



ASSESSMENT OF MEDICINAL PLANTS WITH ANTI DIABETIC ACTIVITY: AN ETHNOPHARMACOLOGICAL APPROACH

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ABSTRACT

Diabetes mellitus is a group of metabolic diseases characterized by high blood sugar (glucose) levels that result from defects in insulin secretion, or action, or both. There are lots of synthetic drugs present in the market for the treatment of diabetes but they are prone to noxious effects to human systems. Herbal medicine is gaining popularity both in developing and developed countries because of their natural origin. Medicinal plants which have potent anti hyperglycemic effect have been identified and proved experimentally by many people around the world. The effects of these plants may delay the development of diabetic complications and correct the metabolic abnormalities. In this review an attempt has been made on most popular medicinal plants with potential antidiabetic significance, their modes of action together with the method used for their assessment. The study recovered 37 plants of 27 families, with Papilionaceae showed more (4) plant species. The list of plants with proven antidiabetic and allied beneficial effects and of herbal drugs used in management of diabetes is compiled. This work stimulates the researchers to promote research on the prospective use of medicinal plants having antidiabetic potential, in the field of pharmacology and therapeutics.

KEYWORDS: Diabetic mellitus, Medicinal plants, Hyperglycemic effect, Insulin secretion.

INTRODUCTION

Diabetes is a chronic disorder of carbohydrate, fat and protein metabolism characterized by increased fasting and post prandial blood sugar levels. The global prevalence of diabetes is estimated to increase from 4% in 1995 to 5.4% by the year 2025. Diabetes mellitus is a multifaceted metabolic disorder resulting from either insulin insufficiency or insulin dysfunction. Insulin, a hormone that is produced in the sufficient quantities in the β - cells of the islets of Langerhans in the pancreas is the chief regulator of the glucose content in the blood. In diabetes the body metabolic process is completely disturbed either due to the lack of insulin or due to ineffectiveness of insulin that can produce.^[1]

In recent times, the World Health Organization (WHO) recommended the use therapeutic plants for the management of diabetic mellitus and further encouraged the expansion of the frontiers of scientific assessment of hypoglycemic properties of various plant species.^[2] Consequently, recent estimates showed that over 70% of the worldwide population applies resources derived from conventional medicine for the management and mitigation of diabetic mellitus and its complications.^[3,4] There is an increasing demand by patients for the use of natural products and other dietary modulators with anti diabetic activity. This tendency is because insulin, to

date, cannot be used orally and its repeated injections have many undesirable adverse effects. In addition, certain oral hypoglycemic agents are not effective in lowering the blood sugar in chronic diabetic patients.^[5]

Natural herbal medicines involve the combination of large number of therapeutic practices and useful experiences of indigenous systems of medicine that may cross several previous generations, which frequently supply precious guidelines to the selection, synthesis and application of herbal formulation with a vision to providing therapeutic benefits. Treatment of sickness and maintenance of health/comfort with herbal medicines is the oldest and most accepted form of healthcare tradition known to humanity that has been practiced by all cultures in every age's right through the history of civilization.

Currently, medicinal plants continue to play an significant role in the management of diabetic mellitus, particularly in developing countries, where many people do not have access to conventional anti-diabetic therapies.^[6,7] In current review paper, an effort has been made to compile the reported hypoglycaemic medicinal plants accessible in different scientific journals and may be valuable to the health professionals, scientists, researchers and natural medicinal follower running in the

field of pharmacology and therapeutics to develop evidence based alternative remedy to treat different kinds of diabetes in human being and animals. This review covers the common name of a medicinal plant, families, the parts that are commonly used as a remedy sources, varied extracts, doses, test model, and the degree of hypoglycemic activity. The number of plants described (37 plant species belonging to 27 families) evidently demonstrated the significance of herbal plants in the treatment of diabetes. This work stimulates the researchers for promoting research on the prospective use of medicinal plants having antidiabetic potential. The important anti-diabetic potential herbal plants given in the table 1. Moreover different extract have been used in the reports were also shown fig. 1.

2. Antidiabetic effect of medicinal plants

2.1 *Aegle marmelos* (Rutaceae)

The effect of methanol extracts of leaf and callus of *Aegle marmelos* in the diabetic Swiss albino rabbits were studied for different durations. Among the various solvent extracts, methanol extract produced the maximum reduction of sugar level, and the highest reduction was observed on the tenth days. The demonstration was statistically proved that, among different treatments, methanol extracts count of blood sugar level were much reduced with leaf extract treatment and callus extract treatment over control blood sugar level. With examination, it revealed that the *in vitro* callus culture of plant has as much prospective in diabetes management as the original leaf extract.^[8]

2.2 *Carica papaya* (Caricaceae)

Seed extract was administered at two different doses of 100 mg/kg, 200 mg/kg to Streptozotocin -Nicotinamide treated diabetic rats caused significant ($P < 0.001$, $P < 0.01$) reduction of blood glucose levels which was related to dose and duration of treatment. On 14th days of treatment maximum reduction was observed of group CSET (200 mg) and group CSET (100 mg) as compared to diabetic control group. The examination were also proved on SGOT, SGPT levels and were decreased ($P < 0.01$, $P < 0.05$). Lipid profile was also decreased significantly ($P < 0.01$, $P < 0.05$).^[9] Similar evaluation was conducted on antidiabetic and chemical characterization of aqueous roots extracts of *C. papaya* in alloxan induced diabetic rats. Under 15 days of observations, blood was withdrawn for glucose determination on 0, 1, 10 and 15 days respectively. At doses of 100 and 200 mg/kg showed significant in blood glucose when compared to diabetic control group. The study also enclosed on primary evaluation to confirmed the presence of many phytoconstituents.^[10]

