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SHORT COMMUNICATION

Antihyperglycemic and hypolipidemic effects of *Melothria maderaspatana* and *Coccinia indica* in Streptozotocin induced diabetes in rats

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KEYWORDS

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Abstract Antihyperglycemic and hypolipidemic effects of ethanol extract of aerial parts of *Melothria maderaspatana* and *Coccinia indica* were evaluated in STZ induced diabetes in Sprague–Dawley rats. The rats were concurrently treated with 100 or 200 mg/kg b.w. p.o. for 14 days. The changes in fasting blood glucose level and body weight were measured in 5 days interval. After 14 days experimental period, rats were sacrificed by cervical decapitation, blood and liver samples were collected. Biochemical estimation of plasma glucose, cholesterol, triglycerides, LDL, HDL, SGOT, SGPT and ALP were done from blood sample. The liver glycogen content was estimated using standard procedure from homogenized liver sample. Administration of EE*Mm* or EE*Ci* to STZ-diabetic rats caused significant antihyperglycemic and hypolipidemic effects ($p < 0.001$). The extracts were also found to be significantly effective ($p < 0.001$; $p < 0.05$) on recovery of altered biochemical parameters and decreased body weight in treated animals. Glibenclamide (0.5 mg/kg b.w.) was used as standard in present study.

1. Introduction

Diabetes mellitus (DM) has been defined by a persistently elevated blood glucose concentration, leading to complications that can be acute and long term (Greenbaum and Harrison, 2008). Globally, DM presents enormous and increasingly important public health issues. The prevalence of DM in all age groups was estimated to be 2.8% (170 million) in 2000 and the rate is expected to rise to 4.4% (366 million) in 2030 (Fonseca, 2006). The occurrence and consequences associated with diabetes are found to be high in countries like India (31.7%), China (20.8%) and USA (17.7%). The rate is expected to rise to 79.4%, 42.3% and 30.3%, respectively, by 2030 in the above countries (Wild et al., 2004). The worldwide survey on diabetes reveals that among the entire diabetes cases more than 90% are account to type-II (National Diabetes Fact sheet, 2005). The overall death rate in people with diabetes is about twice that of people without diabetes (Harrigan et al., 2001).

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The beneficial uses of medicinal plants in traditional system of medicine of many cultures are extensively documented. Several plants have been used as dietary adjuvant and in treating the number of diseases even without any knowledge on their proper functions and constituents. This practice may be attributed to the uncompromised cost and side effects of synthetic hypoglycemic agents (Taylor and Triggle, 2006). Since antique era, plants with medicinal properties are enormously used in treating diabetes throughout the world. Many recent scientific investigations have also confirmed the efficacy of plant preparations, few of which are remarkably effective (Marles and Farnsworth, 1995).

Cucurbitaceae is a plant family well known to have about 125 extant genera including 960 species. It is considered to be one of the important families of plants with potent hypoglycemic effects (Bnouham et al., 2006). In modern drug discovery from medicinal plants, the importance of cucurbitaceae species has been markedly recognized in empirical control of DM. A significant number of species (*Bryonia alba* L., *Citrullus colocynthis* (L), Schrad, *Coccinia indica* Wight et Arn., *Cucumis sativus* L., *Momordica charantia* L., *Momordica cymbalaria* Hook., *Momordica foetida* Schumach. Et Thonn., *Tricosanthes dioica* Roxb) in this family were reported to cause notable hypoglycemic activity (Atta-Ur-Rahman and Zaman, 1989; Ivorra et al., 1989; Marles and Farnsworth, 1995; Roman-Ramos et al., 1995; Abdel-Hassan et al., 2000; Jayasooriya et al., 2000).

Melothria maderaspatana (Linn) Cogn. Syn. *Mukia maderaspatana, Cucumis maderaspatana or Mukia scabella* (Family: Cucurbitaceae) is a monoecious plant having scandent or prostrate stems, very hispid, leaves are variable in size, densely covered with white hairs. The plant is used as drug in the compound preparation for chronic diseases, in which cough is a predominant symptom (Kirtikar and Basu, 1975). Folklore claims the plant as good diuretic, stomachic, gentle aperients, antipyretic and anti-flatulent (Nadkarani, 1971). It is widely recommended in the southern part of Sri Lanka for alleviation of various forms of liver disorders (Jayatilaka et al., 1990). *M. maderaspatana* has also been reportedly found to exhibit anti inflammatory (Ramakrishnamacharya et al., 1996) and anticancer (Hussein and Kingston, 1982) activities. For the first time, extract of aerial parts of this plant was evaluated for antidiabetic and hypolipidemic effects.

