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An Analysis upon Hypolipidemic Influences of Different Medicinal Plants: A Review on Diabetic Rats

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Abstract – Diabetes mellitus is a chronic disorder of carbohydrate, protein, fat and mineral metabolism. The antidiabetic potential of aqueous extracts flower and root of Aerva lanata was evaluated in alloxan induced diabetic rats. Alloxan (150 mg/kg bw) induced diabetic rats showed a hyperglycemic state that led to various biochemical and metabolic alterations. The aqueous extract of flower and root of A. lanata (200 mg/kg bw) was administrated orally to diabetic rats for 45 days. In this study, the levels of fasting blood glucose, glycated hemoglobin (HbA1C), C-reactive protein (CRP), total cholesterol, triglycerides (TG), low density lipoprotein (LDL), very low density lipoprotein (VLDL), urea, and creatinine were significantly increased in diabetic rats. Body weight, hemoglobin, insulin, C-peptide and protein levels in blood were significantly decreased in alloxan induced diabetic rats. After the administration of extracts of flower and root of A. lanata to diabetic rats showed significantly restore the levels as normal rats. The antidiabetic effect of A. lanata was compared with strandard drug glibenclamide (1 mg/kg bw) treated rats. From this study, we concluded that the aqueous extract of A. lanata root have more antidiabetic effect when compared with flower extract. Therefore, the flower and root of A. lanata may be used as the alternative medicine for the treatment of diabetes mellitus.

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INTRODUCTION

Diabetes is one of the major health issues in current scenario and is affecting many people from different walks of life in almost every country of the world (Modak *et al*., 2007). Diabetes is a chronic disorder and is associated with abnormal metabolism of carbohydrate, fat and protein. Elevated levels of both fasting and post-paradinal blood sugar is the specific characteristic of diabetes. Auto-immune and non-auto-immune responses cause destruction of pancreatic β-cells resulting in type 1 diabetes (Kanatsuka *et al*., 2006). There are circulating immune markers against pancreatic islets known as anti-islet cell antibodies or β-cell antigens (Buchanan and Xiang, 2005). That is the reason for patient's dependency on external supply of insulin but those suffering from Type II diabetes known as non-insulin dependent, cannot properly respond to insulin. Type II diabetics can be therefore treated by changes in diet intake, exercise and by use of medicines. Type II diabetes is more prevalent form among two and constitutes about 90% of the whole. Symptoms can be same for both types such as: (i) raised levels of blood glucose; (ii) increased need to drink water; (iii) repeated urine output; (iv) increased food intake and weight loss; (v) blurred vision; (vi) nausea and vomiting; (vii) fatigue and weakness; (viii) restlessness and changes of mood etc.

Adverse side effects are reported by the use of synthetic oral antidiabetic drugs commonly used for the diabetes treatment. On the other hand, these drugs are also not safe during pregnancy. In recent years, use of herbal origin medicines had grown and these medicines are becoming popular in developed as well as developing countries. Natural origin is one of the reasons of increased popularity along with low cost and fewer side effects (Modak *et al*., 2007).

Medicinal plants are in vogue from many centuries for the management of diabetes but very less scientific research had been conducted on these drugs to rule out potentially active constituent and their mechanism of action. *Euphorbia prostrata* commonly known as Hazardani is an annual herb, which belongs to family Euphobeaceae and is abundantly found in India, Pakistan and Africa. The dried leaves and seeds are both slightly aromatic, and are considered as stimulant, astringent, anthelmintic and laxative. The juice from the fresh plant is used to treat ringworm. Among some tribes of India (Nag pur) the pounded whole plant, mixed with sugar and water, is used to stop diarrhea. An essential oil distilled from the plant

is used in medicinal soaps and to treat erysipelas and as a mosquito and fly repellent (Parrotta, 2001).

Several flavonoids like apigenin, quercetin, luteolin (and their glucosides), phenolic acids like gallic acid, ellagic acid and tannins are reported to be present in *Euphorbia prostrata*. These active constituents affect the inflammatory process by means of its action on the enzymes involved such as cyclooxygenase, protein kinase C, hyaluronidase, 5 – lipoxigenase, etc,. The hypoglycemic activity of *Euphorbia prostrata* was reported earlier by Singla and Pathak (1990) but systematic and scientific investigations had not been carried out on *Euphorbia prostrata*.

