Review Article

Antidiabetic Potential of Acanthaceae Family

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ABSTRACT

Plants are the excellent source of various herbal medicines useful in the treatment of various human diseases. Natural products from plants are traditionally used for the treatment of diabetes mellitus mainly in developing countries where the resources are limited and access to modern treatment is a problem. Anti-diabetic activity of the medicinal plants is scientifically evaluated by *in vitro* and *in vivo* studies. The present study deals with the review of information about the anti-diabetic activity of medicinal plants which belong to the family Acanthaceae. This review covers more than 25 medicinal plants which belong to different genus of this family. Acanthaceae is a huge reservoir for variety of phytochemical constituents like terpenoids, glycosides, alkaloids, saponins, β-sitosterol, palmitic acid, stigmasterol, apigenin, kaempferol, tannins, etc. Many compounds were isolated from the plants of Acanthaceae family plants and they possess various pharmacological activities. One of the important hypoglycemic agents isolated from the plant *Andrographis paniculata* is andrographolide and it also imparts variety of therapeutic actions.

Keywords: Diabetes mellitus, Acanthaceae, Medicinal plants, Hypoglycemic effect.

INTRODUCTION

India has been known to be an affluent storehouse of medicinal plants. In India, forest is the principal storehouse for variety of large number of aromatic and medicinal plants; they are largely used as raw materials in manufacture of drugs and related products. Out of the 4, 22, 000 flowering plants, more than 50,000 plants have been used for its medicinal purpose[1]. Allopathic system of medicine has approved a number of plant derivative drugs which forms an important division of the modern pharmacopoeia. In the manufacturing of new drugs, there is a need for many chemical intermediates (β-ionone, solesodine and diosgenin) which are also obtained from plants. Traditional medicines have always played a key role in world health and are being used to treat a vast array of conditions and complaints[2]. Some of the WHO regional offices, including Eastern Mediterranean, African and South East Asian region produced more localized guidelines for regulation and registration of traditional medicines as well as suggestions for marketing requirements.[3,4] WHO has shown great interest for documenting the purpose of medicinal plants used by tribes from different parts of the world.[5] Inspiration of people towards herbal medicines is increasing since it has less side effects compared with synthetic drugs. Natural products are now considered to be a vital source for anti-diabetic compounds and the therapeutic effect of many medicinal plants is frequently attributed to their hypoglycemic activity.[6]

Diabetes

The word diabetes is derived from a Greek word 'Dia' means 'through' and 'betes' means 'to pass'. Diabetes can be conveniently classified into two types' viz. Diabetes mellitus (DM) and Diabetes insipidus. Diabetes mellitus is the clinical condition where the secretion of insulin is reduced leading to hyperglycemia and glycosuria. The common symptoms of DM includes increased urine output (polyuria), increased thirst due to water loss (polydipsia), loss of body weight (due to protein loss), increase in appetite (hyperhagia), whereas diabetes insipidus is noticeable by lack of ADH secretion.[7] DM may result in heart and kidney diseases, impotency, neuropathy and blindness. In United States diabetes is said to be the seventh leading cause of death.[8] In India DM is has become a killer disease next to coronary heart disease. The possible causes for DM may be due to lack of regular physical exercises, sedentary life cycle, obesity, rich food habit etc.[9] The two main types of diabetes mellitus is insulin dependent diabetes mellitus (IDDM), which accounts 10% of diabetes and non-insulin dependent diabetes mellitus (NIDDM) and it accounts to 90%. DM is a chronic medical condition, means that even though it can be controlled, it lasts until lifetime. Chronic control is needed to diminish the risk of long term complications. This is theoretically possible with combination of exercise, diet, weight loss, different diabetic drugs and insulin. The prevalence of diabetes in worldwide for all age groups was estimated to be 2.8% in 2000 and it is expected to be 5.4% in 2025. Commonly available therapies for DM include insulin therapy and various oral anti-diabetic agents like biguanides, sulfonylureas, α-glucosidase inhibitors and glinides. Currently, there is growing attention in herbal remedies due to the awareness of side effects related to the oral hypoglycemic agents which are used for the treatment of diabetes mellitus.[10] Marles and Fransworth estimated that more than 1000 plant species are being used as folk

medicine for diabetes.[11] Medicinal plant products are traditionally used from ancient times in many countries for the treatment of diabetes mellitus. Due to their perceived effectiveness, relatively low cost and fewer side effects in clinical experiences, herbal drugs are prescribed.[12] Traditionally some of the medicinal plants belong to the acanthaceae family have been used as hypoglycemic agents.

