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Pharmacological Screening and Phytochemical Evaluation of Anti-Diabetic Activity of *Asparagasus Racemosus* Leaves in Normal and Alloxan Induced Diabetic Rats

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A B S T R A C T

Diabetes mellitus is a most common endocrine disorder, affecting more than 300 million people worldwide; we studied the anti-diabetic potential of leaves of *A.Racemosus*. The acute oral toxicity studies of the extracts revealed no toxic effects up to the levels of 2000mg/kg b.wt. The aqueous and alcoholic extracts of 20 and 30mg/kg body weight of *A.Racemosus* was screened for the presence of hypoglycemic and antidiabetic activity. In this study diabetes was induced by a single IP dose Alloxan monohydrate in 72hrs fasted rats. The FBGL was carried on 7th, 14th and 21st day and OGTT was measured on 8th, 15th and 22nd day. Glibeclamide was taken as the standard and the results are quite comparable with it. The studies were indicated that the leaves of *A.Racemosus* are effective in regeneration of insulin secreting β-cells and thus possess antidiabetic activity. The aqueous and alcoholic extracts showed significant effect in decreasing the Fasting blood Glucose level and oral glucose tolerance test of rats and it's also showed good hypoglycemic activity in normal glycemic rats. The preliminary phytochemical analysis of the extracts of *A.Racemosus* revealed the presence of alkaloids, tannins, saponins, terpenoids, flavonoids, phenolics and glycoside as the possible biologically active principles.

Keywords: *A.Racemosus* , Alloxan monohydrate, Glibenclamide, FBGL and OGTT

A R T I C L E I N F O

CONTENTS

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1. Introduction

Diabetes Mellitus (DM): Diabetes is one of the most common non-communicable diseases and a serious life-long condition appearing worldwide. The etiology of diabetes is a complex interaction of genetic and environmental factors. It is a heterogeneous group of metabolic disorders characterized physiologically by

dysfunction of pancreatic beta cells and deficiency in insulin secretion or insulin activity and clinically by hyperglycemia or impaired glucose tolerance and other manifestable disorders. It is an endocrinological syndrome abnormally having high levels of sugar in the blood. This may be either due to insulin not being produced at all, is not made at sufficient levels, or is not as effective as it should be. Diabetes is still a serious health problem all over the world since it is associated with increased morbidity and mortality rate. When compared with the general population, mortality and morbidity increase in diabetes is mainly due to the associated chronic complications both specific (microvascular) and nonspecific (macrovascular). Since the disease prevails in both genders and in all age groups, the general public has a concern about its control and treatment[1].

Classification of DM

Diabetes is classified by underlying cause. The most common forms of diabetes are categorized as

Type 1, or insulin-dependent diabetes mellitus (IDDM) - an autoimmune disease in which the body's own immune system attacks the pancreatic beta cells, rendering it unable to produce insulin and

Type 2, or non-insulin-dependent diabetes mellitus (NIDDM) - in which there is resistance to the effects of insulin or a defect in insulin secretion.

Type 2 diabetes commonly occurs in adults associated with obesity. There are many underlying factors that contribute to the high blood glucose levels in these individuals. An important factor is the resistance to insulin in the body essentially ignoring its insulin secretions. A second factor is the decreased production of insulin by the cells of the pancreas. Therefore, an individual with Type 2 diabetes may have a combination of deficient secretion and deficient action of insulin. In contrast to Type 2 diabetes, Type 1 diabetes most commonly occurs in children and is a result of the body's immune system attacking and destroying the beta cells. The trigger for this autoimmune attack is not clear, but the result is the end of insulin production[2]

Treatment: An approach to botanicals

Pharmacological treatment of diabetes mellitus is based on oral hypoglycemic agents and insulin. Different types of oral hypoglycemic agents such as biguanides, sulphonylurea and thiazolididinones are available along with insulin for the treatment of diabetes mellitus. These drug therapies (i.e., oral glucose-lowering agents and insulin injection) along with having adverse effects are not always satisfactory in maintaining glycemia and avoid late stage diabetic complications. Hence, their use is restricted by their limited action, pharmacokinetic properties, secondary failure rates and accompanying side effects. Moreover, these therapies only partially compensate for metabolic derangements seen in diabetics and do not necessarily correct the fundamental biochemical lesion. The complete cure of the disease has been eluding physicians for centuries and the quest for the development of more effective antidiabetic agents is pursued relentlessly. Currently available treatment is far from satisfactory and is expensive. Treatment and care of diabetes represents a substantial portion of the national health care expenditure, over $105 billion annually. This represents a substantial portion of health care expenditure more than one of four Medicare dollars.