Plants have been the major source of drugs in Indian and other ancient systems of medicine in the world. In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity in both developing and developed countries because of their natural origin and less side effects. Many traditional medicines are derived from medicinal plants, minerals and organic matter. A number of medicinal plants, traditionally used for over 1000 years named rasayana are present in herbal preparations of Indian traditional health care systems. In Indian systems of medicine most practitioners formulate and dispense their own recipes. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. India is the largest producer of medicinal herbs and is called as botanical garden of the world. Currently, many research work focuses on herbal drug preparations and plants used in the treatment of diabetes mellitus is a major crippling disease in the world. The global prevalence of diabetes is estimated to increase from 4% in 1995 to 5.4% by the year 2025. Studies were conducted in India in the last decade have highlighted that not only is the prevalence of diabetes is high but also that it is increasing rapidly in the urban population. It is estimated that there are approximately 33 million adults with diabetes in India. This number is likely increase to 57.2 million by the year 2025. Diabetes mellitus is a group of metabolic alterations characterized by hyperglycemia resulting from defects in insulin secretion or action. It is made up of two types such as Type I and Type II. Type I diabetes often referred to as juvenile diabetes, is insulin dependent and known to affect only 5% of the diabetic populations. Type II diabetes is non-insulin dependent, usually develops in adults over the age of 40. It has already been established that chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of organs, especially the eyes (retinopathy), kidneys (nephropathy), nerves (neuropathy), heart (coronary heart disease) and blood vessels (peripheral vascular diseases) .

It has an adverse effect on carbohydrate, lipid and protein metabolism resulting chronic hyperglycemia and abnormality of lipid profile, which leads to series of secondary complications including polyuria, polyphasia, ketosis, glycoma and vascular diseases. In spite of the introduction and extensive utilization of hypoglycemic agents, diabetes and the related complications continue to be a major health problem worldwide, which is affecting nearly 10% of the population all over the world and considered as a major cause of high economic loss which can in turn impede the development of nations . It is projected to become one of the world's main disablers and killers within the next 25 years. Environmental factors such as diet, obesity and sedentary life style increase the risk of diabetes. Other important risk factors include high family aggregation, insulin resistance, nutritional status, age and lifestyle change due to urbanization. The management of diabetes is a global problem until now and successful treatment is not yet discovered. Currently available therapy for diabetes includes insulin and various oral hypoglycemic agents such as sulfonylureas, metformin, glucosidase inhibitors, troglitazone, etc. But these are reported to produce serious adverse side effects such as liver problems, lactic acidosis and diarrhea. About 800 plant species have been reported to possess antidiabetic properties. *Aerva lanata* (Linn.) is an important medicinal plant of Amranthaceae family and known as polpala is a prostrate to decumbent sometime erect herb, found throughout tropical India as a common weed in field and wasteland. The plant is used for curing diabetes, anthelmintic, demulcent and it is helpful in lithiasis, cough, sore throat and wound healing. The plant has been used as diuretic, anti-diabetic, expectorant and hepato-protective in traditional system of medicine. The plant also possesses antimicrobial and cytotoxicity activity, diuretic, urolithiasis and anti-inflammatory activities. It has been reported that Canthin-6-one and β-carboline alkaloids were isolated from leaves of *A. lanata* . The plant has been reported to possess anti-inflammatory, diuretic and nephroprotective actions and alcoholic extract of shoots of *A. lanata* has also shown significant antidiabetic activity. A number of Indian medicinal plants have been used for their antidiabetic activity in the traditional system of medicine, but not all of them have been reported on scientifically. There is no detailed study on antidiabetic activity of leaf, flower and root of *A. lanata*. So the present study was aimed to determine the antidiabetic effect of aqueous extracts of flower and root of *A. lanata* on alloxan induced diabetic rats.