About the Family Acanthaceae

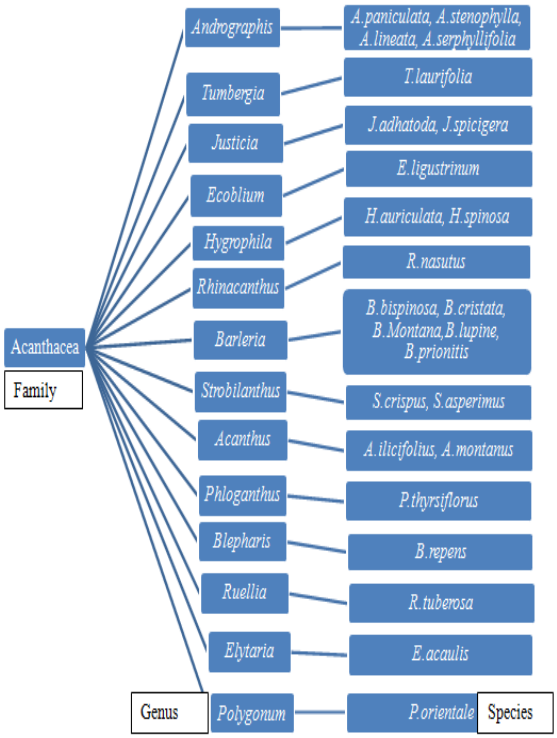

Figure 1: Plants having antidiabetic effect from acanthaceae family

The family Acanthaceae belongs to the taxon dicotyledonous flowering plants, which contains approximately 220 genera and nearly 4000 species concentrated predominantly in tropical and subtropical regions with few species in the temperate regions. The Acanthaceae family consists of almost herbs or shrubs, except for few are trees or vines. This family plant possess simple, decussate leaves arranged in opposite pairs and contain cystoliths (calcium carbonate crystals in enlarged cells). Flowers are pedicellate or sessile, zygomorphic to subactinomorphic, bisexual, usually enclosed by leaf like bracts, often coloured in some species, and is large and showy. Five or four sepals and petals are fused into tubular structures. Fruits are stipitate or not, two valved, the valves are often elastically recurved, the septum spiltting the seeds borne on each half. In majority of the species the seeds are attached to the small, hooked stalk that is ejected from the capsule. The surface of the seeds was smoothened; rarely hispid.[13] Acanthaceae is an important plant family for native people, especially in terms of medicinal use. The leaves and different parts of the plant species are most commonly used for treating various ailments. Many plants in this family reported to have various pharmacological activities like anticancer,[14] antidiabetic, antimicrobial,[15] hepatoprotective[16] and anti inflammatory.[17] One of the important plant *Justicia gendarussa* leaves are used as a contraceptive agent in both male and female,[18] and it reduces the sperm count in male and postpone pregnancy in female. Some important compounds like andrographolide, 14-deoxy andrographolide, neoandrographolide,[19] 3-epi-ursolic acid, lespedin,[20] aurantiamide acetate, lupeol, sitosterol 3-O-β-D-glucopyranoside, campesterol, stigmasterol and β-sitosterol[21] are isolated from different plants and they possess various pharmacological activities. The main objective of the paper is to review on the plants of acanthaceae family having anti-diabetic activity (Figure 1). Anti-diabetic activity of some plants are described in detail while other plants are described with their botanical name, plant part used, solvent and method used are mentioned in Table 1.