The potential role of the medicinal plants as hypoglycemic agents has been reviewed by several authors. Many Indian medicinal plants are reported to be useful in diabetes. Several of the most studied and commonly used medicinal herbs for diabetes include *Ginseng species*, *Momordica charantia* (Bitter Melon), *Trigonella foenum graecum* (Fenugreek), *Gymnema sylvestre* (Gurmar), *Allium cepa* (Onion) and *Allium sativum* (Garlic), *Petrocarpus marsupium*, *Vaccinium myrtillus* (Bilberry), *Atriplex halimus* (Salt Bush), *Aloe vera*. A wide array of plant derived active principles representing numerous chemical compounds like alkaloids, glycosides, polysaccharides, guanidine, steroids, carbohydrates, glycopeptides, terpenoids etc has demonstrated activity consistent with their possible use in the treatment of NIDDM. Medicinal plants have been used for diabetes safely and with reasonable success. Despite the great strides that have been made in understanding and management of diabetes mellitus, serious complications continue to confront patients and physicians. Therefore, search for anti-diabetic plants which are already used but in combination of that are used in this study to show an additive effect when compared to that of individual drug therapy.

2. Materials and Methods

Drugs and Chemicals

Alloxan, Methanol, Alcohol, Glibenclamide.

Experimental animals

Healthy adult albino wistar rats weighing 200-250grams of either sex were selected for the study. Animals were housed in appropriate cages in uniform hygienic conditions and fed with standard pellet diet (Amrul Laboratory Animal Diet) and water ad libitum. They were fasted overnight before the day of experiment, after 72hours of fasting from the day of Alloxan introduction. Animals were housed within the departmental animal house and the room temperature was maintained at 27° C. Animal studies had approval of IAEC.

Plant Material Collection

The leaves of *A.racemosus was* collected from thelocal market in Hyderabad in the month of January and was identified and authenticated from Department of Pharmacognosy. The plant material was cleaned, reduced to small fragments, air dried under shade at room temperature and coarsely powdered in a mixer. The powdered material was stored or taken up for extraction process

Acute Oral Toxicity:

The acute oral toxicity of aqueous and alcoholic extracts of *A.racemosus* was determined by using Albino wistar rats (200-250g) which were maintained under standard conditions. The animals were fasted 12 hour prior to the experiment, up and down procedure OECD guideline no. 425 were adopted for toxicity studies. Animals were administered with single dose of individual extract upto 2000mg/kg and observed for its mortality during 2days and 7days study period (short term) toxicity and observed upto

7days for their mortality, behavioral and neurological profiles.

3. Results and discussion

Acute toxicity testing:

Acute toxicity studies revealed that the alcoholic extracts of *A.racemosus* were safe up to 2000 mg/kg of body weight and approximate LD 50 is more than 2000 mg/kg. No lethality or any toxic reactions was observed up to the end of the study period.

Discussion

- The dried leaves of *A.racemosus*used for this project work were procured locally. The dried leaves of *A.racemosus* were successively extracted with water and alcohol. Therapeutic dose of the extracts were calculated after carrying acute oral toxicity studies in rats. Extracts were tested for their anti-diabetic activity in normal and alloxan induced diabetic rats.

The following parameters were assessed:

- Fasting blood glucose levelsAt 7th, 14th and 21st day in normal and alloxan induced rats.
- Oral Glucose Tolerance Test
- At 8th, 1^{5th} and 22nd day in normal and alloxan induced rats.
- Aqueous and Alcoholic extracts of *A.racemosus* (20 and 30 mg/kg) showed significant effect in blood glucose lowering activity and improved oral glucose tolerance test (OGTT) in short term (7th day) and long term (14th and 21st day) repeated administration in normal and alloxan induced diabetic rats.
- The above studies showed that Aqueous and Alcoholic extracts of *A.racemosus* had potent anti-diabetic activity on repeated administration.

Table 1: Effect of extracts of *A.racemosus* on fasting blood glucose level (FBGL) in normal rats

Treatment	Dose (mg/kg)	Blood glucose level(mg/dl)		
		7th day	14th day	21st day
Normal control	**-**	82.21±5.58	80.29±6.53	82.64±5.28
Glibenclamide	**10**	71.59±2.41	65.36±3.80	61.54±2.54
AQAR1	**20**	82.10±4.60	79.73±4.99	78.49±2.54
AQAR2	**30**	84.10±5.14	81.57±6.99	80.45±5.04
ALAR1	**20**	72.5±3.44	65.58±2.86	62.58±2.45
ALAR2	**30**	73.36±2.67	68.51±2.92	65.45±1.76

Values are expressed as mean± S.E.M. n=6. Significant values were compared with p<0.005, normal control Vs all groups. Parent thesis indicates % reduction in BGL.

Table 2: Effect of extracts of *L.sativum* on 8th, 15th and 22nd day in normal rats

Treatment	Dose (mg/kg)	Blood glucose level(mg/dl)		
		8th day	15th day	22st day
Normal control	**-**	88.64±2.51	89.62±1.68	91.58±1.46
Glibenclamide	**10**	84.24±0.64	80.62±2.57	74.26±2.49
AQAR1	**20**	80.17±2.18	76.28±1.45	72.84±5.81
AQAR2	**30**	85.92±0.64	80.69±0.08	75.68±2.15
ALAR1	**20**	84.62±1.85	78.52±2.64	70.42±0.46
ALAR2	**30**	73.37±2.10	64.58±2.68	62.15±0.84

Values are expressed as mean ± S.E.M. n=6. Significant values were compared with P<0.005. Normal control Vs all groups. Paranthesis indicates % reduction in BGL.