2.3 *Bombax ceiba* (Bombacaceae)

Oral administration of ethyl acetate extract of bark for 21 days resulted in significant reduction of fasting blood glucose at a dose of 600 mg/kg body weight when compared with diabetic control. On the other hand at an initial concentration of dose 200 mg/kg body weight, no

significant reduction in blood glucose level was observed. The investigation was also extended towards the measurement of total cholesterol, triglyceride, HDL and LDL. This dose also significantly ($p < 0.001$) lowered the total cholesterol and triglyceride level in severely diabetic rats. It confirmed that, presence of the triterpenoid compounds in the extract, which may account for its significant hypoglycemic activity.^[11]

2.4 *Calotropis procera* (Asclepiadaceae)

Oral administration of dried extract of plant 300 and 600 mg/kg/day body weight in diabetic rats showed significant reductions in fasting glucose levels of more than 60% already in the first week of treatment when compared to diabetic control and more than 45% in relation to diabetic rats treated with metformin 500 mg/kg group. At the end of treatment, these reductions were of 68 and 51%, respectively, only in relation to diabetic control. With the treatment, the investigation also indicated that the reduction level of blood glucose throughout the evaluation period and improved metabolic status of the animals and ameliorate the oral tolerance glucose test.^[12]

2.5 *Terminalia belerica* (Combretaceae)

As compared with untreated controls, rats animals treated with fruits of *T. belerica* showed much lowered serum glucose level from day 6 onwards. On 9th day, serum glucose in extract treated animals was found to be reduced to 54% ($P < 0.001$) when compared with that of control diabetic animals. However, the plant fruits extract did not have any significant effect on serum glucose level in alloxan diabetic rats during first five days.^[13] Glutathione reductase also was found to be increased in blood and liver. These results suggested that plant fruit extract possessed anti-diabetic and anti-oxidant activity and these activities may be interrelated.

2.6 *Dalbergia sissoo* (Papilionaceae)

Investigation on *D. sissoo* stem-bark alcoholic extracts (250 and 500mg/kg respectively) and aqueous extract (400mg/kg) significantly reduced the blood glucose level ($P < 0.05$) where as hexane soluble extract and butane soluble extract did not reduced the blood glucose level significantly ($P > 0.05$) when compared with glibenclamide. Experimental design includes eight groups animal with six rats in each. Fasting blood glucose levels were determined by glucose oxidase method on day 0th, 7th, 14th and 21st day with commercially available biochemical kit. In conclusions, assessment indicated that plant extracts exerts their hypoglycemic action by stimulation of glucose uptake since promising value for the development of a potent phytomedicine for diabetes.^[14]

2.7 *Moringa oleifera* (Moringaceae)

The finding on effect of *M. oleifera* leave or its ethanolic extract on glucose, HbA1c, insulin and HOMA-IR level were conducted. The experimental design included seven groups of animals (G1 to G7). The active ingredients of

plant were determined through HPLC analysis. A significant increase in blood glucose, plasma and liver; and a significant ($P < 0.001$) reduction in insulin, liver glycogen, protein, super oxide dismutase and total antioxidant capacity level were observed in the STZ-induced diabetic rats. These changes were reversed by treatment with dried leaves of plant or its ethanolic extract. Additionally action of normal rats with plant leave or its ethanolic extract showed a significant decrease (-13, -11% respectively) on glucose level when compared with normal control group and this might be due to its insulin-like activity or presence of terpenoids (stimulate β -cells).^[15] Furthermore, the plant extract was also used for the analysis of anti-hyperglycaemic, anti-Inflammatory and antioxidant activities. Plasma glucose level decreased significantly ($p < 0.05$) in diabetic rats after treatment when compared to diabetic controls. The different parameters were also measured in the experiment and were significantly improved as compared to diabetic animals after the treatment with methanolic leaf extract of plant.^[16]

2.8 *Ficus religiosa* (Moraceae)

The ethanolic extract of the *F. religiosa* fruit, at a dosage of 250 mg/kg body weight, was found to exert a more pronounced antidiabetic activity than a 100mg/kg body weight dose on days 30th of the treatment, on the other hand leaves extract was ineffective to lower the blood glucose level significantly in diabetic rats. Amongst nine group of animals experimental design; 18.15 % reduction of blood glucose level was observed in group seven (diabetic + fruit ext. 250 mg/kg) over group two (diabetic control).^[17] Furthermore, the effect of single dose (250 mg/bwt) of aqueous leaves plant for 21 days in alloxan induced diabetes in rats showed hypoglycemic and antihyperlipidemic activity. It showed moderate decrease in the blood glucose, serum cholesterol, triglyceride and increase phospholipids levels as compared to other test materials.^[18]

2.9 *Madhuca indica* (Sapotaceae)