Medicinal Plants having anti-diabetic activity in Acanthaceae Family

1. Plant name: *Barleria montana*

Synonym: *Barleria purpurea*

Common name: Mountain barleria

Habitat: Mountains of Western Ghats, Southern China, India, Myanmar

Anti-diabetic activity

Methanolic extract of *Barleria montana* aerial part with dose levels of 100 µg/kg, 200 µg/kg and 400 µg/kg body weight (b.wt.) in streptozotocin (STZ) induced diabetic rats produced a reduction of blood glucose levels. At high dose of 400 µg/kg b. wt. produced a highly significant ($P<0.001$) decrease in blood glucose levels at 4th and 8th hour(h). It was due to the presence of polar compounds present in the plant extract and it produces a hypoglycemic activity in a dose dependent manner.[22] *Barleria montana* leaves extract also reduces the blood glucose levels in streptozotocin induced diabetic rats at the dose of 500 mg/kg but it did not produce any effect in normal rats.[23]

2. Plant name: *Ecbolium ligustrinum*

Synonym: *E. viride*

Tamil name: Nilambari

Habitat: Northeastern peninsular India, Tamil Nadu, Kerala, Maharashtra

Anti-diabetic activity

The hydroalcoholic and chloroform extract of *Ecbolium ligustrinum* flowers showed significant ($P<0.01$) anti-diabetic activity against alloxan induced diabetes in rats. The hydroalcoholic and chloroform extract lowered the blood glucose levels in chronic treatment at 300 mg/kg and 200 mg/kg b.wt. respectively compared to the anti-

diabetic control rats. The anti-diabetic effect in diabetic rats and normal rats suggested insulin like effect mediated via the peripheral glucose consumption. Besides the hypoglycemic activity both the extract showed anti-oxidant activity in alloxan treated rats. The peroxidation enzyme levels were similar to the vehicle treated rats.

The anti-oxidant activity of the *Ecbolium ligustrinum* plays a key role in protecting the pancreatic tissues from oxidants produced by alloxan. The histopathological studies of pancreas isolated from diabetic treated rats showed that the extract repaired the pancreas damaged by alloxan.[24]

3. Plant name: *Andrographis paniculata* (Burm. f.) Nees

Synonym: *Justicia paniculata*

Tamil name: Nilavempu

Habitat: Tropical Asian countries, Throughout South India, Sri Lanka, Malaysia, Indonesia

Anti-diabetic activity

Andrographis paniculata extract and its isolated compound andrographolide decreases the blood glucose, triglyceride and LDL (Low Density Lipoprotein) levels in high fat fructose fed induced diabetes in rats.[25,26] The ethanolic and hot water extract of *Andrographis paniculata also* successfully reduces the blood sugar level in alloxan induced diabetes.[27] The possible mechanism of this hypoglycemic effect may be through controlling glucose uptake and oxidation, restoration of insulin signaling molecules in liver and decreasing the serum lipid profile.[28] Aqueous extract of *Andrographis paniculata* leaves stimulates glucose uptake in L-6 skeletal muscle cells[28] also shows α-amylase and α-glucosidase inhibitory effect.[30]

4. Plant name: *Blepharis repens (vahl) roth*

Synonym: *Acanthus repens, Blepharis integrifolia*

Common name: Greeping blepharis

Distribution: Southern and Eastern Africa, China, India, Sri Lanka, Myanmar

Anti-diabetic activity

Ethanolic extract of *Blepharis repens* (100 mg/kg and 200 mg/kg of b. wt.) showed a significant ($p<0.05$) decrease in blood glucose levels after 21 days of treatment in alloxan induced diabetic rats. The serum lipid profiles were near to normal levels in extract treated and glibenclamide (standard) treated rats. In addition to this, the total protein, albumin, globulin and liver marker enzymes like serum glutamate pyruvate transaminases (SGPT), Alkaline phosphatase (AP) and serum glutamate oxaloacetate transaminases (SGOT) were also near to normal levels in diabetic treated rats. These results indicate the ethanolic extract of *Blepharis repens* has significant hypoglycemic, hepatoprotective and hyperlipedemic effects in alloxan induced diabetic rats.[31]

5. Plant name: *Acanthus ilicifolius* Linn

Synonym: *Dilivaria ilicifolia* Juss

Common name/ Tamil name: Attumulli, Kaludaimullai, Kolimulli, Uppukkarinimulli

Distribution: South Africa, Seacoast of India, Philippines, Australia

Anti-diabetic activity

A low dose of 200 mg/kg and high dose of 400 mg/kg of ethanolic extract of *Acanthus ilicifolius* roots exhibited considerable reduction of blood glucose level in acute and repeat dose sub acute study, the reduction of blood sugar was observed at 5th h and 1st day respectively. The histopathological study of pancreas showed the enhanced regeneration of β-cells in drug treated rats.[32]