Table 3: Effect of extracts of *A.racemosus* on fasting blood glucose level (FBGL) in Alloxan induced diabetic rats

Treatment	Dose (mg/kg)	Blood glucose level(mg/dl)		
		7th day	14th day	21st day
Normal control	**-**	82.21±5.58	80.29±6.53	82.64±5.28
Diabetic control	**10**	368.16±10.9	398.20±12.45	412.58±13.46
Glibenclamide	**10**	314.15±16.04	287.32±19.02	221.30±14.69
AQAR1	**20**	290.34±10.58	242.16±14.00	214.47±12.68
AQAR2	**30**	294.15±12.45	272.36±11.57	248.16±16.04
ALAR1	**20**	286.66±13.64	184.52±12.67	168.49±17.25
ALAR2	**30**	240.25±16.02	224.60±14.62	196.31±9.64

Values are expressed as mean ± S.E.M. n=6. Significant values were compared with P<0.05. Normal control Vs all groups. Paranthesis indicates % reduction in BGL.

Table 4: Effect of extracts of *A.racemosus* on 8th, 15th and 22nd day in Diabetic rats.

Treatment	Dose (mg/kg)	Blood glucose level(mg/dl)		
		8th day	15th day	22st day
Normal control	**-**	88.64±2.51	89.62±1.68	91.58±1.46
Diabetic control	**10**	356.20±16.53	374.00±12.48	382.41±6.03
Glibenclamide	**10**	258.6±18.49	154.48±15.64	148.36±14.62
AQAR1	**20**	274.60±14.51	236.60±13.43	224.41±12.68
AQAR2	**30**	280.96±15.62	264.25±10.62	230.29±10.80
ALAR1	**20**	257.30±15.15	168.40±11.00	145.61±12.54
ALAR2	**30**	328.90±14.59	309.50±9.07	284.35±8.57

Values are expressed as mean ± S.E.M. n=6. Significant values were compared with P<0.05. Normal control Vs all groups. Paranthesis indicates % reduction in BGL.

4. Conclusion

In current scenario, herbs are the potent sources of medicines used in the treatment of various disease and disorders. Since, plants are used as medicine there is prompt need of evaluation of plant species, therefore, the present work was conceived to evaluate the phytochemical and pharmacological screening of leaves of *A.racemosus*. The Phytochemical evaluation has revealed the presence of alkaloids, terpenoids, saponins, flavonoids, phenols and tannins. The aqueous and alcoholic extracts had hypoglycemic activity because the presence of flavonoids which are rich in treatment of hypoglycaemia with less side effects. Flavonoids might be producing hypoglycaemic effect by a mechanism independent from insulin secreation e.g. by the inhibition of endogenous glucose production or by the inhibition of intestinal glucose absorption. The present study *A.racemosus* of both aqueous and alcoholic extracts was showed significant effect on glucose tolerance and also showed reduction in fasting blood glucose levels in normal diabetic rats.

The data of the blood glucose level of rats treated with Alloxan (150mg/kg body weight) produced diabetes within 72 hours. After 72 hours of Alloxan administered the blood glucose levels of rats were observed. It was observed that significant lowering of sugar in aqueous and alcoholic extract. The administration of different extracts at a dose of 20 and 30 mg/kg showed significant anti-hyperglycaemic effect at 22nd day which was evident from the 7th day on wards as compared to standard. The aqueous and alcoholic extract of *A.racemosus* has showed better anti-hyperglycaemic effect of the extract on the fasting blood sugar levels on diabetic rats are shown in table. The decreasing blood glucose levels are comparable with that of 10 mg/kg of Glibenclamide. The Glibenclamide (10 mg/kg body weight) shows significant effect on compare to the initial and more significant effect on the 22nd Day compare to the initial. The aqueous and alcoholic extracts of 20 and 30mg/kg body weight shows significant (P*<0.05), effect.

Results of anti-diabetic activity in normal and alloxan induced rats the extracts established the scientific basis for the utility of these plants in the treatment of diabetes. The extracts have shown significant reduction in blood glucose levels in normal and alloxan induced diabetic rats and produced maximum anti-diabetic activity and are higher than the hypoglycaemic activity of Glibenclamide in the diabetic rats. In glucose loaded animals, the drug has reduced the blood glucose to the normal levels. It is possible that the drug may be acting by potentiating the pancreatic secretion or increasing the glucose uptake. In conclusion, these extract showed significant anti-diabetic effect in normal and diabetic rats after administration. Thus the claim made by the traditional Indian systems of medicine regarding the use of these plants in the treatment of diabetes stands confirms.

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