C. indica (Cuccurbitaceae) is a creeper that grows wild and in abundance in major parts of India. The plant has been used since ancient times for treating diabetes mellitus in the Indian system of medicine known as ayurveda. As it was significantly effective in diabetes treatment, *C. indica* was described by some as 'Indian Substitute for Insulin' (Chopra et al., 1958). The plant also gained many reported scientific values as anti diabetic medicine (Mukerjee et al., 1972; Venkatraman and Pari, 2002, 2003).

Because of the professed outcome, negligible side effects or toxic contribution and comparatively cost effective than synthetic drugs, herbal, specifically cucurbitaceae family plants are widely advised choice of drug for diabetes even without their scientific backgrounds. *M. Maderaspatana* is one of such plants used in India for treating diabetes and liver disorders. However, the scientific record on this plant is very poor than *C. indica*. *C. indica* is the primary choice of plant as a drug in diabetes treatment therefore, the present study was undertaken to evaluate the antidiabetic and hypolipidemic effects of extract of aerial parts *M. Maderaspatana* (which is unknown for its antidiabetic activity) against STZ-diabetic rat model. The effectiveness of the plant was experimentally compared to*C. indica* (a known potent antidiabetic plant in cucurbitaceae family).

2. Materials and methods

2.1. Plant material

Aerial parts of *M. maderaspatana* and *C. indica* were collected from Koothiramedu village, Kanchipuram district (Tamil Nadu, India) during the month of October–December. The plant materials were authenticated by Prof. Jayaraman, Director, National Institute of Herbal Science (PARC), Chennai. The voucher specimens (Ref. No. PARC/2009/260 & 261) have been kept there for future reference. The collected plant materials were washed; shade dried and pulverized using a mechanical grinder. The powder materials were kept separately in an air tight container till used further.

2.2. Chemicals

Streptozotocin (STZ) was purchased from Sigma chemical company, Kolkata. All other chemicals used in the experiments were purchased locally (Merck or SD fine Chemicals) and were of analytical grade.

2.3. Preparation of the extract

Pulverized aerial parts of *M. maderaspatana* or *C. indica* were extracted by soaking in 95% ethanol with timely shaking and stirring for 72 h (Maceration), and filtered. The residue was discarded and the filtrate was concentrated in a rotary vacuum evaporator at 50 °C.

2.4. Maintenance of animals and approval of protocol

Adult male Sprague–Dawley rats (180–250 g) of either sex were procured from the University authorized supplier. Animals were maintained in an air-conditioned room (24 ± 2 °C) with relative humidity of 45–55% under a 12 h light/dark cycle. All animals had free access to standard diet and water *ad libitum*. The whole experimental protocol was approved by the Institutional Animal Ethics Committee and constituted in accordance with rules and guidelines of the committee.

2.5. Induction of diabetes to test animals

The overnight fasted animals were induced to diabetics by a single administration of STZ (50 mg/kg b.w. i.p.) in ice cold citrate buffer (pH 7.4). The threshold level of fasting serum glucose to diagnose diabetes was taken as >150 mg/dl and only those animals were included in the study, rest are excluded from the study. The animals were divided into seven groups of six in each group.

2.6. Effect of EEMm or EECi on serum glucose change in STZ-diabetes in rats

A 15 days short term study was chosen to perform to check the effect of *M. maderaspatana* or *C. indica* in STZ-diabetic rats. Animals received extract for a period of 15 days after

recognition of their diabetic condition. The administration of drug or control was followed as below:

Groups	Administrations
I	Vehicle control rats (0.5% CMC solution)
II	STZ induced diabetic rats (negative control)
III	Diabetic rats treated with EE*Mm* 100 mg/kg b.w./day, p.o.
IV	Diabetic rats treated with EE*Mm* 200 mg/kg b.w./day, p.o.
V	Diabetic rats treated with EE*Ci* 100 mg/kg b.w./day, p.o.
VI	Diabetic rats treated with EE*Ci* 200 mg/kg b.w./day, p.o.
VII	Diabetic rats treated with Glibenclamide 0.5 mg/kg b.w./day, p.o

The fasting blood glucose levels and body weight of the animals were determined at 0, 5, 10 and 15 day of treatments. Blood samples were collected from tail or retro-orbital vein.

