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A Review on Study of Anti-Diabetic Activity of Some Herbal Plants in Experimentally Induced Diabetic Rats

Vikram Singh Gurjar*, Yogesh Kumar Sharma

Department of Pharmacology, Jaipur College of Pharmacy, Jaipur, Rajasthan, India

ABSTRACT

Glucose metabolism involves small intestine, pancreas, muscle cell and liver. If there are, some problem with any of this diabetes organ leads to defect in glucose metabolism and can develop diabetes. Western medicine now prevails over "traditional" forms of medicine including herbal medicine systems. The use of a medicinal herb, alone or in combination with other herbs, can be thought of as a type of combination therapy because of the complexity of the phytochemicals and bioactivities in the plant. Diabetes will be induced by intra-peritoneal injection of Alloxan monohydrate and many experimental models were available for anti-diabetic screening on animal studies.

Keywords: Herbal Plants, Antidiabetic activity, Diabetic Rats, Hyperglycemia.

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***Address for Correspondence:**

Vikram Singh Gurjar, Department of Pharmacology, Jaipur College of Pharmacy, Jaipur, Rajasthan, India

1. INTRODUCTION:

The word *diabetes* is Greek for a draw off, referring to the ejection of a more quantity of urine; and *mellitus* is Latin used for sugar. Consequently diabetes mellitus means the passage of huge amounts of sweet urine. This is derived from the information that excess glucose in the blood spills over into the urine, absorbing fluids with it. Diabetes mellitus is a clinically and hereditarily heterogeneous group of disorders characterized by abnormally elevated levels of glucose in the blood. The hyperglycemia is due to lack of insulin secretion or to resistance of the body's cells to the action of insulin, or to a combination of these. Frequently there are also disturbances of carbohydrate, fat, and protein metabolism. Glucose metabolism involves small intestine, pancreas, muscle cell and liver. If there are, some problem with any of this diabetes organ leads to defect in glucose metabolism and can develop diabetes (The expert committee on the diagnosis and classification of diabetes mellitus, 2002). The classical symptoms of diabetes are Polydipsia, Polyuria and Polyphagia; Polydipsia or excessive thirst is a method of restoring the water content of the tissues lost by Polyuria[1]

2. DIABETES MELLITUS SCENARIO IN INDIA:

India goes in front the world with leading number of diabetic patients earning the doubtful distinction of being termed the "diabetes capital of the earth". In India simply, the occurrence of diabetes is expected to rise from 31.7 million in 2000 to 79.4 million in 2030 (Wild et al, 2004). The World Health Organization guess that death from diabetes as well as heart disease cost India about $210 billion each year and is likely to increase to $335 billion in the subsequently ten years.[2]

3. HERBAL MEDICINE AND THEIR POTENTIAL TO TREAT DIABETES MELLITUS:

Long before the birth of orthodox Western medicine, medicinal herbs were applied to treat a wide range of disease categories[2] Due to emphasis on scientism and other complicated reasons, Western medicine now prevails over "traditional" forms of medicine including herbal medicine systems. The use of a medicinal herb, alone or in combination with other herbs, can be thought of as a type of combination therapy because of the complexity of the phytochemicals and bioactivities in the plant. Thus, a single antidiabetic herb with thousands of phytochemicals may have multiple benefits by targeting several metabolic pathways and essentially "killing several birds with one stone." One study supported this principle by demonstrating that a combination therapy of orthodox medicine and herbal medicine exhibited a better (synergistic) effect than either medicine alone [3] Therefore, herbal medicine can

complement orthodox therapy in diabetes mellitus and provides hope for a cure.

