Original Research Article

Evaluation of hypoglycemic and anti-hyperglycemic effect of alcoholic extract of murrayakoenigii in albino rats

Naveen Pokala[1], Nischal shasidher[2*], JayasreeT[3]

[1]Associate Professor,[3]Professor,Department of Pharmacology, Mamata medical college, Khammam, INDIA.
[2]Regional Medical Advisor, Dr Reddy's laboratories. Hyderabad, Telangana, India
Email:nischalshashidhar@gmail.com

Abstract

Objective: To evaluate the hypoglycemic effect in normal rats and Anti-hyperglycemic effect in alloxan induced diabetic rats with alcoholic extract of MurrayaKoenigii leaves.**Materials and methods:** Laboratory breed albino rats of either sex weighing 150-200gm were used in the study. The alcoholic leaf extract of murrayakoenigii was prepared and given to normal and alloxan induced diabetic rats in 100,200 and 400mg/kg per oral doses by dividing the rats into five groups (n=6).normal saline was given in control group and glibenclamide was given in standard group. All were given for 21 days duration. The blood glucose levels were estimated in collected blood by the retro orbital plexus puncture method.**Results:** Alcoholic extract of murrayakoenigii leaves produced a significant reduction in blood glucose levels in the normal and alloxan induced diabetic rats. The bloodglucoseestimationwasdoneatvariousintervalsoftimei.e., 0,30,60,90 and 120 mins. The test drug caused variable reductions in blood glucose levels with its three different doses. There was significant difference in mean blood glucose values with 400mg/kg ($p<0.05$) in both normal and alloxan induced diabetic rats, when compared to the control group and it was comparable with that of the standard. **Conclusion:** The present study demonstrated that the alcoholic extract of Murrayakoenigii (AEMK) leaves possess significant hypoglycemic activity in normal rats and anti-hyperglycemic effect in alloxan induced rats. These effects are may be due to the stimulation of β-cell of the pancreas and subsequent release of insulin, due to the presence of Phytochemical.

Key Word: Alloxan, Anti- hyperglycemic, Hypoglycemic, Murrays Koenigii

***Address for Correspondence:**
Dr.Nischal Shashidhar, Regional Medical Advisor, Dr Reddy's laboratories, Hyderabad, Telangana INDIA.
Email:nischalshashidhar@gmail.com

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INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder in which carbohydrate metabolism is reduced where proteins and lipids metabolism are increased. Hyperglycemia is an end point for all types of DM and is an important parameter to evaluate the efficacy of ant diabetic drugsThough so many drugs are currently available, there is a need for safer agents with fewer side effects, which can be taken for long duration. Ethno botany is the study of the indigenous uses of plants and the relationship between people and plants[1].Recently the search for appropriate hypoglycemic agents has been focused on plants used in traditional medicine. The herbal products are becoming so popular that even many of the modern physicians are beginning to have faith in them. The world is gradually turning to herbal formulations which are very effective against a large number of diseases and ailments. More importantly, they are readily available at affordable prices than allopathic drugs. India is a country with a rich of natural resources and good history of traditional medicine. The World Health Organization (WHO) has recommended that use of herbals should be encouraged in India[2].In many countries medicinal plants are used to control DM. Diabetes is one of the refractory diseases for modern allopathic treatments and suitable herbal drugs

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are to be investigated.*Murrayakoenigii*, commonly known as curry leaf or karipatha, belonging to Family Rutaceae which represents more than 150 genera and 1600 species[3]. *Murrayakoenigii* is a highly valuable plant for its characteristic medicinal values. The whole plant and different parts of the plant are used to cure many human ailments. Apart from many medicinal uses *MurrayaKoenigii* also has anti oxidant, anti dysenteric, hypoglycemic and anti-diabetic activity[3].

MATERIALS

Animals: All the animals included in the study were procured from animal house of Mamata Medical College, Khammam. Wistar albino rats of either sex, weighing 150-200g were used for the study. The animals were maintained under standard laboratory conditions at 25°C, commercial pellet diet with water ad libitum and normal photo period (12hr dark/12hr light). The Institutional Animal Ethics Committee (IAEC) approved the study.

Drugs and Chemicals:

Alloxan monohydrate – Sigma chemicals (St Louis, USA), Tab Glibenclamide 5mg – Dionil, Aventis Parma, (Ankles war). Glucometer – Accu-Chek, (Roche Diagnosis, USA).