2.7. Estimation of liver glycogen

After 15 days experimental period, the 12 h fasted rats were sacrificed by cervical decapitation. The liver tissue (1 g) was collected, placed in a centrifuge tube containing 2 ml of KOH (300 g/L) after washing with saline water and heated for 20 min with occasional shaking. To this, a saturated solution of sodium sulphate (0.2 ml) was added and mixed thoroughly. The glycogen was precipitated by the addition of ethanol (5 mL). The precipitate was removed and dissolved in 10 mL of water. One milliliter of this solution was added to 1 mL of HCl (1.2 mol/l) and boiled for 2 h. After 2 h, the solutions were neutralized by NaOH (0.5 mol/l) using phenol red as indicator. The neutralized solution was diluted to 5 ml and glycogen content was determined. The glycogen content was expressed as mg/g of liver tissue (Sadasivam and Manickam, 1996; Seifter et al., 1950).

2.8. Estimation of biochemical parameters

The blood was collected on day 15 after 12 h of last dose of drug administration. Rats were anesthetized by intraperitoneal injection (1 ml/kg, b.w.) of Pentothal sodium (50 mg/ml in normal saline). Blood was withdrawn from the retro-orbital plexus using capillary (20 mm length × 0.8 mm diameter) and collected in sample tubes containing EDTA (3 mg/ml). Plasma was separated and total cholesterol (TC) (Deeg and Ziegenhorn, 1983). Triglycerides (TG), Low density lipoprotein (LDL), high density lipoprotein (HDL) (Buccolo and David, 1973), serum glutamic oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT) and alkaline phosphatase (ALP) (Reitman and Frankel, 1957) were estimated by Auto-Analyzer (Accucare, Acculab-101) using the standard enzymatic methods and assay kits procured from Accucare, Lab-Care diagnostics (India) Pvt. Ltd.

3. Statistical analysis

All the data are expressed as the mean ± SEM. The statistical analysis was carried out by using Graph Pad Insat version 5. The obtained results are analyzed by ANOVA followed by post test (Bonferroni; one way and two way) and significant levels are $p > 0.05$, $p > 0.01$, $p > 0.001$.

4. Results

Tables 1 and 2 demonstrate the level of blood glucose and changes in body weight of experimental rats at first day and at the end of the 5, 10 and 15 days of treatment. There was significant increase in the plasma glucose level and a significant decrease in body weight in diabetic rats. The administration of EE*Mm* or EE*Ci* to diabetic rats resulted in a significant decrease in level of blood glucose level and a significant dose dependant increase in the body weight of rats. The extract treated groups remained to have higher serum glucose level throughout the experimental period when compared with normal rats. The administration of EE*Mm* or EE*Ci* at the dose of 200 mg/kg b.w. showed a highly significant effect that 100 mg/kg b.w. The results were comparable with the standard.

Table 3 shows the content of liver glycogen in liver tissues of normal and experimental animals. There was interestingly low content of glycogen during diabetes when compared to the respective control group. Administration of EE*Mm*, EE*Ci* and glibenclamide tend to bring the level to near normal,

Table 1 Effect of ethanol extract of EE*Mm* or EE*Ci* on serum glucose level in STZ-diabetes in rats.

Groups	Dose (mg/kg b.w.)	Plasma glucose concentration (mg/dL)			
		0 day	5th day	10th day	15th day
Vehicle control	–	103.5 ± 2.7	106.7 ± 1.9	104.50 ± 3.0	105.0 ± 3.5
STZ control	–	370.7 ± 7.1[a,#]	378.3 ± 5.5[a,#]	390.17 ± 3.9[a,#]	403.3 ± 2.5[a,#]
EE*Mm*	100	367.7 ± 6.2	328.5 ± 2.8[b,*]	270.0 ± 5.4[b,*]	241.5 ± 4.1[b,*]
EE*Mm*	200	358.0 ± 4.45	291.7 ± 5.3[b,*]	219.0 ± 5.8[b,*]	202.3 ± 4.0[b,*]
EE*Ci*	100	360.8 ± 5.09	311.0 ± 3.1[b,*]	271.5 ± 2.4[b,*]	224.2 ± 4.9[b,*]
EE*Ci*	200	365.0 ± 4.41	280.3 ± 4.6[b,*]	234.8 ± 4.9[b,*]	216.00 ± 3.6[b,*]
Glibenclamide	0.5	358.8 ± 5.21	271.2 ± 7.4[b,*]	207.5 ± 3.7[b,*]	187.17 ± 2.8[b,*]

Values are in mean ± SEM, 6 rats in each group. STZ (50 mg/kg b.w.) was injected to control and rest are treated groups.
[a] STZ induced diabetic group *vs.* vehicle control group.
[b] Treated group *vs.* STZ induced group.
[#] $p < 0.001$.
[*] $p < 0.001$.

Table 2 The effect on body weight changes during 14 days treatment of EE*Mm* or EE*Ci*.