6. Plant name: *Polygonum orientale* Linn

Common name: Princess feather

Habitat: Southeastern Asia, Subtropical Himalayas, Bihar, North Bengal, Assam

Anti-diabetic activity

The anti-diabetic activity of *polygonum orientale* was well established in normal, glucose loaded and STZ induced diabetic mice methods. In normoglycemic method *Polygonum orientale* exhibited dose dependent antidiabetic effects in 2 h, whereas in glucose tolerance test the high dose of 200 mg/kg showed greatest improvement and in streptozotocin induced diabetic rat method extract treated rats showed a significant ($P<0.0001$) decrease in blood sugar level by the enhancement of pancreatic secretion of insulin from β-cells of islets. The plant extract also significantly reduces the serum cholesterol level ($P<0.01$) and increase the liver glycogen ($P<0.0001$) in STZ diabetic mice.[33]

7. Plant name: *Justicia adhatoda* Linn

Synonym: *Adhatoda zeylanica*, *Adhatoda vasica* nees

Tamil name: Kattumurungai

Distribution: Throughout India, Sri Lanka, Burma, Malaysia

Anti-diabetic activity

The ethanolic extract of leaves and roots of *Justicia adhatoda* (100 mg/kg b.wt.) and the reference drug glibenclamide (5mg/kg b.wt.) produced significant ($P<0.05$) blood sugar lowering effect in the diabetic rats. After the treatment with plant extract sugar level in blood, urine and tissue lipids were reduced and body weight, cholesterol, free fatty acids, triglycerides and phospholipids returned to normal level. Anti-hyperlipidemic effect of this plant could act as a protective effect against the development of

atherosclerosis and other similar diseases.[34] The synthesized silver nanoparticles using this plant extract also showed good anti-diabetic effect.[35]

8. Plant name: *Hygrophila auriculata* (K.Schum.) Heine

Synonym: *Astercantha longifolia (L) Nees, Hygrophila spinosa T. anders*

Tamil name: Neermulli, Nirmalli

Distribution: Throughout India along the bangs of fresh or stagnant water ditches, Sri Lanka, Malaysia, Nepal

Anti-diabetic activity

The plant extract expresses a significant and dose dependent anti-diabetic activity in amylase inhibition, glucose diffusion inhibition studies[36] and also in streptozotocin induced diabetic rats. A dose of 100 mg/kg and 250 mg /kg b. wt. hydroalcoholic extract of *Hygrophila auriculata* for 3 weeks showed a significant reduction in blood sugar, hyperperoxide, Thiobarbituric acid reactive substance in liver and kidney, increased the levels of glutathione (GSH), glutathione s-transferase (GST), glutathione peroxidase (GPx) and catalase when compared to the control. It also showed decreased level of lipid peroxidation which is associated with increased activity of superoxide dismutase (SOD) and catalase. The hydro alcoholic extract of plant has potent anti-diabetic activity along with significant anti-oxidant activity in diabetic conditions.[37] The aqueous extract also caused the reduction of Alanine transaminase (ALT) and Aspartate transaminase (AST) enzymes in diabetic treated rats.[38]

9. Plant name: *Elytraria acaulis* Lind

Synonym: *Elytraria crenata Vahl, Tubiflora acaulis Kuntze*

Tamil name: Pumikatampam

Habitat: South Africa, India, Nigeria, Sri Lanka, Eastern Himalayas

Anti-diabetic activity

Administration of 200 mg/kg and 400 mg/kg b. wt. of *Elytraria acaulis* methanolic extract to diabetic animals once daily for 4 weeks decreased the fasting blood glucose levels while in the untreated diabetic rats the fasting blood glucose levels remained at higher range. Treatment with *Elytraria acaulis* showed an increase in liver glycogen levels and decrease in glycated hemoglobin levels when compared to untreated rats. The histopathological study of islets of langerhans showed a marked improvement in normal architecture with mild hepatocytes degeneration and showing significantly inhibited glomerular hypertrophy and glomerulosclerosis.[39] The ethanolic extract also produced a highly significant effect in alloxan induced diabetic rats.[40]

10. Plant name: *Pseuderanthemum palatiferum* nees

Synonym: *Eranthemum palatiferum* Nees

Distribution: Cuc phuong forest in Northern Vietnam and expanded throughout the country including the Mekong Delta region