The experiments were conducted on extracts of dried pieces of bark of *M. indica* by using three different solvents viz. methanol, petroleum ether and water. Among these extracts, methanolic extract of plant has shown significant anti diabetic activity against streptozotocin and streptozotocin–nicotinamide induced diabetic models in wistar rats. The count of serum blood glucose level was much reduced in methanolic MI extract (Group G3) as compared to diabetic control (Group G2).^[19]

2.10 *Tamarindus indica* (Caesalpinaceae)

A total number of 30 rats were randomized into 5 groups of six each in the investigation, the oral administration of aqueous extract of *Tamarindus indica* seeds for 45 days decreases fasting blood glucose in group 3 (diabetic control + TiA Set) as compared to group 2 (diabetic control). The investigation concludes that TiASet has potent antidiabetic effect, which was possible due to its

antilipid peroxidative, antioxidant prospective and modulating impact on carbohydrate metabolizing enzymes action in alloxan-induced diabetic animal.^[20]

2.11 *Vitex negundo* (Verbenaceae)

The work carried out on aqueous and ethanol leaf extract of *V. negundo* for its antidiabetic activity using alloxan induced diabetic model in rats. The investigation was conducted on five groups of animals. The aqueous extract showed ($P < 0.01$) significant activity than the ethanol extract at the tested dose level, which were comparable to glibenclamide, a standard antidiabetic drug. There was improved final body weight of animals also, over an initial weight of animal with aqueous extract of treated diabetes group. The body mass return to usual as compared to diabetic rats.^[21] Another assessment was carried out upto 21 days on mice for evaluation of antihyperglycemic and antihyperlipidemic effects on normal and streptozotocin-induced diabetic animals. Comparing the blood sugar level in streptozotocin induced diabetic mice, ethanol leaves extract administered subject showed significant reduction of blood glucose level at $P < 0.001$. In the 7th, 14th and 21st days of experiment with 300 mg/kg b.w., glucose level was decreased by 13.93%, 29.36%, and 45.91% respectively.^[22]

2.12 *Semecarpus anacardium* (Anacardiaceae)

The impact of *S. anacardium* barks extract on blood glucose level in groups SA 100, SA 200 and SA 400, dose-dependent throughout the treatment period were examined. The trial process included total of 30 long evans rats, were divided into six groups for the oral administration of extracts/drugs or vehicle up to for 15 days using intragastric tube. The 15 days survival rate was significantly higher in group SA 400 (400 mg/kg) compared to diabetic control group (DC). The bark extract exhibited significant ($p < 0.05$) anti-diabetic activity. With observations it concluded that stem barks of *S. anacardium* possess strong anti-diabetic and antioxidant potentials and support traditional medicinal use for the treatment of diabetes mellitus.^[23]

2.13 *Tinospora cordifolia* (Menispermaceae)

The research evidently showed that *T. cordifolia* has significant ($P < 0.05$) anti-diabetic activity in diabetic animals and has an efficacy of 40% to 80% compared to insulin. Experimental animals were separated into seven groups, with each group consisting of six animals. Single dosage of either aqueous extract or alcoholic extract was given orally for 10 days and 30 days to specific groups. On 11 days of treatment, the fasting blood glucose count was greatly reduced of group three (diabetic rats treated with 200 mg/kg b.w. aqueous extract of plant) as compared to group two (diabetic control-consisted of streptozotocin induced diabetic rats). However with 31th days of treatment, the same counts were highly decreased. With assessment, it concluded that the probable mechanism by which plant may act as an antihyperglycemic drug was not through insulin secretion

like sulfonylureas. It might through some peripheral mechanisms, such as increasing the glycogen storage in the liver or decreasing the glucose release from the liver.^[24]

2.14 *Cyperus rotundus* (Cyperaceae)

Albino rats of male weighing between 180-220 gms were categorized into five groups, each group consisting of 6 animals. Blood glucose levels were measured with a portable glucometer on 0, 1, 7 and 14 days. The ethanolic extract of *C. rotundus* plant showed the significant decrease in serum glucose level ($p < 0.001$) in both oral glucose tolerance test and alloxan induced diabetic rats. The study were also confirmed that the significant reduction in serum triglycerides, total cholesterol, LDL, and liver enzymes.^[25]

2.15 *Psidium guajava* (Myrtaceae)

Rats were divided into five groups, each group containing five animals. All the treatments were given orally for 30 days, and on the final day the blood samples were collected by retro-orbital plexus puncture process, and the serum glucose levels were measured by glucose-oxidase-peroxidase method. Among the fresh and dry hydro alcoholic plant extracts, fresh leaf extract showed significant anti hyperglycemic activity than the dry leaf extract which was nearly produced equal decrease in serum blood glucose levels to that of standard glibenclamide 10mg/kg.^[26] Moreover, administration of ethanolic extracts of *P. guajava* leave at doses 1.00 and 0.50 g/kg significantly ($P < 0.05$) decreased blood glucose levels in oral glucose tolerance test model as well as 0.75 g/kg dose in alloxan induced diabetic test model in wistar rats ($P < 0.001$). Results exhibited the significant antidiabetic activities of plant leave in rats.^[27]

2.16. *Syzygium cumini* (Myrtaceae)

