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Amelioration of Streptozotocin Induced Diabetes Mellitus and Lipid Profile in Rats by *Mukia Maderaspatana Linn*

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ABSTRACT

Diabetes is a condition primarily defined by the level of hyperglycemia giving rise to risk of micro vascular damage (retinopathy, nephropathy and neuropathy).Over 400 traditional plant treatments for diabetes have been reported, although only a small number of these have received scientific and medical evaluation to assess their efficacy. The World Health Organization Expert Committee on diabetes has recommended that traditional medicinal herbs be further investigated. In the Indian system of medicine, Mukia maderaspatana Linn was used for different pharmacological activities. But the pharmacological and scientific evidence for its antidiabetic effect is yet to be proved. So, based on above fact it can be evaluated for antidiabetic and antioxidant property in streptozotocin (STZ) induced diabetic rats for 21 days. Diabetes was induced using streptozotocin (50 mg/kg i.p) and after the induction of diabetes the animals were given with MEE (100 mg/kg, 200 mg/kg), MCF (100 mg/kg) and MBF (100 mg/kg) orally for 21 days. Blood glucose levels were determined by using GOD-POD method with diagnostic kits. After 21 days the parameters like HDL, LDL, VLDL, TC, TG, Albumin, Creatinine, total protein and glucose were estimated. The treatment with the extracts and fractions of Mukia maderaspatana Linn improved the lipid level and lipoprotein level to a normal condition which may be attributed to its potent antidiabetic activity.

Keywords: *Mukia Maderaspatana Linn, Hyperglycemia, Streptozotocin, Antidiabetic Activity.*

1. INTRODUCTION

Diabetes mellitus is a serious complex chronic condition that is major source of ill health worldwide. This metabolic disorder is characterized by hyperglycemia and disturbances of carbohydrate, protein and fat metabolisms, secondary to an absolute or relative lack of the hormone insulin. The number of people in the world with diabetes has increased dramatically over recent years. The diabetes control and complications trial (DCCT) research group stated that tight control of blood glucose is an effective strategy in reducing clinical complications of diabetes mellitus significantly but even optimal control of blood glucose could not prevent complications suggesting that alternative treatment approaches are needed. The use of herbal medicine is widespread, which are used by the people for the treatment of disparate diseases even at this modern era. There are diverse medicinal plants in the world, which are the impeding sources of the drugs. These drugs are invariably single plant extracts or fractions or mixtures of extracts/fractions from different plants, which have been carefully standardized for their safety and efficacy. (1)

Now a days, scientists and researchers are very much tiring on research of natural plant products all over the world and a large number of substantiation have shown the immense potential of medicinal plants used traditionally. In addition to the known plants, there are unexplored group of plants used by tribal and folk medical practitioners which are a promising source of effective antidiabetic agents. Despite its ancestral use in the treatment of diabetes mellitus there are insufficient scientific data to support folkloric medicine. This formed the basis of present study which was aimed at investigating the effects of oxidative stress, nephropathy and dyslipidemia in streptozotocin-induced diabetic rats by oral administration of extract and fractions of *Mukia maderaspatana.* (2, 24)

Herbal medications are the most commonly used alternative therapy for blood sugar control; however, their safety and efficacy need to be further evaluated by well-designed, controlled clinical studies.In the Indian system of medicine, *Mukia maderaspatana Linn* was used as a bitter, sweet, refrigerant, carminative, sudorific, expectorant, anodyne and tonic.