Anti-diabetic activity

The ethanolic extract of *Pseuderanthemum palatiferum* leaf has been proved as an active hypoglycemic agent in streptozotocin induced diabetic rats. After 14 days of treatment the *Pseuderanthemum palatiferum* extract at a dose of 250 mg/kg showed higher effect than the standard drug glibenclamide at a dose of 0.25 mg/kg and also the serum insulin levels were increased, this was due to the degeneration of pancreatic β-cells. The increasing levels of HDL and decreasing levels of Total cholesterol (TC), LDL, Blood Urea Nitrogen (BUN), ALP, total protein and albumin indicate that the ethanolic extract of *Pseuderanthemum palatiferum* can improve the liver and renal function.[41] Aqueous extract of *P. palatiferum* leaf at doses of 0.25 g/kg and 0.50 g/kg showed hypoglycemic effects in both oral glucose tolerance test (OGTT) and streptozotocin-nicotinamide-induced diabetic rats.[42]

11. Plant name: *Barleria bispinosa* (Forssk.) Vahl

Tamil name: Kikkiri, Ikkiri

Distribution: Sri Lanka, South India

Anti-diabetic activity

In normal and streptozotocin diabetic rats the methanol extract of aerial part of *Barleria bispinosa* produced hypoglycemic effect. The possible mechanism of these hypoglycemic effects may be through the insulin like activity and the increase of glucose uptake in lipocytes or stimulation of activity of pancreatic β-cells (synthesis, release and cell revitalization). The plant extract also possess hypolipedemic effects and could be helpful in decreasing the complication of lipid profile in some cases of diabetes in which the hypercholesterolemia and hyperglycemia to exist.[43]

12. Plant name: *Barleria cristata* Linn

Tamil name: Nilachemmulli, Udamulli, Semmulli, Vellainilambaram

Distribution: Throughout India, Subtropical Himalaya, Khasi hills, Sikkim

Anti-diabetic activity

The alcohol extract of *Barleria cristata* seeds has a good effect to lower blood glucose levels. The oral administration of alcoholic extract of *Barleria cristata* seeds at a dose of 200 mg/kg for 7 days showed a significant $p<0.01$ decrease in blood glucose levels in the alloxan induced diabetes rats model.[44]

13. Plant name: *Acanthus montanus* (Nees) T. Anderson

Common name: Mountain Thistle

Habitat: Africa, Greece, Australia, Eastern Mediterranean

Anti-diabetic activity

The hypoglycemic effect of an *Acanthus montanus* was investigated in normal and alloxan induced diabetic rats. Oral administration of ethanolic and aqueous extract at a dose of 200 mg/kg once daily for 14 days, the ethanolic extract treated group showed a decrease in blood glucose level when compared to aqueous extract treated rats. This effect was due to the ethanolic extract has maximum flavonoid content; the anti-oxidant property of flavonoids is one of the contributing factor for the reduction of blood glucose levels. The possible mechanism of *Acanthus montanus* extract support in the recovery of destroyed beta cells and release of insulin.[45] Plant drug produced noticeable reduction of blood sugar level in both the normoglycemic and alloxan-induced diabetic rats.[46]

14. Plant name: *Justicia spicigera* Schltdl

Common name: Muicle or mohuite

Distribution: Native from Mexico and extending into South America

Anti-diabetic activity

The hypoglycemic activity of *Justicia spicigera* leaves in diabetic rats showed that the ethanolic extract of *Justicia spicigera* significantly (P<0.01) decreased fasting blood glucose levels in normal and streptozotocin induced diabetic rats similar to those produced by the anti-diabetic drug glibenclamide by enhancing insulin secretion in pancreatic β-cells. *Justicia spicigera* ethanolic extract stimulates the human subcutaneous adipocytes and 2-NBDG uptake in insulin sensitive murine 3t3-F442A in a concentration dependent manner.

The possible mechanisms for reducing the blood glucose levels in diabetic rats are the involvement of an anti-oxidant system, activation of enzyme system generating cyclic AMP, modulating insulin secretion or insulin action and enhancement of β-cells glucose metabolism or phospholipids derived messenger.