Diabetes mellitus, a leading world-wide metabolic disorder, is characterized by hyperglycemia associated with impairment in insulin secretion and/or insulin action as well as alteration in intermediary metab-olism of carbohydrate, protein and lipids. Several reports indicate that annual incidence rate of diabetes mellitus will increase in future worldwide, especially in the developing countries.

Lipid abnormalities occur most commonly in diabetes in type 2 diabetic subjects, even in those who have reasonable glycaemic control. The characteristic pattern of blood lipids in type 2 diabetes is called

'diabetic dyslipidaemia' and consists of elevated serum total and VLDL (very low-density lipoprotein) triglyceride, low HDL (high-density lipoprotein) cholesterol and essentially normal total and LDL (lowdensity lipoprtein) cholesterol concent-rations. The distribution of LDL subfrac-tions, however, is altered, with a predomi-nation of small dense LDL particles (sometimes called the 'type B' pattern) which are strongly related to vascular disease in the general population. Dysipidaemia is also present in patients with impaired glucose tolerance. Diabetic dyslipidaemia is a component of the insulin resistance syndrome (syndrome X), i.e. central or truncal obesity, hypertension, glucose intolerance, accelerated atherosc-lerosis, dyslipidaemia and insulin resistance (Reaven, 1998).

INDIAN MEDICINAL PLANTS WITH ANTIDIABETIC POTENTIAL

Diabetes mellitus is a chronic endocrine disorder caused by an absolute or relative lack of insulin and/or reduced insulin activity that results in hyperglycemia and abnormalities in carbohydrate, fat and protein metabolism. Diabetes has emerged as a major healthcare problem in India. A national urban survey in 2005 observed that the
prevalence of diabetes in urban India in adults was 15.1%.
Recent data have illustrated the impact of socio-economic
transition occurring in rural India. The transition has occurred in the last 15 years and the prevalence has risen from 2.4% to 6.4%.

In India, indigenous remedies have been used in the treatment of diabetes mellitus since the time of Charaka and Sushruta. Plants have always been an exemplar)' source of drugs and many of the currently available drugs have been derived directly or indirectly from them. The ethnobotanical information reports that about 800 plants may possess
anti-diabetic potential). Several such herbs have shown anti-diabetic activity when assessed using presently available experimental techniques. A wide array of plant derived active principles representing numerous chemical compounds has demonstrated activity consistent with their possible use in the treatment of insulin dependent diabetes mellitus. Among these are alkaloids, glycosides,
galactomannan gun, polysaccharides, peptidoglycans, hypoglycans, guani-dine, steroids, carbohydrates, glycopeptides, terpenoids, amino acids and inorganic ions. Even there is the discovery of widely used hypoglycemic drugs, metformin came from the traditional approach by
using Galega officinalis. Thus, plants are a potential source of antidiabetic drugs (and others too) but this fact has not gained enough momentum in the scientific community. Out of the several medicinal plants used in the treatment of diabetes, some were reviewed in the present study.

1. Acacia arabica (A. arabica) (Leguminosae)

Powdered seeds of A. arabica demonstrate significant hypoglycemic effect at 2, 3 and 4 gm/kg in normal rabbits by initiating the release of insulin from pancreatic 2 cells. No acute toxicity and behavioral changes were observed at these doses). Yasir et al evaluated an aqueous and hydro alcoholic extracts of A. arabica for its hypoglycemic property and found that both extracts possess significant hypoglycemic property at 400 mg/kg. The hydro alcoholic
and chloroform extracts of A. acacia bark demonstrate significant antidiabetic property at 250 and 500 mg/kg dose dependendy in alloxan induced diabetic rats.

2. Aegle marmelos (Rutaceae)

The aqueous extract of leaf normalizes the blood glucose and lipid parameters in streptozotocin induced diabetic mice at a dose of 300 mg/kg. Also the same extract show's hypoglycemic effect by releasing insulin in vitro. Methanolic extract of leaf and callus possesses significant antidiabetic effect at a dose of 1 g/kg in streptozotocin
induced diabetic rabbits comparable to petroleum ether, benzene and chloroform extracts. Oral administration of leaves of plants at 5 g/day significantly ameliorates blood glucose level in non insulin dependent diabetes mellitus patients.