Groups	Dose (mg/kg b.w.)	Body weight (g/day)			
		0 day	5th day	10th day	15th day
Vehicle control	–	208.2 ± 5.0	232.5 ± 6.9	248.2 ± 13.3	273.2 ± 9.1
STZ control	–	180.7 ± 11.8[a,#]	179.3 ± 10.8[a,#]	173.2 ± 0[a,#]	168.0 ± 8.9[a,#]
EE*Mm*	100	177.0 ± 7.9	183.5 ± 10.3	176.7 ± 8.8	175.8 ± 5.9
EE*Mm*	200	181.3 ± 13.4	185.7 ± 13.4	190.7 ± 16.1[b,*]	195.8 ± 19.1[b,***]
EE*Ci*	100	185 ± 8.6	190.8 ± 9.2	174 ± 14.6	185.5 ± 8.3 [b,*]
EE*Ci*	200	179.8 ± 9.4	184.7 ± 9.2	191.7 ± 9.8[b,*]	199.5 ± 10.1[b,***]
Glibenclamide	0.5	181.7 ± 12.2	191.5 ± 6.6	203.5 ± 6.7[b,***]	218.7 ± 5.4[b,***]

Body weight degreases with injection of STZ. Body weights were measure with 5 days interval for 15 days. Each value is the mean ± SEM; $n = 6$.

[a] STZ induced diabetic group *vs*. vehicle control group.

[b] Treated group *vs*. STZ induced group.

[#] $p < 0.001$.

[*] $p < 0.001$.

[***] $p < 0.001$.

Table 3 Effect of EE*Mm* and EE*Ci* on liver glycogen level in STZ-diabetes in rats.

Groups	Dose (mg/kg b.w.)	Liver glycogen (mg/g of liver)
Vehicle control	–	47.8 ± 1.8
STZ control	–	15.2 ± 0.9[a,#]
EE*Mm*	100	29.5 ± 1.8[b,*]
EE*Mm*	200	33.8 ± 1.8[b,*]
EE*Ci*	100	27.5 ± 1.6[b,*]
EE*Ci*	200	32.6 ± 1.6[b,*]
Glibenclamide	0.5	38.7 ± 1.9[b,*]

Values are in mean ± SEM, 6 rats in each group. STZ (50 mg/kg b.w.) was injected to control and rest are treated groups.

[a] STZ induced diabetic group *vs*. vehicle control group.

[b] Treated group *vs*. STZ induced group.

[#] $p < 0.001$.

[*] $p < 0.001$.

Table 4 Effect of EE*Mm* or EE*Ci* on biochemical parameter in STZ-diabetes in rats after 14 days treatment.

Groups	Dose (mg/kg b.w.)	Cholesterol (mg/dl)	Triglycerides (mg/dl)	LDL (mg/dl)	HDL (mg/dl)
Vehicle control	–	144.5 ± 1.34	114.3 ± 1.6	128.17 ± 1.11	53 ± 1.07
STZ control	–	266.7 ± 2.4[a,#]	230.3 ± 1.8[a,#]	232.8 ± 2.8[a,#]	31.2 ± 1.2[a,#]
EE*Mm*	100	196.7 ± 1.5[b,*]	175.33 ± 2.5[b,*]	173.3 ± 1.4[b,*]	34.7 ± 0.8
EE*Mm*	200	165.5 ± 1.8[b,*]	149.50 ± 2.5[b,*]	144 ± 1.4[b,*]	42.7 ± 0.9[b,*]
EE*Ci*	100	203.0 ± 2.2[b,*]	183.5 ± 2.2[b,*]	177.8 ± 1.8[b,*]	33.7 ± 1.4
EE*Ci*	200	168.5 ± 1.9[b,*]	151.8 ± 1.3[b,*]	143 ± 1.6[b,*]	43.5 ± 1.0[b,*]
Glibenclamide	0.5	160.8 ± 1.6[b,*]	139.5 ± 1.3[b,*]	139 ± 1.2[b,*]	43.67 ± 0.9[b,*]

Values are mean ± SEM, 6 rats in each group. STZ (50 mg/kg b.w.) was injected to control and rest are treated groups.

[a] STZ induced diabetic group *vs*. normal group.

[b] Treated group *vs*. STZ induced diabetic group.

[#] $p < 0.001$.

[*] $p < 0.001$.

which has been indicated by the higher levels of hepatic glycogen in the drug treated diabetic animals.

Table 4 shows the concentration of concentration of TC, TG, LDL and HDL. There was significant increase in the concentration of TC, TG, and LDL and significant decrease in HDL during diabetes when compared to corresponding control groups. Administration of EE*Mm*, EE*Ci* and glibenclamide tend to bring the level to near normal.