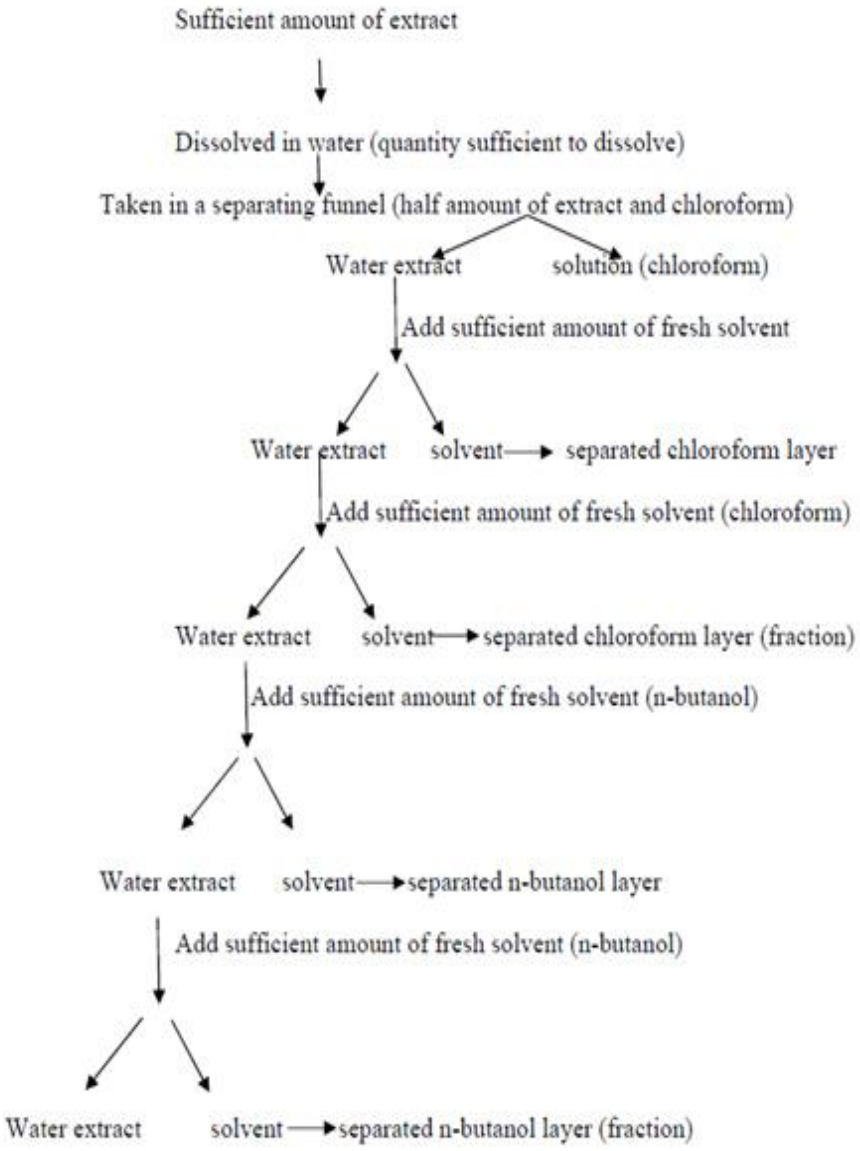
2. OBJECTIVE

The pharmacological and scientific evidence for the antidiabetic effect is yet to be proved. So, the main objective of the study is to find the antidiabetic property and lipid profile in streptozotocin (STZ) induced diabetic rats.

3. MATERIALS AND METHODS

3.1 Chemicals used: Streptozotocin from Aldrich and Ascorbic acid, Nitro blue tetrazolium (NBT), sodium nitroprusside, dimethyl sulphoxide, potassium chloride and sodium chloride from Ranbaxy Laboratories Ltd., Mohali, India. Sulphanilic acids, sodium bicarbonate from E Merck (India) Ltd, Mumbai, India. Disodium hydrogen phosphate, nutrient broths were obtained from Hi-Media Lab PVT. Ltd, Mumbai. All other chemicals used in the studies were analytical /laboratory grades procured from the following manufacturers, Loba chemie, ACROS Organics, Merck lab, S.D.Fine chemicals, Fluka., diagnostic kits, MEE (100 mg/kg and 200 mg/kg), MCF (100 mg/kg) and MBF (100 mg/kg). (3, 4, 18, 19)

The plant was collected from the forests of polavaram in WG district of A.P and was authenticated by the botanist. The collected fresh plant materials were dried in shade (2 days) and then dried in a hot air oven at 250C for three days and they were made in to coarse powder with the use of mixer grinder. The powder of entire plant of Mukia maderaspatana obtained were weighed separately and transferred to a round bottomed flask and then went with soxhlet extraction using 95% ethanol for 24 hour. Then the extract of ethanol was concentrated and then the marc was stored for fractionation. The alcoholic extract was fractionated with chloroform and n-butanol respectively as shown in the figure.