3. Agrimonia eupatoria (Rosaceae)

Zhang and Cheng, isolated nine compounds viz. apigenin-7-0-3-D-glucopyranoside, catechin, quercetin, rutin, kaempferol-3-0-alpha-L-rhamnoside, kampferol-3-O-beta-D-glucopyranoside, lutcolin-7-0-beta-D-glucopyranosidc, 19alpha, 24-dihydroxy ursolic acid, 3,3'-di-0-mcthyl ellagic acid4-()-beta-D-glucopyranoside form agrimony which reduce blood glucose level.

4. Allium cepa (Liliaceae)

Oral administration of juice of onion regulates blood glucose level and biochemical parameters in alloxan induced diabetic rats at a dose of 120 mg/kg. Furthermore, extract also normalizes the concentration of thiobarbituric acid reactive substances and the activity of glutathione S-transferase in plasma, liver, testes, brain, and kidney which were increased in alloxan-diabetic ratsU). Administration of onion powder in high fat diet streptozotocin diabetic rats causes increase in insulin secretion. The onion extract intake was effective in

lowering plasma glucose concentrations and body weight in diabetes.

5. Allium sativum (A. sativum) (AUiaeeae)

The intraperitoneal administration of (250 mg/kg) petroleum ether, ethyl aeetate and chloroform fractions of the methanol extract of garlic reveals significant antidiabetic, antihyperlipidemic and hepatoprotective properties. Administration of aqueous extract of A. sativum to diabetic subjects causes a significant antidiabetic and hypolipidemic effect. Furthermore, an administration of alcoholic extract of garlic significantly reduces Candida albicans concentrations in liver and kidneys homogenates in infected control and streptozotocin induced diabetic rats. The herbal formulation, DRF/AY/500I, containing a garlic, elicits hypoglycemic/antidiabetic effect in both normal and experimentally induced hyperglycemia (epinephrine and alloxan) rats at a dose of 500 mg/kg. Mahesar el al reported a significant anti-hyperglycaemic effect of garlic (1% solution/kg) in alloxan-induced rabbits.

6. Aloe vera (A. iera) (liliaceae)

Rajasekaran et al reported that, ethanol extraet of A. vera leaf gel shows significant antihyperlipidaemic effect in streptozotocin induced diabetic rats at 300 mg/kg for 21 days. The treatment of A. vera in diabetic rats showed a marked increase in body weight, liver glycogen, decreased blood and urine glucose levels and normalized serum lipids. Oral administration of processed A. vera gel for 8 weeks in diet induced non-insulin dependent diabetes mellitus in mice inhibits significantly plasma glucose level. The high molecular weight (MW) fractions of A. vera containing less than 10 ppm of barbaloin and polysaccharide (MW: 1 000 kDa) with glycoprotein, verectin (MW: 29 kDa) showed a significant hypoglycemic as well as antihyperlipidaemic activity. Oral administration of polyphenol-rich A. vera extracts (350 mg/kg) with known concentrations of aloin (181.7 mg/g) and aloe-emodin (3.6 mg/g) for 4 w'eeks to insulin resistant ICR mice decreases
significantly both body weight and blood glucose levels. The lophenol and cycloartanol, phytosterols isolated from A. vera gel inhibits blood glucose level at 25 g/kg/ day respectively for 44 days in animal model of type-2 diabetes.

7. Brassica juncea (Brassicaceae)

Admninistration of (200 mg/kg) aqueous extract of seeds to streptozotocin induced diabetic rats daily once for one month causes significant antidiabetic and antihyperlipidaemic activity.

8. Caesalpinia bonducella (Cisalpineaceae)

The fraction isolated from seeds shows hypoglycemic activity in type-2 acute diabetic models and also shows insulin secretagogue activity in isolated islets. Oral administration of seed extract produces significant antihyperglycemic action due to blocking glucose absorption in alloxan induced diabetic rats at 300 mg/kg.