The isolated compound mycaminose (50 mg/kg), ethyl acetate (EA) and methanol (ME) extracted compounds of *S. cumini* seed (200 and 400 mg/kg) was used to evaluate anti-diabetic activity up to 15 days of treatment on eight group of animal rats against streptozotocin (STZ)-induced diabetic rats. Amongst eight groups, blood sugar level count, were lowest in group – VI (STZ induced diabetic animals received methanolic extract at the dose of 400 mg/kg daily p.o. for 15 days) compared to group – II (STZ induced diabetic animals received 1% SCMC 10 ml/kg, p.o. for 15 days). The results were confirmed significant ($p < 0.05$) reduction in blood glucose level. Experiment indicate that isolated compound ‘Mycaminose’, ethyl acetate and methanol extracts possess anti-diabetic effects against STZ-induced diabetic rats.^[28] Out of different doses of ethanol plant extract, 25 µg dose found suitable and for highest decrease (63.88 % and 61.15 %) in total glucose content and total cellular content respectively in diabetic human.^[29]

2.17 *Feronia limonia* (Rutaceae)

On four weeks treatment of ethanolic extract of *Feronia limonia* fruits, the fasting blood glucose level in 400 mg kg⁻¹ group was lowest as compared to in diabetic control group. At the end of four weeks treatment on albino rats, the decrease of blood glucose level count were 39% and 54.5 % respectively in 200 and 400 mg kg⁻¹ b.wt. group of *F. limonia* extract. The experimental design included seven groups of animals treated differently. The investigation concluded that plant extract showed significant ($p < 0.05$) decrease in blood glucose level when compared to the *Artocarpus heterophyllus* extract, the another plant used for same experiments.^[30]

2.18 *Asparagus racemosus* (Asparagaceae)

Powder of entire plant of *A. racemosus* was prepared. During investigation healthy, adult wistar rats of both sexes were divided into five groups of 6 animals each. At the end of 21 days study period, blood samples were collected under fasting conditions. Oral administration of ethanolic extract of plant (EEAR) 200 and 400 mg/kg/b.w for 21 days significantly decreased the blood glucose level, fluid intake and very much increased the body weight of diabetic induced rats. The count of blood glucose were minimum and maximum respectively in diabetic + EEAR (400 mg/kg) group, and diabetic control group, and concluded that EEAR may be regarded as a promising natural and safe medicine for prevention of diabetic difficulty.^[31]

2.19 *Cissus quadrangularis* (Vitaceae)

The serum glucose level was estimated at 0, 2, 4, 6 and 24 h after drug administration in acute study. The subacute investigation involved repeated administration of the drugs for 28 days and serum glucose level estimated weekly upto 28 days. Aqueous extracts of leaves of *C. quadrangularis* showed more significant reduction in blood glucose level in alloxan induced diabetic rats as compared to control and glibenclamide treated rats. The study was indicated that antihyperglycaemic activity of plant may probably be due to the presence of several bioactive components.^[32]

2.20 *Emblica officinalis* (Euphorbiaceae)

The fruit of *E. officinalis* aqueous extract treated groups of animal showed significant ($p \leq 0.001$) reduction in blood glucose levels in the fifth and sixth weeks compared to the metformin-treated group. Both extract doses (200 and 400 mg/kg) produced significant decrease ($p \geq 0.05$) in serum glucose. On the other hand, body weight of diabetic control group was not significantly different ($p < 0.05$) from those of the extract-treated groups. The investigation was carried out on four groups of animal up to 11 weeks and also focused on impact of these in cholesterol and triglyceride levels. With observations, it concluded that the aqueous fruit extract of amla has a potential as an antidiabetic natural product.^[33]

2.21 *Aloe vera* (Liliaceae)

The comprehensive research conducted on histology of liver and small intestine of diabetic animals, observed granular cytoplasm, dilated sinusoids, shrunken nuclei and inflammation, and excess proliferation of epithelium were reduced after feeding with *Aloe vera* (L.) crude plant extract. The significant reduction in sugars, protein and antioxidant contents were observed after the treatment of plant extract. Out of four groups of animal study, the fasting plasma glucose levels count on third weeks of treatment were low in group-IV (diabetic + *Aloe*) and high in group-III (diabetic control) respectively. It also noticed in report that, excess increase of epithelium in the small intestine was observed in diabetic rats, which was reduced after plant extract feeding.^[34]

2.22 *Ocimum sanctum* (Lamiaceae)

A total of 60 human patients were selected for the observations up to 90 days, and fasting blood glucose level were measured on 30th and 90th days. The study incorporated 30 type 2 diabetic cases who received only Glibenclamide and 30 type 2 diabetic cases received Glibenclamide plus *O. sanctum* tablet. The group which received Glibenclamide, showed more mean fasting blood glucose on first day however, it was low on 90th days. The group which received Glibenclamide plus *O. sanctum*, showed maximum, mean fasting blood glucose on first day however, it was minimum on days 90. Assessment confirmed that the drop in the fasting mean blood glucose levels obtained by Glibenclamide plus *O. sanctum* was more than Glibenclamide, when used alone. Further it suggested that this plant can be used as an adjuvant in type 2 diabetes mellitus patients.^[35]

2.23 *Acacia catechu* (Mimosaceae)

