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EVALUATION OF ANTIDIABETIC ACTIVITY OF STEM BARK OF *MURRAYA KOENIGII* ON EXPERIMENTAL ANIMALS

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ABSTRACTS

The current study is an effort to examine the effect of *Murraya koenigii* stem bark extract on streptozotocin induced diabetes in Wistar rats. Two groups of streptozotocin persuaded diabetic rats were orally treated through *Murraya koenigii* stem bark extract (200 and 400 mg/kg) respectively. The blood glucose level, body mass, Glycosylated hemoglobin, liver glycogen, lipid profile, Antioxidant status were measured at the finish of the study that is after 28 days of treatment. Murraya koenigii stem bark extract were originate to be significant ($p < 0.001$) in dropping the blood glucose level, glycosylated hemoglobin, triglyceride, cholesterol, blood urea, lipid profile, while both the treatments improved body weight, liver glycogen satisfied status once compared to the diabetic control. It have been concluded that *Murraya koenigii* stem bark extract, in adding to the antidiabetic activity in the streptozotocin induced diabetic model.

INTRODUCTION

The term diabetes is often used to mean "diabetes mellitus". Diabetes is a group of metabolic illnesses that cause chronic high blood sugar levels and is a major health problem currently recognized simultaneously of the top some causes of death worldwide.

The WHO (World Health Organization) estimates that the number of diabetic patients in the world is steadily increasing. The occurrence of diabetes international is assessed at 2.8 present in 2000 and 4.4% in 2030. The whole figure of persons with diabetes is probable to increase from 171 million in 2000- 366 million by 2030.

For many people, diabetes mellitus is a fact that they have to live with every day. Diabetes kills one person every 10 seconds and infects two people at once. This is the horrible truth behind the silent killer who is taking his own lives around the world rather than AIDS and cancer.

Rendering to the Nationwide Diabetes and Diabetic Retinopathy Study provide through the Ministry of Health and Family Welfare, the occurrence of diabetes to India has been 11.8% over the past 4 years.

A survey conducted by the Rajendra Prasad Center of Ophthalmic Sciences in New Delhi in 2015-2019 also revealed which the occurrence of identified diabetes cases was 8.0 % and new diabetes cases 3.8%. The prevalence of diabetes in men is 12% compared to women, which is 11.7%, 67.3% of participants with known diabetes, and 32.7% of those with new diabetes. The highest prevalence was observed at the age of 70–79 years at 13.2%. The report states that 40% of cases of diabetes known 1-4 years ago were diagnosed and 5.3% of cases of diabetes were diagnosed last year.

MATERIAL AND METHOD

The stem bark of the plant is composed nearby from the herbal Botanical Garden of Botany Central Council of Investigation Ayurvedic and Siddha India. The shrub was recognized, authenticated through contrast with Herbarium samples. The stem bark of Tecomastens (L.) Jas xkunt was verified by contrast thru herbarium samples and certification number.

Coarse powders were weighed by consecutive solvent extraction by means of a Soxhlet apparatus using different solvents.

Chemicals and Drugs

Streptozotocin, citric-acid, sodium-citrate is released at a private biochemical stockpile in Delhi. Alcohol, HCL, - $C_{10}H_8$, H_2So_4, Fehling A&B, Benedict mixture, Sodiumhydroxide - Extra essential chemicals used in phytochemical examination.

Nitricacid, ammonia, leadacetate, ninhydride, sudan red-III reagent, glycerine, picricacid, chloroform, acetic-anhydride, ferricchloride, zinc, Dragendroff's mixture, wagner chemical, and Wagner chemical, transalam college of pharmacy for medical education and research,. All chemicals used in the study in the analysis phase.

Extraction Procedure
The stem bark of the dried up plant in the shadow are prudently removed and ground using a mixer. The maximum energy found thus used to be extracted by the abstraction machine using a series of solvents.

Alcoholic extract
The marker obtained from the above extract was dried for 36 h using a socket with 2.5 liters of ethanol (90%) and collected. The resulting discharge is collected and concentrated by vacuum distillation. Focused discharge is dried on a vacuum desiccator.

Phytochemical Analysis
The phytochemicals found in plants are naturally active, logically happening in chemicals that provide health benefits to humans compared to those given to macro-nutrients and micro-nutrients. Plant activities are part of the plant components of medicinal activities. These releases are subject to quality testing to identify the various parts of the plant.