The *Justicia spicigera* plant could have a remarkable hypoglycemic activity; it stimulates the glucose uptake in insulin sensitive and insulin resistant adipose cells and exhibits anti-oxidant effect,[47] also shows excellent effect in α-glucosidase and lipase inhibition studies.[48]

15. Plant name: *Ruellia tuberose* Linn

Siddha/Tamil name: Tapas-Kaaya

Distribution: Native to Central America, Grown in Indian gardens

Anti-diabetic activity

Methanolic extract and solvent fractions of *Ruellia tuberose* produces a significant hypoglycemic activity in normoglycemic as well as alloxan induced diabetic rabbits. The acute toxicity study in rabbits did not expose any behavioral changes and toxic effect up to 5000 mg/kg body weight dose. The ethyl acetate fraction and hexane fraction (150 mg/kg) showed highest and moderate anti-diabetic activity respectively when compared to the anti-diabetic drug tolbutamide (100 mg/kg). The water fraction did not show blood glucose lowering activity in normal as well as diabetic rabbits.[49]

16. Plant name: *Eranthemum roseum* Vahl. R. Br

Tamil name: Nila-mulli

Habitat: Western Ghats (of India), Peninsular India

Anti-diabetic activity

The saponin fraction of *Eranthemum roseum* significantly (P<0.01 and P<0.05) reduces the blood sugar level in the dose dependent manner. The oral administration of saponin fraction of plant extract and glibenclamide to STZ induced diabetic rats the elevated levels of hepatic enzymes like ALT and AST, serum creatinine, thiobarbituric acid reactive substances (TBARS) levels recovered to normal levels. It indicates that the plant has probable activity to prevent liver damage. It also reduces the levels of cholesterol and triglycerides followed by increased level of HDL. All these finding indicated that the plant extract exhibited hypocholesterolemic, hypotriglyceridemic, hypoglycemic and anti-oxidant activity in diabetic condition. The histopathological examination of rat pancreatic section revealed restoration of β-cells followed by occasional trophy in saponin fraction and glibenclamide treated rats.[50]

CONCLUSION

Plants have been an excellent source of medicine since ancient times. Medicinal plant products are traditionally used in many countries for the treatment of diabetes mellitus. Due to their perceived effectiveness, fewer side effects in clinical practice and relatively low cost herbal drugs are prescribed. In this review, we discussed the medicinal plants having anti-diabetic activity in Acanthaceae family. Treating diabetes mellitus with herbal compounds seems highly attractive because they are easily accessible, do not require laborious pharmaceutical synthesis, they delay the development of diabetic complications and correct the metabolic defects.[69,70] In this review, an effort has been made to explore the anti-diabetic medicinal plants and more investigations must be carried out to evaluate the mechanism of action of medicinal plants with anti-diabetic effect.

Table1: Some other medicinal plants with their anti-diabetic effect

S. No	Plants name	Extract used	Parts used	Method used	References
1.	*Hemigraphis colorata*	Whole plant	Water extract	Alloxan induced	51
2.	*Phlogacanthus thyrsiflorus*	Stem bark and leaf	Methanol	Streptozotocin induced	52,53,54
3.	*Strobilanthes asperimus*	Leaves	Ethanol	Alloxan induced	55
4.	*Andrographis stenophylla*	Leaves	Dichloro ethane	Oral hypoglycemic	56
5.	*Adhatoda zeylanica*	Leaves	Ethanol	Alloxan induced	57
6.	*Rhinacanthus nasutus*	Leaves	Methanol	Streptozotocin	58
7.	*Hygrophilla spinosa*	Roots	Chloroform, Ethyl acetate, alcohol	Alloxan induced	59
8.	*Thunbergia laurifolia*	Leaves	Aqueous	Alloxan induced	60
9.	*Barleria lupine*	Aerial part	methanol	Streptozotocin induced	61
10.	*Barleria prionitis*	Leaf and roots	Alcohol	Alloxan induced	62
11.	*Graptophyllum pictum*	Leaves	Aqueous	Alloxan induced	63
12.	*Strobilanthes crispus*	Leaves	Aqueous	Streptozotocin induced	64
13.	*Asystasia gangetica*	Leaves, Flowers	Methanol Anthocyanin extract	α-Glucosidase and α-Amylase	65, 66
14.	*Andrographis lineata*	Leaves	Methanol	Streptozotocin induced	67
15.	*Andrographis serpyllifolia*	Whole plant	Ethanol	Alloxan induced	68

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