Solvent- solvent fractionation

3.2 Animals used:

Healthy, adult Wistar rats of both sexes (150-220g) were obtained from the central animal house facility. The animals were kept in a well ventilated room and the animals were exposed to 12 hrs day and night cycle with a temperature between 20±3 ^{0} C. The

animals were housed in large spacious, hygeinic polypropylene cages during the course of the experimental period. The animals were fed with water and rat feed *ad libitum*,. All the experiments were performed after obtaining prior approval from IAEC.

3.3 Induction of diabetes:

Non-Insulin dependent diabetes mellitus (NIDDM) was induced by a single intraperitoneal injection (i.p.) of 50mg/kg streptozotocin. The rats with permanent NIDDM (250-350 mg/dL) were used for the study.

3.4 EXPERIMENTAL MODELS:

Oral glucose tolerance test (OGTT):

Rats divided in to six groups (n-6) were administered with 10 mg/kg Glibenclamide, 100 mg/kg, 200 mg/kg ethanolic extract, 100 mg/kg chloroform fraction, and 100mg/kg n-butanol fraction, respectively. Glucose (2 g/kg) was fed 30 min. after the administration of extracts. Blood was withdrawn from the retro orbital sinus under ether inhalation at 0, 30, 60, 90, and 120 min. of extract administration. The fasting blood glucose levels were estimated by glucose oxidase-peroxidase method**.** (5, 6)

STZ Induced Diabetic Model:

The Wistar rats (180-220 gm) of either sex were used for the experimental study. The animals were divided into seven groups of 6 animals each.

GROUPING OF THE ANIMALS

GROUP I	-	Untreated Control
GROUPII	-	Diabetic control
GROUPIII	-	Positive control (Glibenclamide 10 mg/kg i.p)
GROUPIV	-	MEE 100 mg/kg
GROUPV	-	MEE 200 mg/kg
GROUPVI	-	MCF 100 mg/kg
GROUPVII	-	MBF 100 mg/kg

The test doses were administered orally for 21 days. Urine sugar, glucose was analyzed every week and lipoprotein profile from serum was analyzed after 21 days. Total protein, albumin, creatinine, urea were also analyzed by serum.

4. RESULTS

OGTT:

The treatment with MEE, MCF and MBF showed the tolerance towards glucose when compared with that of normal animals.

S.No	TREATMENT	Blood glucose concentration(mg/dL)				
		0 min	30min	60min	90min	120min
1.	Untreated Control	88.16±1.25	110.5±1.33	103.1±0.73	102.5±0.76	96.33±0.98
2.	Glibenclamide(10mg/kg)	82.50±0.76	94.2±4.01 ###	80.5±2.18 ###	78.1±2.12 ###	66.5±0.76 ###
3.	MEE(100mg/kg)	80.10±1.40	110.3±2.51 **	101.8±3.81 **	89.5±2.86 ***	85.6±2.21 **
4.	MEE(200mg/kg)	77.83±2.60	94.2±2.61 ***	89.2±1.90 ***	85.8±2.77 ***	79.2±2.61 ***
5.	MCF(100mg/kg)	80.50±3.30	110.5±2.42 ***	93.1±3.20 **	89.3±4.11 ***	82.3±3.6 2**
6.	MBF(100mg/kg)	76.67±2.30	103.5±5.31 ***	92.7±5.91 **	90.6±3.13 ***	81.17±3.30 **

All value are expressed as mean ± SEM

***P<0.001, **P<0.01, as compared to Glibenclamide

P<0.001, as compared to untreated control

EFFECT OF EXTRACTS ON SERUM GLUCOSE:

The treatment with MEE, MCF and MBF in STZ induced diabetic rats significantly decreased the elevated serum glucose levels from first week onwards