Animals were classified into 6 groups; group 1 was kept as control, 2 was treated with glibenclamide, 3 to 6 were treated with ethanolic extract and water insoluble fraction of ethanolic extract of barks of *A. catechu* at two dosage levels (200 and 400 mg/kg). In the investigation, biochemical parameters including glucose, urea, creatinine, serum cholesterol, serum triglyceride, high density lipoprotein, low density lipoprotein, haemoglobin and glycosylated haemoglobin were also assessed. At the end of the 7th day, the rats were fasted for 16 h and blood parameters were determined. Both the ethanolic extract and its fraction exhibited significant ($p < 0.05$) hypoglycaemic activity and the activity was dose-dependent. Comparatively, the fraction prepared from ethanolic extract was more active. After 7 days, values of blood glucose decreased in all the treated groups and the diabetic rats showed a slight increase in blood glucose level.^[36]

2.24 *Abrus precatorius* (Papilionaceae)

The ground seed of *A. precatorius* was stored dry and used throughout the study. The crude extract was regarded as chloroform- methanol extract. Three groups of healthy male rabbits ($n = 3$) with average weight of

1.6 kg were used for analysis. Blood glucose level was determined using O-toluidine method.^[37] The peak % reduction of chloroform- methanol was 69.1% after 30 hours while that of chlorpropamide was 61.3% after 20 hours of administration. The blood glucose percentage reduction was 56.6 and 51.8 after 60 and 168 hours respectively; There was a significant difference ($P < 0.001$) between the reduction patterns of chloroform-methanol to that of chlorpropamide. With such observations, it suggested that the chloroform-methanol extract of plant seed has some antidiabetic properties similar to that of chlorpropamide.^[38]

2.25 *Dioscorea alata* (Dioscoreaceae)

The powdered tubers plant material was extracted with ethanol. With plant extract (200 mg/kg, p.o.); the blood glucose level was found to be 82.33 ± 1.61 (mg/dl) after 120 min. The pre-treatment with *Dioscorea alata* ethanol extract (100 and 200 mg/kg) and metformin (250 mg/kg) elicited reduced serum glucose level significantly ($P < 0.001$) as compared to the control group. On repeated oral administration of the vehicle, plant extract or metformin, for 21 days, a sustained and significant ($P < 0.001$) decrease in the serum blood glucose of the diabetic rats was observed at a dose of 100 (47.48% fall) and 200 mg/kg (52.09% fall), in a dose dependent method as compared to the vehicle treated group. Serum lipid levels, total protein, albumin, and creatinine were reversed toward near usual in treated animals as compared to diabetic control.^[39]

2.26 *Eucalyptus globulus* (Myrtaceae)

The aqueous extract of *E. globulus* leaves was used in the study and experiments was carried out on 50 matured normoglycaemic male albino rats of Wistar strain weighing 200–250 g, separately housed in cages. Treatment of TD1, 2 rats with *Eucalyptus* extract displayed a significant, hypoglycaemic effect in STZ-induced diabetic rats in comparison to the corresponding D rats. Moreover, with treatments decreased the weight loss and increase of water and food intake in the treated diabetic groups in comparison to the STZ-induced diabetic (D) group. Plant treatment partially restored cellular deterioration of β -cells of islets in treated diabetic animals. Volume density and total amount of β -cells improved 21% and 65%, respectively, in the TD2 group, but it was not statistically significant compared to the diabetic group ($p > 0.05$). This observations suggested beneficial effect of *Eucalyptus* in the treatment of diabetes.^[40]

2.27 *Cynodon dactylon* (Poaceae)

The dried leaves of *C. dactylon* extracted with chloroform, ethanol and methanol for experimental purpose. Male albino rats with body weight of 160- 220 gm were divided into seven groups of five rats each. With 21 days, in diabetic rats, significant decrease in blood glucose level was observed after the treatment of different extracts. Blood glucose level of methanolic extract of plant treated rats showed very much less and it

was parallel to blood glucose level of normal rats. The value is found to be more than 50% less to alloxan induced rats (negative control) which had 345 ± 6.2 mg/100 ml. Variation in the plasma cholesterol level of the entire groups were observed at the end of 21 days of treatment ($P < 0.05$). Moreover, the reduction in triglycerides was by 50% in the diabetic rats treated with methanol extracts. It was also noticed that 45% reduction in urea level in the diabetic animals treated with extracts of chloroform and methanol.^[41]

2.28 *Zizyphus lotus* (Rhamnaceae)

Aqueous extracts from different parts, i.e. root, leaf, and seed of plant were prepared and administered orally to the animals at the dose of 300 mg/kg for 21 days. The leaf and root extracts significantly decreased glucose levels during 3 weeks, i.e. from 7th day to 21st day of treatment. The concentrations of different vitamins (vitamin A, C and E) in diabetic rats were also modulated by leaf and root, but not seed, extracts. Report confirmed that plant extracts from roots and leaves exerted antidiabetic and antioxidant effects in diabetic rats and suggested further, that plant seems to be a good candidate to lower, in addition to conventional antidiabetic drugs, the hyperglycaemia in diabetic subjects.^[42]

2.29 *Erythrina indica* (Papilionaceae)

Animals were divided into seven groups. The authors used alcoholic and aqueous extracts of stem bark of *E. indica*. In general alloxan-induced diabetic rats; both the extracts decreased blood sugar levels with significant improvement in glucose tolerance and body weight at the end of 1st, 2nd and 3rd week after test extract treatment. The experimental data showed that the aqueous extracts (200 and 400 mg/kg) treatment for 21 days in diabetic rats has caused a reduction in blood glucose level when compared to the alcoholic extract, indicating the potency of aqueous extract. It further recommended that extracts contain carbohydrates, alkaloids, flavonoids, saponins, phytosterols, phenolics and tannins; these phytoconstituents might be responsible for the hypoglycaemic activity of the plant.^[43]