9. Coccinia indica (C. indica) (Cucurbitaceae)

Combined extracts of Musa paradisiaca and C. indica ameliorate indices of protein metabolic disorders in streptozotocin induced diabetes rats. Aqueous extract of leaf shows antidiabetic activity in streptozotocin induced diabetes rats. The ethanolic extract of aerial parts, normalizes blood glucose level and lipid parameters in streptozotocin induced diabetic rats at 100 or 200 mg/kg. Chronic administration of fruit extracts (200 mg/kg) for 14 days reduces the blood glucose level in alloxan induced diabetic rats.

10. Eucalyptus globulus (Myrtaceae)

Administration of leaves extract to alloxan induced diabetic rats ameliorates blood glucose by enhancement of peripheral glucose uptake and oxidative stress by increase in catalase, superoxide-dismutase and gluthatione-peroxidase activities in liver and kidney.

11. Mangifera indica (M. indica) (Anacardiaceae)

Intraperitoneal administration of aqueous extract of stem bark (50-800 mg/kg) produces significant hypoglycemic effect in streptozotocin induced diabetic rats in a dose dependent manner. The oral administration of peel extract at 200 mg/kg to streptozotocin induced diabetic rats possesses significant antidiabetic and antihyperlipidemic
activityf6i). Mangiferin, a polyphenol isolated from M. indica significantly prevents progression of diabetic nephropathy and improves renal function in diabetic nephropathy rat model and cultured rat mesangial cells.

12. Punica granatum (Punicaceae)

The oral administration of methanol extract of flowers at 500 mg/kg inhibits glucose loading-induced increase in plasma glucose levels in Zucker diabetic fatty rats. Parmar and Kar, reported that, fruit peel extract normalizes all the adverse changes induced by alloxan mice, revealing the antidiabetic and anti peroxidative potential at 200 mg/kg. In addition to this, oral administration of aqueous extract of
flowers (250 and 500 mg/kg) ameliorates blood glucose, lipid parameters and oxidative stresses in streptozotocin induced diabetic rats. Administration of pomegranate seed oil reduces blood glucose level and lipid parametars in mice.

HYPOLIPIDEMIC ACTIVITY OF *ASPARAGUS RACEMOSUS*

Since ancient times, plants have been an exemplary source of medicine. Ayurveda and other Indian

literature mention the use of plants in treatment of various human ailments. India has about 45000 plant species and among them, several thousands have been claimed to possess medicinal properties. Researchers conducted in last few decades on plants mentioned in ancient literature or used traditionally for diabetes have shown anti-diabetic property. There are many plants and their products (active, natural principles and crude extracts) that have been mentioned or used in the Indian traditional system of medicine and have shown experimental or clinical anti-diabetic activity. Among the major phytochemical constituents of plants credited with hypoglycemic action are glycosides, alkaloids, glycans, triterpenes, mucilages, polysaccharides, oils, vitamins, saponins, glycoproteins, peptides, amino acids and proteins.

Over 400 traditional plant treatments for diabetes have been reported, although only a small number of these have received scientific and medical evaluation to assess their efficacy. The hypoglycemic effect of some herbal extracts has been confirmed in human and animal models of type 2 diabetes. The World Health Organization Expert Committee on diabetes has recommended that traditional medicinal herbs should be further investigated. Diabetes mellitus (DM) is caused due to deficiency in production of insulin by the pancreas, or by the ineffectiveness of the insulin produced. It is the global problem and number of those affected is increasing day by day.

The abnormalities in lipid metabolism generally lead to elevation in the levels of serum lipids and lipoproteins that turn play an important role in occurrence in premature and severe atherosclerosis which affects patients with diabetes. The most common lipid abnormalities include hypertriglyceridaemia and reduced high density lipoprotein (HDL) cholesterol levels.

Diabetes is associated with oxidative stress, leading to an increased production of reactive oxygen species (ROS), including superoxide radical, hydrogen peroxide and hydroxyl radicals or reduction of antioxidant defence system. Implication of oxidative stress in pathogenesis of diabetes is suggested not only by oxygen free radical generation but also due to non-enzymatic protein glycosylation, auto oxidation of glucose, impaired antioxidant enzyme and formation of peroxides. Lipid peroxidation is a key marker of oxidative stress results in extensive membrane damage and dysfunction.