S.No	TREATMENT	Serum glucose (mg/dL)			
		0 day	7th day	14th day	21th day
1.	Untreated control	84.83±5.41	85.33±5.87	84.66±5.77	84.83±5.09
2.	Diabetic control	298.16±17.20	367.33±4.70 ###	413.83±16.61 ###	410.00±2.05 ###

3.	Diabetic+Glibenclamide(10mg/kg)	280.33±2.44	205.33±1.14 **	165.00±1.29 ***	114.83±1.302 **
4.	Diabetic+MEE (100 mg/kg)	319.33±6.76	217.83±6.46 **	147.17±5.36 ***	121.00±2.67 ***
5.	Diabetic+MEE (200 mg/kg)	322.17±10.20	217.17±9.10 **	142.17±7.10 ***	115.00±4.50 ***
6.	Diabetic+MCF (100 mg/kg)	316.83±15.30	251.17±13.17 **	152.33±8.17 ***	120.50±2.52 ***
7.	Diabetic+MBF (100 mg/kg)	310.17±15.10	245.67±14.84 **	144.5±4.78 ***	121.50±3.88 ***

All value are expressed as mean ± SEM (n=6).

***P<0.001, **P<0.01 as compared to diabetic control;

$^{##}$P<0.01, $^{###}$P<0.001 as compared to untreated control

EFFECT OF EXTRACTS ON SERUM LIPID AND LIPOPROTEIN PROFILE:

The treatment with the extracts and fractions of *Mukia maderaspatana Linn* improved the lipid level and lipoprotein level to a normal condition, which may be attributed to its potent antidiabetic activity.

S.No	TREATMENT	TC(mg/dL)	TG(mg/dL)	HDL(mg/dL)	LDL(mg/dL)	VLDL(mg/dL)
1.	Untreated control	86.50±0.76	54.83±1.14	54.80±0.69	18.38±0.40	8.79±0.40
2.	Diabetic control	156.68±0.72 ###	183.5±11.59 ###	21.33±0.44 ###	37.73±6.75 ###	37.10±2.85 ###
3.	Diabetic+ Glibenclamide (10mg/kg)	69.33±2.81***	116.5±5.21***	32.63±2.30 ***	16.27±1.39 ***	23.96±1.13 **
4.	Diabetic+MEE (100 mg/kg)	73.18±4.59 *	123.3±6.32 **	41.13±0.52 **	18.48±1.51 ***	23.90±0.87 ***
5.	Diabetic+MEE (200 mg/kg)	66.15±7.50 **	120.33±5.37 ***	31.62±1.74 ***	15.27±0.79 ***	20.00±1.49 ***
6.	Diabetic+MCF (100 mg/kg)	72.15±5.52 *	152.66±6.81*	36.48±3.3 **	17.57±3.05 ***	23.05±1.95 ***
7.	Diabetic+MBF (100 mg/kg)	65.72±13.26 **	140.16±7.89 *	33.78±7.12 **	16.80±4.03 ***	27.20±1.03 **

All value are expressed as mean ± SEM (n=6),
* P<0.05,** P<0.01, *** P<0.001, as compared to diabetic control
$^{##}$ P<0.01, $^{###}$ P<0.001,as compared to untreated control

5. DISCUSSION

Glucose tolerance signifies the ability of the body to dispose of additional glucose entered into the body. It is useful in distinguishing a person with normal glucose tolerance and a person with impaired glucose tolerance namely diabetic.

Serum lipid profile is usually raised during diabetes and presents a risk for the coronary heart disease.

The diabetic hyperglycemia induces elevation of the serum levels of urea, creatinine which are considered as significant marker of renal dysfunction.

Reduction in serum total protein and albumin level was observed in diabetic rats.

6. CONCLUSION

The present study was an attempt to investigate the effect of extracts and fractions of *Mukia maderaspatana Linn* on glycemia, lipid and lipoprotein level in STZ induced diabetic rats.

The administration of extracts and fractions of *Mukia maderaspatana Linn* showed a significant activity on blood parameters such as glucose, lipid and lipoprotein profiles.

Further clinical studies on the plant may reveal it as a potent andiabetic agent.

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