Plant Material and Extraction Procedure:

The leaves of *Murraya koenigii*collected from the local market, were identified and authenticated by Head of the Department of Botany, Government degree college Khammam. The leaves were shade dried and powdered. The preparations of alcoholic leaf extract of *Murraya koenigii* were done byContinuous hot percolation process by Soxhelts appartus[4]in the Department of Pharmacology, Mamata Medical College,Khammam.

METHODOLOGY

Acute toxicity study

Normal albino rats were divided into four groups of six animals each. Different doses (500, 1000, 1500 and 2000 mg/kg body weight) of leaf extract was administered orally. The rats were observed for three days continuously and no lethality was observed.

Procedure for the hypoglycemic activity[5]: Albino rats of either sex weighing 150-250gms were included in the study. The animals included in the study were fasted overnight and were divided into five groups, six in each group.

Group I (Control): Animals of this group were administered with 1 ml of sterile normal saline only.

Group II (Standard): Animals were administered with 0.5mg/kg of glibenclamide dissolved in distilled water.

Group III: Animals were administered with 100mg/kg doses of alcohol extract of *Murrayakoeinigii*

Group IV: Animals were administered with 200mg/kg doses of alcohol extract of *Murrayakoeinigii*

Group V: Animals were administered with 400mg/kg doses of alcohol extract of *Murrayakoeinigii*

Procedure for the anti-hyperglycemic activity[6]

induction of diabetes: The overnight fasted animals were administered injection Alloxan monohydrate reconstituted in sterile normal saline in the dose of 150 mg/kg body weight, intraperitoneally after taking their fasting blood glucose values. Then they were allowed to have free access to food and water. The blood glucose levels were repeated after 3 days and then again on the 7th day. The animals with fasting blood glucose levels between 250mg/dl – 350mg/dl were included in the study.

Estimation of blood glucose: In both the procedures the treatment is given for 21 days. The blood glucose levels were estimated by puncturing the retro orbital plexus from overnight fasted rats under light ether effect. The blood glucose estimation was done at 30, 60, 90 and 120 mins after the administration of doses using a Glucometer (Accu-Chek, Roche Diagnostics, USA).

Statistical analysis: The statistical analysis of data was done using one way analysis of variance (ANOVA) followed by Dunnett's test using the software "SPSS VERSION16". P value < 0.05 was considered to be significant

RESULTS

The effect of *Murray Koenigii* on blood glucose was studied in vivo in non-diabetic albino rats and in alloxan induced diabetic albino rats. There was significant reduction in blood glucose levels with peak reduction observed at 120 mins of its administration in both the studies as shown in the Tables I and II and it was comparable to that of Glibenclamide.A "dose response relationship" exists with the alcoholic extract of *MurrayaKoenigii* as maximum response was obtained with 400mg/kg of alcoholic extract as in the Tables I, II in both the studies.

Hypoglycemic activity: The different doses of Alcoholic extract of *MurrayaKoenigii*(AEMK) were tested for its hypoglycemic activity on albino rats. The overnight fasting blood glucose levels of rats were recorded before the administration of drugs.Control group (Group I) the mean blood glucose level was 122±2.88 at 0 minutes and 110±2.778 at 120 minutes as shown in Table I. In the Standard group (Group II) the mean blood glucose level was 118±2.683 at 0 minutes. After administration of the standard drug Glibenclamide, there was significant ($p<0.05$) decrease in blood glucose levels at 30 mins, there after there was highly significant ($p < 0.001$) reduction in blood glucose levels from 60 minutes to 120 minutes as shown in Table I. In Test -1 (Group III)

Alcoholic extract of *MurrayaKoenigii* (AEMK) when given in the dose of100mg/kg the mean blood glucose levels at 0 minutes was 126±5.071. There was no significant fall in blood glucose levels till 120 minutes when compared to the standard as shown in Table I. In Test – 2 (Group IV)/ Alcoholic extract of*MurrayaKoenigii* (AEMK) when given in dose of 200 mg/kg the mean blood glucose levels at 0 minutes was 120±4.017. There was no significant fall in blood glucose levels till 120 minutes when compared to the standard as shown in Table IIn Test – 3 (Group V)/ Alcoholic extract of *MurrayaKoenigii* (AEMK) when given in the dose of 400mg/kg the mean blood glucose levels at 0 minutes was 124±1.857. There was significant ($p<0.05$) decrease in blood glucose levels at 30 mins, thereafter there was highly significant ($p<0.001$) reduction in blood glucose levels from 60 minutes to 120 minutes as shown in Table I.