Asparagus racemosus constitute of alkaloids, flavonoids, tannins, saponins, phenols, terpenes, polysaccharides and steroids. *Asparagus racemosus* root extract which contains highest amount of flavonoids, polyphenols and vitamin-C exhibits the greatest antioxidant activity. *Asparagus racemosus* was used as a bitter, sweet, emollient, cooling, nervinetonic, constipating, galactogogue, diuretic, carminative, appetizer, stomachic, antispasmodic and tonic. It is also used in nervous disorders, dyspepsia, diarrhea, dysentery, tumors, inflammation, burning sensation, hyperdipisia, nephropathy, agalactia and general debility. But the pharmacological and scientific evidence for its antidiabetic effect is yet to be proved.

METHODOLOGY

Collection and preparation of plant material - The medicinal plant *Aerva lanata* was collected from in and around Mayiladuthurai at Nagapattinum District, Tamilnadu, India. The plant was identified and authenticated by Dr. S. John Britto, Director, Rapinat Herbarium and Centre for Molecular Systematics, Department of Botany, St. Joseph's College, Tiruchirappalli, and Tamilnadu, India. The leaf, flower and root of *A. lanata* were separated and washed thoroughly in running tap water to remove soil particles and adhered debris and then finally washed with sterile distilled water. The leaf, flower and root of *A. lanata* were dried under shade separately and ground well into powder. The powdered materials were stored in air tight containers till the time of use.

Preparation of aqueous extracts - 30 g powder of leaf, flower and root were soaked separately in distilled water for 12 to 16 hours and boiled and then it was filtered through muslin cloth and then Whatmann no. 1 filter paper. The aqueous extracts were concentrated and made the final volume to one-fifth of the original volume. The paste form of extracts was stored in air tight container at 4ºC until the time of use.

Acute oral toxicity study - Acute oral toxicity study was conducted as per the OECD Guidelines 423 (acute class toxic class method) . The female *wistar* albino rats weight about 140-160 g (6-8 weeks) were selected and divided into 4 groups with 6 rats in each group. Animals were fasted overnight, but allowed water *ad libitum*. Group 1 being the control group and received only distilled water and the groups 2, 3 and 4 were the test group and received aqueous extracts of leaf, flower and root of *A. lanata* at the dose of 2000mg/kg, p.o. Since the formulation is relatively nontoxic in clinical practice the highest dose of 2000 mg/kg, p.o (as per OECD guidelines "unclassified'') was used in the acute toxicity study. All the animals were observed at the time interval of 1, 2, 4, 6 and 24 hrs from 2-14th day, then sacrificed 15th day for gross pathological examination of different organs including heart, lungs, liver, kidneys, sex organs and brain. The animals were observed closely for behavioral toxicity. There is no toxicity was observed in behavior and differentiation in organs.

Oral glucose tolerance test - Oral glucose tolerance test was performed by the method of Du and Karr .

The overnight fasted rats were divided into 5 groups of six rats each, pretreatment fasting blood glucose levels of each group were evaluated. Group 1 served as a control, the doses of 100, 200 and 300 mg/kg bw of aqueous leaf, flower and root extracts of *A. lanata* were given orally to the groups 2, 3 and 4 respectively. Blood glucose level of each group was evaluated after 1 hour of the treatment and considered as 0 h value. 2 g/kg bw of glucose solution was given to all the groups and their blood samples were withdrawn from retro-orbital site at intervals of 1, 2 and 3 h of glucose administration.

Experimental animals - Albino *wistar* rats weight ranges between 150-200 g of both sexes were used in this study. They were housed in polypropylene cages under standard laboratory conditions (12-h light/ 12-h dark cycle, 21 ± 2 ºC, and relative humidity 55 %). The animals were given standard rodent pellets and water *ad libitum*.

The rats were acclimatized to laboratory condition for 7 days before commencement of experiment. Ethical clearance for handling animals for this study was obtained from Institutional Animal Ethical Committee (IAEC) of SASTRA University, Thanjavur, and Tamilnadu, India. The experiments were conducted as per the guidelines of CPCSEA, Chennai, India. (Approval no: 211/ SASTRA /IAEC/RPP) .