2.30 *Jatropha gossypifolia* (Euphorbiaceae)

The study was confirmed antidiabetic and hypolipidemic efficacy of active fractions (chloroform fraction of 95 % ethanolic extract and butanol fraction of aqueous extract) of plant. Amongst 3 extracts, the 95% ethanolic extract and aqueous extract showed significant decrease on OSTT to the tune of 26.2% ($p < 0.01$) and 26.5% ($p < 0.01$) while the standard antidiabetic drug Metformin showed improvement on OSTT by 27.3% ($p < 0.01$) at 100 mg/kg in normal rats. The stem extract have positive effect in bringing down the severity of hyperglycemia, hyperlipidemia, modulating effect on carbohydrate metabolizing enzymes, decline the amplified level of renal and hepatic function markers and also improving glucose tolerance activity. In conclusion, the study verified that chloroform fraction of 95% ethanolic extract

of plant stem, was a valuable candidate for the search of antidiabetic ingredients from natural sources and as a possible candidate in the treatment of type 2 diabetes associated with hyperlipidemia.^[44]

2.31 *Annona squamosa* (Annonaceae)

The assessment was carried out on demonstration of the hypoglycaemic and antidiabetic activity of aqueous (hot) leaves extract of *A. squamosa* in diabetic rabbits and rats with a view to explore its use for the treatment of diabetes mellitus in humans. With extract at a dose 350 mg/kg bw, reduced fasting blood glucose (FBG) level slightly by 6.5% within 1 h and the peak blood glucose at 1 h during glucose tolerance test (GTT) was reduced by 15% in normal healthy rats. The same dose showed antidiabetic activity in two species of animals with induced diabetes. It was observed that serum insulin level enhanced by 27.6% in diabetic animals during GTT and insulin release by 38.1% from isolated pancreatic islets. The assessment reveals that plant has equally hypoglycaemic and antidiabetic activity. It seems to act by enhancing insulin level from pancreatic islets, increased consumption of glucose in muscle and inhibited the glucose output from liver.^[45] Likewise other report confirmed that, out of petroleum ether, chloroform, ethyl acetate, ethanol and aqueous bark extract of plant; ethanol achieved best results after 10 days (300 mg/kg, p.o., once daily). The count of blood glucose level was found to be more in diabetic +control and was reduced in diabetic+ extract. The whole of the study was performed on albino wistar rats. It was further confirmed that extract of plant reversed the weight loss of diabetic rats and they returned to near normal.^[46]

2.32 *Catharanthus roseus* (Apocynaceae)

Feeding with aqueous extract of *C. roseus* leaves in alloxan-induced diabetic rats, significantly ($P < 0.001$) decreased blood glucose levels and has brought down TC, LDL, VLDL and TG close to normal level. Adult four groups of healthy albino rats each with eight (wistar strain) aged about 3 months weighing between 400-420 g were used in the experiments. The fasting blood glucose was decreases rapidly from in experimental group of animals within 30 days of treatments. It further noticed that, the behavior of diabetic rats appeared sluggish and abnormally active, consumption of food increased initially, but both were returned to normal after a week of treatment.^[47]

2.33 *Curcuma longa* (Zingiberaceae)

The animals were randomized into 4 groups of 5 each for the estimation of anti-diabetic activity. There was a significant ($p < 0.05$) increase in the level of blood glucose and others molecules including body weight of the diabetic untreated rats. However with oral administration of aqueous extract of *C. longa* rhizome at a dose of 200 mg/kg, body weight for 28 days to diabetic rats resulted in a reversal of the diabetic situation. Phytochemical analysis of three extract revealed the presence of alkaloids, cardiac glycoside and resins while

flavonoids, tannins, saponins, balsams and phenols were not detected in all solvent extracts. From this report it recommended that the extract of plant rhizome used in the study possesses anti-diabetic activities and could be used for the management of diabetes and allied metabolic alterations.^[48]

2.34 *Ricinus communis* (Euphorbiaceae)

Administration of the effective ethanolic extract dose of *R. communis* roots (RCRE) to eight groups of five animals each; the diabetic rats for 20 days showed favourable effects not only on fasting blood glucose, but also on total lipid profile and liver and kidney functions on 10th and 20th days. Fasting blood glucose (FBG) decreased very much at the 8th h from an initial value with the dose of 250 and 500 mg/kg b.wt. of the extract. A dose-dependent outcome was observed on FBG up to a dose of 500 mg/kg b.wt. Ethanolic extract of plant roots seemed to have a high margin of safety as no mortality and no statistically significant variation in alkaline phosphatase, serum bilirubin, creatinine, serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase and total protein was observed even after the administration of the extract. Hence authors suggested that plant have a promising value for the development of a potent phytomedicine for diabetes.^[49]

2.35 *Trigonella foenum-graecum* (Papilionaceae)