Table 5 illustrates the effect of administration of EE*Mm*, EE*Ci* and glibenclamide on serum biochemical markers. The

Table 5 Effect of EE*Mm* and EE*Ci* on serum biomarkers in STZ induced diabetes in rats after 14 days treatment.

Groups	Dose (mg/kg b.w.)	SGOT (μ/L)	SGPT (μ/L)	ALP (μ/L)
Vehicle control	–	62 ± 1.1	63.2 ± 1.1	124.2 ± 1.0
STZ control	–	153 ± 1.4[a,#]	146.2 ± 1.2[a,#]	250.3 ± 1.1[a,#]
EE*Mm*	100	99 ± 1.2	77.2 ± 1.4[b,*]	151.2 ± 4.0[b,*]
EE*Mm*	200	63.2 ± 1.0[b,*]	66.2 ± 0.5[b,*]	126 ± 1.1[b,*]
EE*Ci*	100	97.8 ± 1.5	115.3 ± 0.9	178.2 ± 1.1
EE*Ci*	200	68.5 ± 1.7[b,*]	75.3 ± 1.2[b,*]	140.7 ± 1.2[b,*]
Glibenclamide	0.5	66.7 ± 1.2[b,*]	72.5 ± 1.2[b,*]	136.8 ± 1.6[b,*]

Values are mean ± SEM, 6 rats in each group. STZ (50 mg/kg b.w.) was injected to control and rest are treated groups.
[a] STZ induced diabetic group *vs.* normal group.
[b] Treated group *vs.* STZ induced diabetic group.
[#] $p < 0.001$.
[*] $p < 0.001$.

concentration of SGOT, SGPT and ALP was significantly increased in diabetes condition when compared with normal control. Administration of EE*Mm*, EE*Ci* and glibenclamide was found to increase the levels near to normal values. The effect of EE*Mm* at the dose of 200 mg/kg b.w. was more prominent than glibenclamide.

5. Discussion

The traditional system of medicinal plants and practices have been a imperative resource in many countries to control various complications of diabetes mellitus as they are considered to be less toxic and free from side effects than synthetic molecules. Cucurbitaceae is one of the important families of the plants with potent hypoglycemic effect (Bnouham et al., 2006; Ghosh et al., 2004; Mukherjee et al., 1972) to be used as best choice of alternative medicine for treating diabetes throughout India. The current study dealt with two plants, one is well known (*C. indica*) for antidiabetic activity and the other is less known (*M. maderaspatana*).

The observed significant increase in of blood glucose level in diabetes rats could be due to the destruction of pancreatic β-cells by STZ administration and decreased glycogen formation during diabetes. The concurrent treatment of EE*Mm* and EE*Ci* for 14 days caused significant reduction ($p < 0.001$) in blood glucose level in STZ-diabetic rats and significant increase in glycogen formation. The increased content of glycogen in drug treated experimental animals could be contributed to the decreased endogenous glucose output from the liver.

The priorities of lipid goals are LDL and non-HDL cholesterol lowering, followed by HDL rising. The strong hypolipidemic activity observed in treatment with EE*Mm* and EE*Ci* could be through the control of hyperglycemia, as it is a major determinant of TC, LDL and TG concentrations during diabetes. The level of HDL-cholesterol, which increased after administration of EE*Mm* or EE*Ci*, might be due to the increase in the activity of lecithin cholesterol acyl transferase, which may contribute to the regulation of blood lipids.

The derangements of metabolic processes in disease are often associated with alteration in serum enzymatic activities. Hence the assay of serum enzymes has become an important goal during diabetes. The transaminase (SGOT, SGPT and ALP) activity is increased in serum during diabetes (Ghosh et al., 2004). The increased level in SGOT, SGPT and ALP, which are active in the absence of insulin, with the availability of amino acids in blood of diabetics, are responsible for the increased formation of gluconeogenesis and ketogenesis observed in diabetics (Mukherjee et al., 1972).The remarkable reduction in the level of SGOT, SGPT and ALP of treated diabetes rats could also contribute to reduction of glucose level by inhibiting gluconeogenesis process. In the present study, EE*Mm* at the dose of 200 mg/kg b.w. was found to bring the serum transaminase activity more significantly than glibenclamide towards normal.

6. Conclusion

The plant *M. maderaspatana* is as effective as *C. indica* in treating the STZ-diabetic rats. Hence, this plant may be used as a substitute for *C. indica* in treating diabetes. Combination of these two plants in treating diabetes may be expected to produce better significant results. However, further study is required to evaluate using a long term study and adverse and beneficial effects of their combination.

Conflict of interest statement

There are no conflicts of interest.

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