TOXICITY STUDIES
Acute toxic study
Research has been done to investigate the toxic effects of the release. Guidelines for the Organization for Cooperation and Development (OECD) no. According to 423 the study was conducted. Mice are used for this determination. Animals fasted overnight, only water was given, after which the discharge was controlled with a gauge with a body weight of 2000 mg / kg in appropriate groups and groups were given continuously 24 h for behavioural, neurological and anatomical profiles and 24 h for any a bad situation. 72 h. The animals were tested for toxicity for 14 days. According to the guidelines, if death is detected in 2 or 3 animals, the dose to be given is determined as a toxic dose. When death is detected in an animal, the same dose is repeated to confirm the toxicity. If death is not detected at all, plant extraction is considered non-toxic. Alternatively, the toxicity test can be started with 5mg / kg body weight and repeated in other doses such as 50, 300, 2000 mg / kg body mass.

Choice of Experiment animals
Referred adult female rats aged 8-12 weeks. Comfort with non-pregnant animals was obtained at the Meerut Medical Education and Research Centre at Centralized Animal House of Translam and is usually maintained for 1 week prior to dosing.

Feeding condition and housing of experimental animals
Temperature: The temperatures of animal house are maintained at $23^0C \pm 5^0C$/OECD guideline-420.

Moisture
The relative humidity of the animal's apartment is upheld at 50 to 60 %, rather not more than 70% (OECD guideline 423, 2001). Else there might be an increase in food consumption due to injuries such as ring tail.

Lights: 12 hour's bright and 12 hours dark.

Caging
Polypropylene cages with solid walls and solid bottoms are used. The bottles are made of stainless steel that can hold both feed and water.

Drug administration
The animals came before the dose (diet but liquid would not be stopped overnight). Animals are weighed and tested equipment is provided. Healthy rats were engaged and distributed into 4 different groups. The exam material is supplied in one volume by an orally gauge using a stainless steel feed needle lined with a ball.

Experimental Design
In present work, four groups of six rats were assumed by 5, 50 and 300 and 2000 mg/kg abstract (PO). Meals should be discontinued for 3 hours after drug administration. Animals should be seen regularly for the first two hrs after treatment, occasionally for six hrs and every day for 14 days to observe any signs of poisoning and death. Skin and hair, eyes and mucous membranes (nose), autonomic paraphernalia (saliva, lacrimation, gait and pilerection) and central nervous system (gait, tremors and seizures) observed daily and changes noted (OECD, 2001).

Clinical Observation
Totally animals are observed for signs of toxicity up to 4 hours after dosing. Additional observations will also be made over the next 14 days for some extra behavior or clinical ciphers. Weight change is calculated. The animals are weighed at the end of the test. LD50 standards are recognized by the formula.

Pharmacological Studies
Selection of Exam rat
Male Wistar mice assessing 150–200 g were used for the current work. The animals used aimed at trial had kept in the animal house at Translam institute of pharmaceutical education and research Meerut under standard laboratory conditions. Approved by the Control and Monitoring Committee (IAECNO. KU / IAEC/ M.Pharm /169) for experiments on animals with a 12 hour dark / light cycle and a controlled temperature of 24^0 C. Under 2 ° C. they get free food and water. Prior to the start of the experiment, the animals were accustomed to the laboratory for 7 days.

Overview of Diabetes in Investigational Animals
Investigational diabetes was persuaded with a single intra-peritoneal injection
After 15 minutes of intra-peritoneal inoculation of 25mg / kg of streptozotocin, nicotinamide (110 mg / kg) was prepared with common salt, recently mixed in a cold citrate-buffer (pH4.5). Rats with Glycosuria (not eat plasma glucose above 200mg/dL) were detected 7 days after STZ given was used for research.

Examination of diabetes

Diabetes was diagnosed 48 hours later the injection of streptozotocin, plasma samples had collected from the tail vein and glucose level was tested using the glucose oxidase method (Accu Check glucometer activated). Mice with a plasma glucose level faster than 200mg/dL) were designated and used for the current work.

Glucose-Tolerance Test

The Orally Glucose Tolerance Assessment determines the body capability to absorb glucose, the bodys chief energy source. Glucose tolerance tests were achieved on normal mice by fasting overnight (18 hours).