Medicinal herbs have never become obsolete and still play a prominent role in human health care. Among them, over 1200 plants have been claimed to be remedies for diabetes. Over 400 plants as well as 700 recipes and compounds have been scientifically evaluated for T2D treatment. Metformin was developed based on a biguanide compound from the antidiabetic herb, French lilac, and is now a first-line drug for T2D. Medicinal herbs contain diverse bioactive compounds and can have multiple actions on insulin action, insulin production, or both. Ayurvedic preparations remarkably effective in controlling blood glucose levels. This was particularly true of case 2, for which the HbA1c decreased from 8.3 to 6.9% [4-6]

Some of the plants available in India that are reported to have antidiabetic properties are *Achyranthes aspera, Aegle marmelos, Anacardium occidentale, Areca catechu, Artemesis pallens, Bauhinia forficate, Beta vulgaris, Calmellia sinensis, Cassia auriculata, Cassia fistula, Ceiba pentendra, Enicostemma littorale, Euphorbia protrata, Ficus hispida, Ganoderma lucidum, Gum arabic, Gymnema sylvestre, Lepechinia caulescens, Memecylon umbellatum, Momordica charantia, Musa sapientum, Nigella sativa, Ocimum sanctum, Opuntia fukiginosa, Pterocarpus marsupium, Rhizoma polygonati, Salacia reticulata, Smallantus sonchifolius, Terminalia catappa, Tinospora cordifolia and Vinca rosea* [7-13] Though many of the plants are reputed in the indigenous systems of medicine for their hypoglycemic activities, several are unknown to the medical community, since these remain to be scientifically established along with their active compounds.

4. MECHANISM OF ACTION OF HERBAL ANTIDIABETICS:

The antidiabetic activity of herbs depends upon variety of mechanisms. The mechanism of action of herbal anti-diabetic could be grouped as-

- Stimulation of insulin secretion (*Teucrium polium, Allium sativum, Allium cepa, Panax ginseng*) (Pulok et al, 2016).
- Inhibition in renal glucose reabsorption (*Fraxinus excelsior*) (Eddouks and Maghrani, 2014).
- Stimulation of glycogenesis and hepatic glycolysis (*Momordica charantia*) (Miura et al., 2011).
- Protective effect on the destruction of the beta-cells (*Thea sinensis*) (Kim et al, 2013).
- Improvement of digestion and reduction of blood sugar and urea (*Aegle marmelos*) (Krishnan, 1968).
- Prevents pathological conversion of starch to glucose (*Eugenia jambolina, Pterocarpus marsupium*) (Sepha and Bose, 1956).
- Increasing the use of glucose by tissues and effect on adrenergic receptors (*Panax ginseng, Allium sativum, Allium cepa*)
- Potentiates the action of exogenously injected insulin
- Cortisol lowering activities (*Boerhaavia diffusa, Ocimum sanctum*) (Gholap and Kar, 2014).
- Inhibition of alpha-amylase (Heidari et al, 2015).
- Inhibition of β -galactocidase and α- glucocidase (Sharma and Mujumdar, 1990).
- Preventing oxidative stress that is possibly involved in pancreatic ß-cell dysfunction found in diabetes (Kaneto et al, 2015).
- Regenerating and/or repairing pancreatic beta cells (Mohamed et al, 2016).

5. STEPS INVOLVED IN SCREENING OF ANTIDIABETIC HERBAL DRUGS:

5.1 Plant material

5.1 Collection, identification and authentication of plant parts

5.3 Preparation of extracts

For the extraction soxhlet apparatus will be used and the extraction yield of the extracts from plant species is vastly depends on the solvent polarity, which find out both qualitatively and quantitatively the extracted compounds. Ethanol and water are the commonly used solvent for the extraction because of their low toxicity and high extraction yield with the advantage of modulating the polarity of the solvent by using mixtures at different ratios[14]

5.4 Animals

Healthy adult Male albino Wistar rats, weighing 150–200 g and will be used for the Screening methods.

5.5 Investigational model for induction of diabetes

Diabetes will induce by intra-peritoneal injection of Alloxan monohydrate (150 mg/kg b.w.) dissolved in the in normal saline. Blood was withdrawn (0.1 ml) from the tip of the tail of each rat under mild ether anaesthesia. The blood glucose level was checked before alloxanisation and after alloxanisation regularly in 24h intervals. Animals were considered diabetic when the blood glucose level was raised beyond 200 mg/100 ml of blood.[15] This condition was observed at the end of 72 h after alloxanisation.