Induction of diabetes mellitus - Diabetes was induced by intraperitoneal injection of alloxan at the dose of 150 mg/kg bw. The alloxan was dissolved in distilled water, and then used to induce diabetes mellitus in rats. Fasting blood glucose of the animals was measured after 14 days of alloxan injection using glucometer. Rats with fasting blood glucose above 200 mg/dl were considered as diabetic rats and used for further study.

Collection of blood sample - After the experimental period, the animals were kept fasted overnight and sacrificed by cervical dislocation under mild anesthesia. Blood was collected on decapitation and plasma and serum were separated by centrifugation at 2500 rpm for 15 min. The collected plasma and serum samples were used for various biochemical estimations.

Statistical analysis - The results of the present study were subjected to statistical analysis and all the results were expressed as means ± SE. The statistical significance was evaluated by one way analysis of variance (ANOVA) using SPSS (statistical package for social sciences) Ver. 11 and the individual comparison were obtained by Duncan's Multiple Range Test (DMRT). The values were considered statistically significant at 5% level ($p \leq 0.05$). Values with identical letter are not significant different according to DMRT at 5% level.

RESULTS

Acute oral toxicity - Aqueous extracts of leaf, flower and root of *A. lanata* administered rats showed no mortality or behavior changes at the single dosage of 2000 mg/kg bw during 14 days of study. Hence there is no lethal and toxic effect was observed on plant extracts treated rats.

Oral glucose tolerance test - The oral glucose tolerance test was evaluated in normal rats by treated with different concentrations (100 mg, 200 mg and 300 mg/kg bw) of leaf, flower and root extracts of *A. lanata*. The blood glucose level was estimated at 0, 1, 2 and 3 hours. The plant extracts treated rats suppress the increases of blood glucose levels. The highest inhibition of glucose absorption in blood was observed in root (62.66±1.18 mg/dL) and flower (70.66±0.98 mg/dL) extracts of *A. lanata* treated groups at the concentration of 200mg/kg b.w. when compared to leaf and standard drug glibenclamide.

Diabetes mellitus is a life threading metabolic diseases and it is estimated that its annual incidence rate will continue to increase in the future worldwide. Hyperglycemia is the primary clinical manifestation of micro and macro vascular diabetic complications. Alloxan is a beta cytotoxin, and islets of langerhans of pancreatic beta cells are destroyed and decreased the production of endogenenous insulin secretion and for the reduced utilization of glucose by tissue. In recent years, herbal medicines have started to gain importance as a source of hypoglycemic agents. Marles and Farnsworth estimated that more than 1000 plant species are being used as folk medicine for diabetes. Biological actions of the plant products used as alternative medicines to treat diabetes are related to their chemical composition. Herbal products are flavonoids, terpenoids, phenolic compounds, coumarins, and other constituents which showed reduction in blood glucose levels. Several species of medicinal plant possess antidiabetic activity have been described in the scientific and popular literature.

CONCLUSION

Most popularly used drugs of modern medicine such as atropine, quinine, artimisinine, digitalis, reserpine, metformin, etc have been originating from plant source. About less than 1% of estimated higher plants have been screened pharmacologically for diabetes mellitus. The main undesirable effects of current treatment include hypoglycemia, allergy, gastrointestinal disturbances, heart failure, lactic acidosis, etc. which may limit the use of these drugs in diabetes mellitus. It was reported that XI. charanlia, E. jambolana, T. foenum graecum, 0. Sanctum, etc. have shown varying degree of hypoglycemic and anti-hyperglycemic activity. This review' of ethnomedicinal value of these plants may be helpful in the treatment of diabetes.

In this study, the antidiabetic effect of aqueous extracts of flower and root of *A. lanata* on alloxan induced diabetic rats was confirmed. Antidiabetic activity was high in root extract treated rats when compared to flower extract of *A. lanata*. From this study, we concluded that flower and root extracts of *A. lanata* has significance hypoglycemic and hypolipidemic effects.

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