Experimental Design

Ordinary mice are distributed addicted to 4 groups, every containing of 6 mice. Normal group-control (refined liquid). Group II and group III animals expected a variety of extracts. 200 mg / kg and 300mg/kg, in that order. Glibenclamide (GL) is common in Group IV animals weighing 10 mg / kg. In group-II and group III animals the single dose was 200mg /kg and 300mg/kg respectively. Treatment 30 minutes after administration of the drug Glucose (2 g / kg) given to tubes. Control animals are kept in equal amounts of aqueous. Plasma is drawn from the tail vein at zero, one, two, three and four h after glucose taken. Percentages after glucose loading at different times were calculated according to the following glycaemia (% IG) control and treatment groups.

$$\%IG = (Gx - Go) / Go \times 10$$

Here to go first glycaemia (mg/dL) and Gx-glycemia (mg/dL) at dissimilar times later oral glucose weight.

Hypoglycemic Activity

Dosage is designated for STZ induced diabetic rat sample study, based on OGTT studies in usual, diabetic mice.

RESULTS AND DISCUSSION

EXTRACTION

The extraction of solvent is done as solvents in the dry part of the Murraya koenigii powder using stem bark and water. The highest extraction rate was found in leaf alcohol extraction.

PHYTOCHEMICAL ASSESSMENT

Phytochemicals are plant organisms linked to protecting human wellbeing from chronic degenerative illnesses. Phyto-chemical examination of ethanolic abstraction reveals Alkaloids, Carbohydrates, Saponins, and Proteins, aminoacids, flavonoids and tannins. The mixture of the abovementioned phytochemicals can create anti-diabetic properties in this plant.

PHARMAACOLOGICAL STUDIES

Result of ethanol abstract on Glucose Loaded Rats (OGTT Model)

Table No.1: Result of ethanolic abstract on serum-glucose levels in OGTT model in normal rats.

S. No.	Drug /control	Body Wt.	Body glucose level(mg/dl)				
			0 hr	1 hr	2 hr	3 hr	4 hr
1	Grup I Control (distilled water)	181.0 ±3.0	91. ±2.6	133.0 ± 3.5	118.0 ± 0	120± 1.0	101.5 ± 1.6
2	Group II extrect (200mg/kg)	165.2±3.8	103.0 ±1.1	124.0 ± 0	108.0 ± 2.0	102.0 ± 3.0	99.0 ± 2.0
3	Group III extrect (400mg/kg)	150.7 ±2.5	99.5 ± 1.6	121.0 ± 1.5	101.0 ± 2.5	97.0±3.0	83.5 ± 1.5
4	Group IV GLI (10 mg/ kg body weight)	152.9 ±1.5	112.0 ± 4.6	122.0 ± 3.2	118.0 ± 3.7	115.0 ± 2.6	113.5±1.23

Standards be characterized as mean±SEM (n = 6 mice). Standards were statistically important at *P< 0.05,**P <0.01. GLI =Glibenclamide.

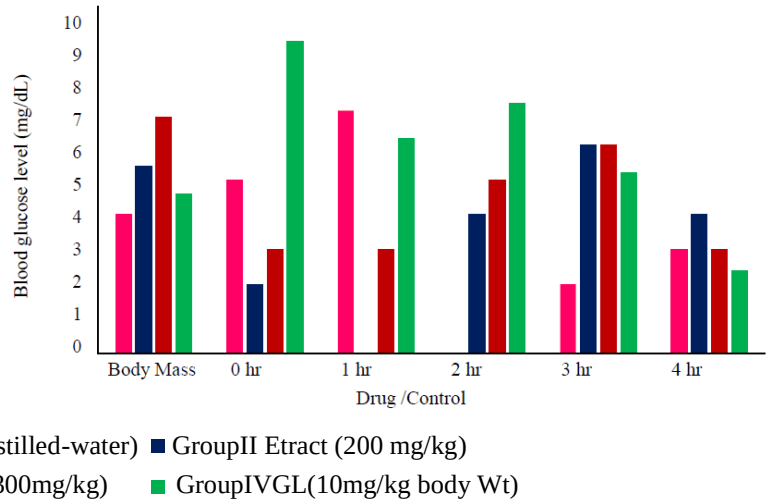

Fig.1: Result of ethanol abstract on blood glucose levels in OGTT model in normal rats.

Effect of ethanolic extract on serum glucose level of diabetic rats

Table no.2: action of 27days treatment of ethanol abstract on blood glucose levels of STZ- induced diabetics rats.

S. No.	Treatments	Initial	7thdays	14thdays	21stdays	28th days
1	Normal Control	90.5 ± 4.9	92.0 ± 1.6	96.1 ± 2.1	93.9 ±3.2	90.1 ±2.3
2	Diabetic Control	222.5 ±3.3	268.3 ±3.5	311.3 ±3.3	384.0 ± 2.9	406.4 ± 3.3
3	Diabetic + glibenclamide (10mg/kg)	282.0 ±0.8	262.0 ± 3.7	154 ±4.9	141.1 ±3.2	130.5 ±3.8
4	Diabetic + *M. koenigii* (400 mg/kg)	241.1± 3.3	211.6 ± 3.4	161.2 ± 4.8	122.3 ±1.5	98.9 ±1.9

Standards are characterized as Mean±SEM (n = 6 mice).