5.6 Maintenance of animals and Exposure Conditions

Earlier to the experiments, the selected animals shall house in acrylic cages in standard environmental conditions (conditions (temp: 20–25 ^{0}C; relative humidity: 45-55 % under 12 h light/dark cycle), fed with standard rat feed for 1 week in order to adapt to the laboratory conditions and water *ad libitum*. They were fasted overnight (12 h) before experiments, but were allowed free access to water. Six animals were used for each group of study.[14-15]

5.7 Blood glucose level determination

Fasting blood glucose concentration will determine using a Glucometer (Optium), based on the glucose oxidase method. Blood samples were collected from the tip of tail at the defined time patterns.

5.7.1 Principle of glucometer system in measuring blood glucose level

A glucose meter (or glucometer) is a medical machine for determining the fairly accurate concentration of glucose in the blood. It is a main element of home blood glucose monitoring (HBGM) by citizens with diabetes mellitus or hypoglycemia. A small drop of blood, obtained by pricking the skin with a lancet, is placed on a disposable test strip that the meter reads and uses to calculate the blood glucose level. The meter then displays the level in mg/dl or mmol/l. Glucose meters provide fast analysis of blood glucose levels and allow management of both hypoglycemic and hyperglycemic disorders with the goal of adjusting glucose to a near-normal range, depending on the patient group.[3]

5.8 Acute model (In single dose treated alloxan induced hyperglycemic rats)

The acclimatize animals shall kept fasting for 24 h with water *ad libitum* and injected intraperitoneally a dose of 150 mg/kg of alloxan monohydrate in normal saline. After 1 h, the animals were provided feed *ad libitum*. The blood glucose level was checked before alloxanisation and 24 h after alloxanisation as above. Animals were considered diabetic when the blood glucose level was raised beyond 200 mg/100 ml of blood. This condition was observed at the end of 72 h after alloxanisation. The animals were segregated into seven groups of six rats in each. Group I served as normal control, Group II served as diabetic control and received vehicle (2 ml/kg) through the oral route. Group III received glibenclamide (5 mg/kg). Groups IV to VII received alcohol and extracts of *herbal drug/drugs* at doses of 200 and 400 mg/kg. Blood glucose level of each rat was estimated at 1, 2, 4, 6, 8 and 10 h, respectively.[16]

5.9 Sub acute model (In multi dose treated alloxan induced hyperglycemic rats)

The animals shall kept fasting for 24 h with water *ad libitum* and injected alloxan monohydrate intraperitoneally at a dose of 150 mg/kg in normal saline. After 1 h, the animals were provided rat diet *ad libitum*. The blood glucose level was measured 72 h after administration of alloxan. The animals showing blood glucose level beyond 200 mg/dl were considered for the study. The diabetic animals were segregated into seven groups of six rats each. Group I served as normal control, Group II served as diabetic control and received only vehicle (2 ml/kg) through the oral route. Group III received glibenclamide (5 mg/kg); Groups IV to VII received alcohol and extracts of *herbal drug/drugs* at doses of 200 and 400 mg/kg for 11days. The Group I served as normal reference. The blood glucose level was measured on 0, 3, 7 and 11th day of treatment.[15-17]

6. CONCLUSION:

India has a rich source of indigenous medicinal plants, which are traditionally being used in various health care purposes. Recent research works are involved to establish the medicinal values of the plants on a scientific platform. The Indian indigenous drugs have great importance both from professional and economic point of view. Numerous plants have been used for the treatment of diabetes mellitus in Indian system of medicine and in other olden systems of the world, out of these only a few have been evaluated as per the modern system of medicine. Various extracts of diverse parts of medicinal plants have been shown to possess antidiabetic and hypoglycemic effect. Most of them look to act directly on pancreas (pancreatic effect) and stimulate insulin level in blood. Some have extra pancreatic effect by acting directly on tissues like liver, muscle, etc and alter favorably, the activities of the regulatory enzymes of glycolysis, gluconeogenesis and other pathways.

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