The comprehensive study was carried out in four groups of five each animals to evaluate antidiabetic effect of *Trigonella foenum - graecum* seed extract (TFSE) and including glucose content in blood, liver and pancreas of normal and alloxan induced diabetic mice. In the 1st day experimental animals, the blood glucose level dropped and there was a gradual reduction in the 3rd and 5th day. A near normal value of 96.72 ± 0.05 mg / 100 ml was observed in the 7th day experimental animals. The investigation assumed that the compounds present in the extract might have caused regeneration of β -cells effecting normal secretion of insulin.^[50] Moreover, the chloroform extract of the plant applied to diabetic human, at a dose 25 μ g, 34.72 % and 36.69 % of total glucose content and total cellular content were reduced respectively.^[29]

2.36 *Nerium indicum* (Apocynaceae)

The *N. indicum* chloroform extract (NICE) and ethanolic extract (NIEE) showed significant ($P < 0.001$) antidiabetic activity. In alloxan induced model, blood glucose level on the 17th days of assessment were lowered in both the extract in comparison of diabetic control animals. These extracts also prevented body weight loss in diabetic rats. Phytochemical screening of the plant extract have been also carried out and confirmed various constituents like alkaloids, steroids, triterpenoids, carbohydrates and amino acids. Authors concluded that the NICE and NIEE have potent antidiabetic impact in alloxan-induced

diabetic rats; and suggested that investigation has also opened avenues for further research particularly with reference to the progress of potent formulation for diabetes mellitus from plant leaves.^[51]

2.37 *Costus speciosus* (Zingiberaceae)

The antidiabetic effect of ethanolic extract of *C. speciosus* rhizome was determined. The experiments were conducted on four groups of wistar albino rats, each consist of five animals (150-180gms). The diabetic rats treated with rhizome extract 200 mg/kg, reduces blood sugar level on seventh and fourteen days of measurements in comparison to the initial count. With extract treatment also showed significant reduction in glycosylated haemoglobin, blood urea, serum uric acid, serum creatinine, triglycerides, total cholesterol, phospholipids, low density lipoprotein (LDL) and very low density lipoprotein (VLDL); on the other hand liver glycogen, insulin and lactate dehydrogenase (LDH) were increased. It was concluded that the mechanism of action of extract in alloxan induced diabetic rats enhances insulin secretion by the islets of langerhans, enhances peripheral glucose consumption and increases serum protein levels.^[52] Moreover the rhizome samples of *C. speciosus* plant from forests of Indonesia was used to carry out the experiments on Swiss albino male mice of 3-4 months aged with mass 20-30 grams for the investigation. After many filtration and processed plant rhizome powdered were actually used in the experiment, diosgenin. Beside this, the conduction of research was also extended towards the measurements on other parameters i. e. body and testis weight, spermatogenic cells counts, sperm counts as well as sperm motility and viability. In alloxan-induced mice, at the end of 14 day, application of diosgenin 20% and 30% or taurine solely significantly lowered the blood glucose levels. In addition, the glucose levels in alloxan-induced mice significantly decreased by treatment of crude diosgenin extract combined with taurine ($P = 0.016$).^[53]

Table 1: Data of Medicinal plants traditionally used for the management diabetes mellitus.