Standards are statistically substantial at **P<0.01,*** P<0.001. Diabetic+ ethanol abstract associated by diabetic+glibenclamide and normal-control mice.

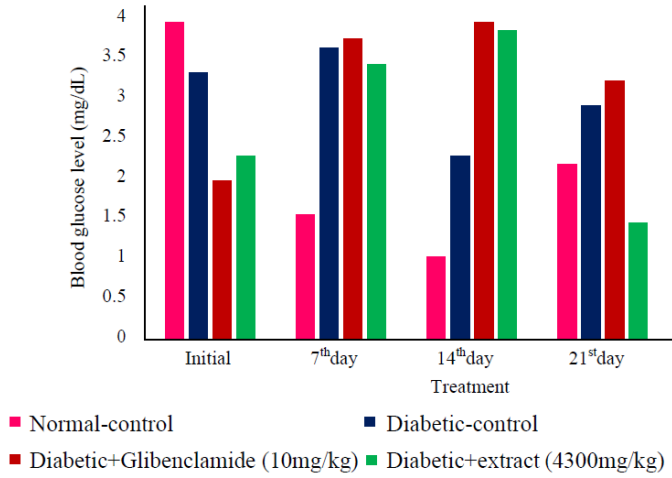

Fig.2: Result of 27thdays treatment of ethanol abstract on serum glucose levels of STZ induced diabetic rats.

Outcome of ethanol abstract treatment on body mass

Table no.3: - Result of ethanolic abstract treatment on body weight in STZ persuaded diabetic rats on 21st day and 28th day

S. No.	Drugs/ control	Body mass (g)		
		Baseline	21stdays	28th ays
1	Normal-control	181.1±3.1	181.0±4.3	183.3±4.2
2	Diabetic-control	165.2 ± 8.2	156.0±8.1	124±11.3**
3	Diabetic+glibenclamide (10 mg/kg)	153.7± 9.5	154.9±9.6**	156.2±7.8***
4	Diabetic+extracts (400 mg/kg)	152.4±8.4	153.0±6.2**	157.1±8.4***

Standards are characterized as Mean ± SEM (n = 6 mice). Standards are statistically substantial at ** P<0.01, *** P<0.001. Diabetic + ethanol abstract associated thru diabetic+glibenclamide & common control mice.

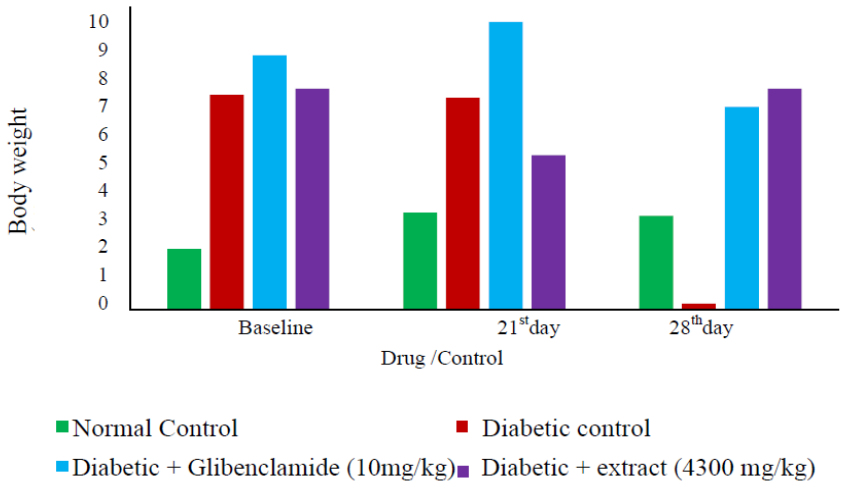

Fig. 3: Result of ethanol abstract treatment on body wt. in STZ persuaded diabetic rats on 21stday and 28thday

SUMMARY AND CONCLUSION

Current research on diabetes faces serious challenges. Over time it will require an assimilated approach to the wellbeing upkeep arrangement. There is a developing attention in environmental research on therapeutic plants. Those are very different from the solid structure and practical application of their philosophical and epistemological foundations. In the case of diabetes, both drug regimens have different treatment options depending on the severity of the disease. Medication use can reduce the symptoms and signs of the illness.

