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Review Article

A COMPREHENSIVE REVIEW ON ANTI-DIABETIC AGENTS OF HERBAL ORIGIN

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ABSTRACT

Diabetes mellitus is one of the oldest diseases known to mankind and yet with the tremendous scientific advances witnessed in this century, medical science cannot claim that it knows all that needs to be known about this disease, including its management. This is the main reason for the persistent interest all over the world to explore alternative remedies from the so-called "alternative systems" of medicine. It is the fact that diabetes can it be cured and it has never been reported that someone had recovered totally from diabetes. The rapidly increasing incidence of diabetes mellitus is becoming a serious threat to mankind health in all parts of the world. Plants have been the major source of drugs in medicine and other ancient systems in the world. Herbals are a traditional medicine or folk medicine practice based on the use of plants and plant extracts. This review presents the profiles of plants with hypoglycaemic properties, reported in the literature. The profiles presented include information about the scientific name, family, methodology used.

Keywords: Diabetes mellitus, Insulin, Blood glucose, Herbal sources

INTRODUCTION

The adulteration and substitution of herbal drugs is the major problem causing treat to the herbal drug industry and to the research on commercial natural products [1]. Diabetes mellitus is a clinical syndrome characterized by inappropriate hyperglycemia caused by a relative or absolute deficiency of insulin or by a resistance to the action of insulin at the cellular level [2].

It is the most prevalent chronic disease in the world affecting nearly 25% of the population .There is an estimated 143 million people worldwide suffering from diabetes which is almost five times more than the estimates ten years ago. This number may probably double by the year 2020 [3]. It is caused by inherited and/or acquired deficiency in production of insulin by the pancreas, or by the ineffectiveness of the insulin produced. It results either from inadequate secretion of hormone insulin, an inadequate response of target cells to insulin, or a combination of these factors [4]. In type I insulin dependent diabetes mellitus [IDDM], previously called juvenile diabetes, there is an absolute lack of insulin. The condition is caused by a lesion in the beta cells of the pancreas [5].

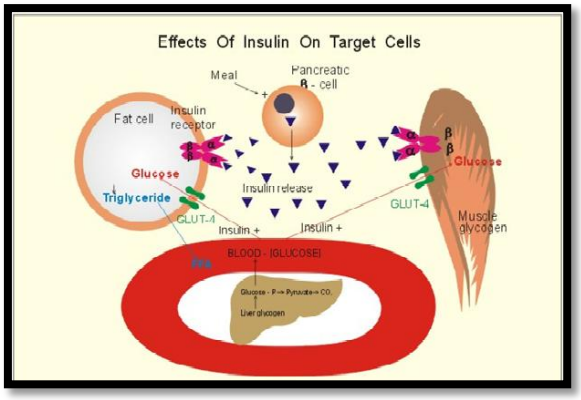

Fig. 1: Effect of insulin on target cells [6].

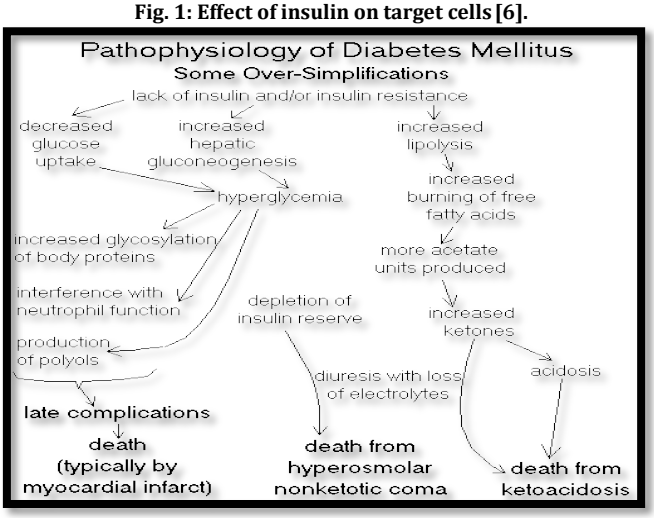

Fig. 2: Pathophysiology of Diabetes Mellitus [7].

