgements

The authors express sincere thanks to J.S.S College of pharmacy, Ooty for animal experiment support to this research work. We are also grateful to A. Basak, Department of Chemistry, Indian Institute of Technology Kharagpur for NMR studies and M. Senthilkumar, Prathyusha Institute of Technology

and Management (PITAM), Chennai for his valuable support in this research work.

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