When diabetes is identified, the patient would takings lifelong treatment. Long-term treatment of diabetes with modern medicine is dangerous for the reason that the side effects of the drug are stark. However in the case of Ayurveda medicine the side effects of modern medicine are small related to the current medicine arrangement as it has a natural origin.

Phytochemicals plant organisms that protect human health from degenerative and incurable diseases. Phytochemicals study of ethanol extraction revealed alkaloids, carbohydrates, Saponins, Proteins, Amino-acids, Flavonoids, and Tennis. The chemical composition of the phytochemicals said above might be similar in structure to a computer.

The concentration of Ethanol in the toxicology was 2000 mg / kg even though herbal goods stand broadly well thought-out to be less expensive than artificial medications; they are not totally unrestricted from the effects of toxins or extra side effect. Therefore, toxicity testing of plant-obtained substance, as well as abstracts, is an important portion of precise proof of herbal medicine. However, toxic plants are everywhere,

Herbal medicine is used by 80% of people in emerging states. The care of the use of herbs has newly been interrogated unpaid to rumors of diseases and adverse events such as nephrotoxicity and hepatotoxicity 42-43.

Extensive toxicity studies have shown that the release of ethanol at a dose of 2000 mg/kg showed no signs of toxicity or death. Medically LD50 and ED50 are estimated at 2000 mg/kg and 200 mg/kg, correspondingly. Although LD_{50} be 2000 mg/kg, it is usually considered safe (GRAS). These findings are consistent with Clark and Clark, who reported that any combination drug or low dose estimated to exceed 1000 mg/kg of LD50 body mass would be measured non-toxic and safe. However, variables for example animal species, age, sex, food, bedding, near temperature, cage situations and period of day may completely mark the available LD_{50} standards and it is suggested that LD50 should be excluded. There is a lot of uncertainty. With the species found in other species. These findings suggest that LD50 cannot be considered biologically stable.

Administration of ethanolic excretion at 200, 500, or 1000 mg / kg body weight daily for 28 days did not show any signs of toxicity or death. Animals did not show any changes in normal behavior or other physical activity and were found to be normal throughout the study.

The 28 day study provides information on the effects of repeated exposure and highlights the need for longer-term studies. It also provides details on the choice of long-term concentration subjects. All animals were treated twice daily for sickness and death. Nothing remarkable

Changes in body weight, diet and water intake were observed in mice given ethanolic release (200, 500 and 1000 mg/kg) associated by the control-group later a 28-day study period. every animals are weigh up before the start.

Try again after seven days. Meals of diet and water are too done 1 a week. Ethanol release resulted in a significant statistical increase ($p < 0.01$) to the body mass in Group-III animals. It's essential to amount of water ingesting no less than once a week. Not show the symptoms of toxicity, behavioral changes or extra abnormalities and physique were detected for the duration of the test.

Stz be maybe the more broadly used substance in experimental animals that cause insulin dependent diabetes and noninsulin dependent diabetes mellitus. that is a combination of glucosamine nitrosouria that tenet a significant decrease in beta cells in the Langerhans Islands. Within three days, streptozotocin swells the pancreas and eventually causes a decrease in beta cells in the Langerhans islands and also causes diabetes mellitus. It's too alters common breakdown to diabetic rats compared to common mice. Long-term taken of STZ may reduce the beta-cell of the Langerhans Islands to yield insulin. The effect of let fall the infusion glucose in mice caused by STZ diabetes can also be due to increased glucose uptake. Many other plants show hypoglycemic activity by reducing insulin secretion.

Diet and food intake, increased serum glucose in diabetic animals compared to normal mice, but also lowered seruminsulin, C peptide, and body mass levels. Weight loss will be followed by fatigue and constant tiredness. When treated for the release of 56 diabetic rats, weight loss was tested and modified.

The various ingredients (alcoholic and liquid) of TecomaStanswere are subject to physico-chemical analysis. Examination of carbohydrates, phenols, tannins, alkaloids, flavonoids, fats, glycosides, steroids, amino-acids, Carbohydrates, amino-acid, Flavonoids, Saponins, Phenols, Tannins can be involved. Factors with a large number of phyto elements and a specified excretion (ethanolic) were used in the following experiments. Toxicology studies with safety of release and toxic and

robust studies with toxins up to 500 mg / kg show no toxic symptoms.

The discharge had been tested at a previous clinic compared to samples of diabetes mice caused by STZ.

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