Table 1: Comparison of blood glucose values of Control, Standard, and Test groups of AEMK in albino rats.

Sl no.	Groups	0 min	30min	60min	90min	120min
1	Group I Control NS 0.9%	122 ±2.88	118±2.404	118±3.04	112±2.985	110±2.778
2	Group II Standard Glibenclamide 0.5mg/kg	118±2.683	80±2.683*	74±2.104	70±1.961	62±1.713**
3	Group III AEMK 100mg/kg	126±5.071	118±5.071	116±5.431	110±5.661	106±5.207
4	Group IV AEMK 200mg/kg	120±4.017	112±4.017	106±5.83	106±3.998	100±6.997
5	Group V AEMK 400mg/kg	124±1.857	82±1.857*	76±3.117	72±1.932	70±2.206**

*Values expressed as mean ± S.D, * significant ($p<0.05$), ** highly significant ($p = 0.001$)*

Anti-hyperglycemic activity: The different doses of Alcoholic extract of *MurrayaKoenigii* (AEMK) were tested for its anti-hyperglycemic activity in diabetes induced albino rats as explained in the methodology. The overnight fasting blood glucose levels of rats were recorded before the administration of drugs. Control group (Group I) the mean blood glucose level was 292.83±15.44 at 0 minutes and 335.33±5.2 at 120 minutes as shown in Table II. In the Standard group (Group II) the mean blood glucose level was 299.33±16.97 at 0 minutes. After administration of the standard drug Glibenclamide, there was significant ($p<0.05$) reduction in blood glucose levels from 30 minutes to 120 minutes as shown in Table II.In Test -1 (Group III)/ Alcoholic extract of *MurrayaKoenigii* (AEMK) when given in the dose of100mg/kg the mean blood glucose levels at 0 minutes was 297.33±16.12. There was significant difference ($p<0.05$)in blood glucose levels when compared to control but they were lesser when compared to that of standard as shown Table IIIn Test – 2 (Group IV)/ Alcoholic extract of *MurrayaKoenigii* (AEMK) when given in dose of 200 mg/kg the mean blood glucose levels at 0 minutes was 302.66±10.96. There was significant difference ($p<0.05$)in blood glucose levels when compared to control but they were lesser when compared to that of standards shown in Table II.In Test – 3 (Group -5)/ *Murraya Koenigii* when given in the dose of 400mg/kg the mean blood glucose levels at 0 minutes was 302.83±10.79. There was significant ($p<0.05$) reduction in blood glucose levels from 30 minutes to 120 minutes and it was comparable with that of the standard as shown in Table II. The blood glucose estimation was done at various intervals of time i.e., 0,30,60,90 and 120 mins. The test drug caused variable reductions in blood glucose levels with its three different doses. There was significant difference in mean blood glucose values with 400mg/kg ($p<0.05$) when compared to the control group and it was comparable with that of the standard.

Table 2: Comparison of blood glucose values of Control, Standard, and Test groups of AEMK in albino rats.

Sl.no.	Groups	0 min	30min	60min	90min	120min
1	Group I Control NS 0.9%	292.83±15.44	352±6.89	349.33±6.3	342.16±5.98	335.33±5.2
2	Group II Standard Glibenclamide 0.5mg/kg	299.33±16.97	254.5±12.98*	192.83±7.96	205.83±6.86	217.83±5.31*
3	Group III AEMK 100mg/kg	297.33±16.12	288.66±14.19	270±13.33	255.5±11.8	257.5±12.3
4	Group IV AEMK 200mg/kg	302.66±10.96	282.5±8.76	267.66±8.11	228.66±3.01	240.33±5.28
5	Group V AEMK 400mg/kg	302.83±10.79	278.83±6.36*	260.16±10.49	204.5±3.64	217.33±4.17*

Values expressed as mean ± S.D, * significant ($p < 0.05$)