SN	Plant species	Common Name	Family	Habit	Type of Plant extract	References
1	<i>Aegle marmelos</i> (L.)	Bengal Quince / Bael tree	Rutaceae	Shrub or tree	Methanol extracts of leaf	[8]
2	<i>Carica papaya</i> (L.)	Papaya	Caricaceae	Shrub or small tree	Aqueous extract of seed and root	[9,10]
3	<i>Bombax ceiba</i> (L.)	Shaalmali/ Katsaver	Bombacaceae	medium size tree	Ethyl acetate extract of bark	[11]
4	<i>Calotropis procera</i> (Ait.) R.Br	Milk Weed/ Rui	Asclepiadaceae	Evergreen shrub	Hydroalcoholic extract of the leaves	[12]
5	<i>Terminalia belerica</i> Roxb,	Behada	Combretaceae	Medium size tree	Methanolic extract of fruits	[13]
6	<i>Dalbergia sissoo</i> Roxb. ex	Sissoo/ Seesham	Papilionaceae	Tree	Alcoholic extracts of stem bark	[14]
7	<i>Moirnga oleifera</i> (L.)	Shewaga/ Horse-Radish	Moringaceae	Shrub or small tree	Ethanolic and methanolic extract of leaf	[15,16]
8	<i>Ficus religiosa</i> (L.)	Peepal	Moraceae	Tree	Ethanolic fruit; aqueous leaves extract	[17,18]
9	<i>Madhuca indica</i>	Mahua/ Moha.	Sapotaceae	Tree	Methanol, petroleum ether and water bark extract	[19]
10	<i>Tamarindus indica</i> (L.)	Tamarind tree/ Chinchaa	Caesalpiniaceae	Tree	Aqueous extract of seeds	[20]
11	<i>Vitex negundo</i> (L.)	Nirgundi/ Sambhalu	Verbenaceae	Shrub or smaller tree	Aqueous and ethanol leaf extract	[21,22]
12	<i>Semecarpus anacardium</i> (L.)	Marking-Nut/ Biba	Anacardiaceae	Shrub or medium size tree	Ethanolic stem barks extract	[23]
13	<i>Tinospora cordifolia</i>	Guduchi/ Amrita	Menispermaceae	Climbing shrub	Aqueous or alcoholic extract	[24]
14	<i>Cyperus rotundus</i> (L.)	Nutsedge/ Nutgrass	Cyperaceae	Herb	Ethanolic extract	[25]
15	<i>Psidium guajava</i>	Psidium/ Peru	Myrtaceae	Shrub or small tree	Hydro alcoholic leaf extracts; ethanolic extracts	[26,27]
16	<i>Syzygium cumini</i> (L.)	Black Plum/ Jambolan	Myrtaceae	Tree	Ethyl acetate and methanol seed; ethanol plant extract	[28,29]
17	<i>Feronia limonia</i>	Wood Apple/ Kavath	Rutaceae	Medium size tree	Ethanolic extract of fruits	[30]
18	<i>Asparagus racemosus</i> Willd.	Satavari/Satmuli	Asparagaceae	Herb or shrub	Ethanolic extract of entire plant	[31]
19	<i>Cissus quadrangularis</i>	Hadjod/ Kandvel	Vitaceae	Perennial climber	Aqueous extracts of leaves	[32]
20	<i>Emblica officinalis</i> Gaertn.	Indian gooseberry/Amla	Euphorbiaceae	Small tree	Aqueous fruit extract	[33]
21	<i>Aloe vera</i> (L.)	Ghikanvar	Liliaceae	Herb	Crude plant extract	[34]
22	<i>Ocimum sanctum</i>	Tulsi	Lamiaceae	Herb	Drug tablet	[35]
23	<i>Acacia catechu</i> (Linn. f.) Willd.	Khair/ Katthaa	Mimosaceae	Small tree	Crude aqueous extracts	[36]
24	<i>Abrus precatorius</i> Linn.	Gunjaa/ / Lal Gunj	Papilionaceae	Herb	Chloroform-methanol extract	[38]
25	<i>Dioscorea alata</i> Linn.	Yam	Dioscoreaceae	Herb	Ethanolic extract	[39]
26	<i>Eucalyptus globulus</i> Labill.	Neelgiri	Myrtaceae	Tree	Aqueous extract	[40]
27	<i>Cynodon dactylon</i> (L.)	Durva/ Doob	Poaceae	Herb	Chloroform, ethanol and methanol	[41]
28	<i>Zizyphus lotus</i> (L.)	Jujube/Ber	Rhamnaceae	Small tree	Aqueous extracts	[42]
29	<i>Erythrina indica</i>	Coral tree/Pangara	Papilionaceae	Tree	Alcoholic and aqueous extracts of stem bark	[43]
30	<i>Jatropha gossypifolia</i> (L.)	Tua-Tua/ Eranda	Euphorbiaceae	Shrub	Ethanolic and aqueous	[44]
31	<i>Annona squamosa</i> (L.)	Custard apple /Sugar apple	Annonaceae	Shrub and small tree	Aqueous leaves extract, ethanol extract of bark	[45,46]
32	<i>Catharanthus roseus</i> (L.)	Madagascar Periwinkle/Sadaabahaar	Apocynaceae	Herb and Shrub	Aqueous leaves extract	[47]
33	<i>Curcuma longa</i> (Linn.)	Turmeric/ Haldi	Zingiberaceae	Perennial herb	Aqueous rhizome extract	[48]
34	<i>Ricinus communis</i> (L.)	Erandi/ Castor oil bean	Euphorbiaceae	Shrub	Ethanolic roots extract	[49]
35	<i>Trigonella foenum-graecum</i> (Linn.)	Fenugreek/ Methi	Papilionaceae	Herb	Aqueous seed extract	[50,29]
36	<i>Nerium indicum</i>	Indian oleander	Apocynaceae	Evergreen shrub	Pet. ether, chloroform, alcohol and aq. leaves extracts	[51]
37	<i>Costus speciosus</i> (Koenig) Sm.	Wild Ginger/ Kebuka,	Zingiberaceae	Herb	Ethanolic rhizome extract	[52,53]

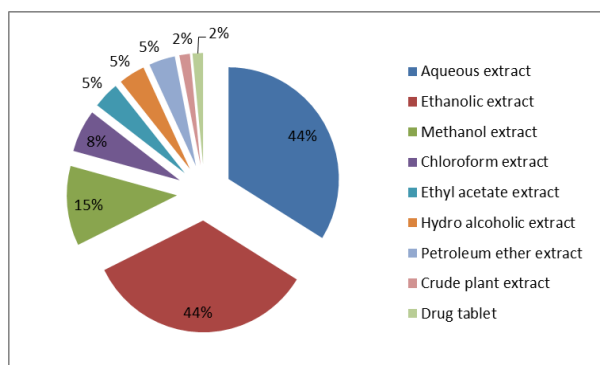


Fig 1: Frequency of diverse extract used in the different report.

3. CONCLUSIONS

Uncontrolled diabetes resulting to numerous chronic difficulties such as cardiac failure, blindness, renal failure and many more. It is known to be a dreadful disease that is found in all parts of the world with a serious threat to the health of mankind. In order to check this alarming health trouble, expansion of novel hypoglycaemic and potentially antidiabetic agents is of immense interest. There has been rising demand by patients to use the natural products with antidiabetic activity. The majority of *in vivo* and *in vitro* investigations confirmed the prospective of medicinal plants in the managing diabetes mellitus. From whole of the story it confirmed that the presences of bioactive chemicals are mainly responsible for this antidiabetic action. However, it equally important to explore many other active agents obtained from plants has not been well characterized. Therefore more investigations must be carried out to evaluate the mechanism of action of medicinal plants with antidiabetic effect.

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