DISCUSSION

In normal albino rats glucose estimation was done at 0,30,60,90 and 120 minutes after feeding three doses of AEMK i.e., 100mg/kg, 200mg/kg and 400mg/kg respectively. After the 21 days of treatment the test drug caused variable reduction in blood glucose levels with these three different doses. In group III (100mg/kg) reduction at 120 min was 106 ± 5.207, in group IV (200mg/kg) it was 100 ± 6.997 and in group V (400mg/kg) it was 70 ± 2.206 which was highly significant when compared to the control as shown in Table I.Studies on *Moringa oleifera* leaves[7-10] have shown glucose lowering effect on normoglycemic and hyperglycemic albino rats. In a comparative hypoglycemic study of extract of *Aloevera*, *Murrayakoeinigii* and *Azadirachtaindica* showed hypoglycemic effect in Wistar rats[11].In alloxan induced diabetic albino rats the test drug AEMK leaves was given in doses of 100,200 and 400mg/kg in group III, IV and V respectively and blood glucose estimation was done at 0,30,60,90 and 120 min. There was reduction in blood glucose levels with above 3 doses. In group III (100mg/kg) there was significant reduction in blood glucose levels when compared to control ($p<0.006$). In group IV (200mg/kg) there was significant reduction in blood glucose levels ($p<0.008$) when compared to control. In both the groups the reduction in blood glucose was lesser when compared to that of standard as shown in table II.In group V (400mg/kg) there was a significant reduction ($p<0.05$)in blood glucose levels from 30 min to 120 min and was comparable with that of the standard as shown in table II. Studies on *Moringa oleifera* leaves[7-10]showed hypoglycemic and anti-hyperglycemic activity of its aqueous extract in normal albino rats and alloxan induced diabetic rats. Significant decrease in blood glucose levels were seen at 2hrs ($p<0.001$) innormal albino ratsand diabetic albino rats ($p<0.001$) with 200mg/kg.Studies on ethanol extract of *Murrayakoenigii* stem[12] also showed significant reduction ($p<0.05$) in elevated blood glucose levels in comparison to untreated diabetic animals. A study with ethanolic and aqueous extracts of *Murrayakoenigii* rootsin alloxan induced diabetic rats[13] exhibited significant reduction in blood glucose levels in a dose dependent manner. In another study with aqueous and ethanol extract of *Murrayakoenigii* leaves powder showed similar anti-hyperglycemic effects[14].In the present study with Alcoholic extract of *MurrayaKoenigii* (AEMK) leaves at a dose of 400mg/kg body weight showed profound hypoglycemic and anti-hyperglycemic effect on normal albino and the diabetic albino rats respectively. The present results are in consensus with the previous studies mentioned above. The probable mechanism of action of alcoholic extract of *Murrayakoenigii* (AEMK) could be either due to insulin secretogogue effect[15] or increased glycogenesis or decreased glycogenolysis or gluconeogenesis[16]. The mechanism of action seems to be similar to that of Glibenclamide. Studies on several alkaloids have shown to possess similar anti-diabetic effects of Glibenclamide[17].The Phytochemical analysis of *Murrayakoenigii* leaves showed the presence of alkaloids, flavonoids, saponins, tannins and glycosides[18]. These flavonoids and carbazole alkaloids have strong anti-oxidant and anti-inflammatory properties and also have the capacity to scavenge hydroxyl radicals and lipid-peroxy radicals[19]. These free radicals are responsible for chronic diseases such as diabetes mellitus, cardiovascular diseases, Alzheimer's disease and Parkinson's disease. Flavonoids and carbazole alkaloids in curry leaves may be the basis for using them in the above diseases. Literature suggests that *Murrayakoenigii* leaves exert a protective effect in diabetes mellitus by preventing pancreatic β-cell damage and decreases oxidative stress[20]. So this present study suggests that the phytochemicals in *Murrayakoenigii* leaves exhibited significant hypoglycemic and anti-hyperglycemic effects at a dose of 400mg/kg in albino rats. Most probably the carbazole alkaloids might have been the reason for the hypoglycemic and anti-hyperglycemic effects as mentioned in the above studies.

CONCLUSION

The present study demonstrated that the alcoholic extract of *Murrayakoenigii* (AEMK) leaves possess significant hypoglycemic activity in normal rats and anti-hyperglycemic effect in alloxan induced diabetic rats. These effects are may be due to the stimulation of β-cell of the pancreas and subsequent release of insulin, due to the presence of phytochemicals. It can be concluded that the extract of Murrayakoenigii can be suggested as an adjuvant therapy along with other hypoglycemic drugs in both insulin dependent diabetes mellitus (IDDM) and non-insulin dependent diabetes mellitus (NIDDM). The exact Phytochemical causing this effect and its mechanism of action should be elucidated by further extensive research and the lead compound can be included in the one class of anti-diabetic drugs in the future.

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