List of Herbal Sources Possessing Potent Antidiabetic Activity

S. No.	Botanical name	Family	Part used	Active Extract	Model used
1.	*Anacardium occidentale* L. [8]	Anacardiaceae	Leaves	Methanol	SID
2.	*Annona squamosa* [9]	Annonaceae	Roots	Aqueous	SID
3.	*Acacia catechu* willd [10]	Leguminosae	Bark	Petroleum ether, chloroform, acetone, ethanol, aqueous and crude aqueous	AID
4.	*Allium cepa* [11]	Liliaceae	Bulb	Aqueous	AID
5.	*Achyranthes aspera* Linn. [12]	Amarathaceae	Aerial parts	Aqueous	AID
6.	*Achyranthes aspera* [13]	Amaranthaceae	Whole plant	Aqueous and methanolic	AID
7.	*Allium sativum* L. [14]	Liliaceae	Bulbs	Ethanolic	SID
8.	*Aloe vera* [15]	Liliaceae	Leaves	Water	AID
9.	*Berberis aristata* [16]	Berberidaceae	Stem bark	Aqueous	SID
10.	*Capparis decidua Forsk Edgew* [17]	Capparidaceae	Stem	Aqueous, ethanolic	AID
11.	*Casearia esculenta* Roxb. [18]	Samydaceae	Roots	Ethanolic	AID
12.	*Cocculus hirsutus* (L) Diels [19]	Menispermaceae	Aerial part	Methnolic	SID
13.	*Cassia glauca* [20]	Fabaceae	Bark	Aqueous	SID
14.	*Cassia auriculata* Linn. [21]	*Caesalpiniaceae*	Flower	Hydromethanolic and ethyl acetate and n-butanol fractions	AID
15.	*Cassia kleinii* [22]	Piniaceae	Leaves	Ethanol	SID
16.	*Cassia grandis* [23]	Leguminosae	Whole plant	Aqueous and ethanolic	AID
17.	*Croton zambesicus* muell [24]	Euphorbiaceace	Leaves	Ethanolic	AID
18.	*Cajanus cajan* [25]	*Fabaceae*	Leaves	Methanol	AID
19.	*Dalbergia sissoo* L. [26]	Leguminosae	Leaves	Ethanolic	AID
20.	*Eugenia jambolana* [27]	Myrtaceae	Seeds	Ethanolic	SID
21.	*Emblica officinalis* [28]	Phyllanthaceae	Seeds	Methnolic	SID
22.	*Ficus glomerata* [29]	Moraceae	Leaves	Ethanol	AID
23.	*Ficus krishnae* L. [30]	Moraceae	Leaves	Petroleum ether	AID
24.	*Gongronema latifolium* [31]	Asclepiadaceae	Leaves	Aqueous and methanol	AID
25.	*Ipomoia digitata* [32]	Convolvulacea	Root	Hydro-ethanolic	AID
26.	*Leucaena Leucocephala* (lmk) [33]	Mimosaceae	Seeds	Methanol	AID
27.	*Myristica Fragrans* [34]	Myristicaceae	Seeds	Petroleum ether	AID
28.	*Ocimum sanctum* [35]	Labiate	Leaves	Ethanolic	AID
29.	O*lea-europea* [36]	Oleaceae	Leaves	Ethanolic and Petroleum ether	AID
30.	*Psidium guajava* [37]	Myrtaceae	Leaves	Ethanolic	AID
31.	*Pterocarpus Marsupium* [38]	Papilionaceae	Heart woods	Ethylacetate	AID
32.	*Phyllanthus amarus* [39]	Euphorbiacea	Leaves	Ethanolic	AID
33.	*Salvadora oleoides* [40]	Salvadoraceae	Aerial part	Ethanolic	AID
34.	*Sphaeranthus indicus* Linn [41]	Asteraceae	Flower head	Petroleum ether	AID
35.	*Suaeda fruticosa* [42]	Chenopodiaceae	Aerial part	Aqueous	SID
36.	*Thespesia Populnea* [43]	Malvaceae	Bark and leaves	Ethanol	SID
37.	*Terminalia catappa* Linn [44]	Combretaceae	Fruit	Petroleum ether, methanol, and aqueous	AID
38.	*Trigonella foenum-graecum* [45]	Fabaceae	Seeds	Ethanol	AID
39.	*Tamarindus indica* [46]	Caesalpiniacae	Seeds	Aqueous	SID
40.	*Vinca rosea* [47]	Apocynaceae	Whole plant	Methanolic	AID

AID- Alloxan Induced Diabetes, **SID**- Streptozotocin-induced diabetes.

Achyranthes aspera [13]

Blood glucose levels of normal and alloxan diabetic rabbits were determined after oral administration of various doses of *Achyranthes aspera* powdered whole plant and certain aqueous and methanolic extracts. Oral administration of 2, 3 and 4 g/kg of *A. aspera* powder produced a significant dose-related hypoglycaemic effect in normal as well as in diabetic rabbits. The water and methanol extracts also decreased blood glucose levels in normal and alloxan diabetic rabbits.

***Allium sativum* L.** [14]

Oral administration of garlic extract (0.1, 0.25 and 0.5 g/kg body wt.) for 14 days on the level of serum glucose, total cholesterol, triglycerides, urea, uric acid, creatinine, aspartate amino transferase (AST) and alanine amino transferase (ALT) in normal and streptozotocin-induced diabetic rats were evaluated. Oral administrations of the garlic extract significantly decreased serum glucose, total cholesterol, triglycerides, urea, uric acid, creatinine, AST and ALT levels.

***Casearia esculenta* Roxb.** [18]

The hypoglycemic effect of ethanolic extract of *Casearia esculenta* was investigated on alloxan induced diabetic rats. The blood glucose levels were measured at 0, 1, 2 and 3 h after the treatment. The ethanolic extract of *C. esculenta* (250 mg/kg) reduced the blood glucose of normal rat from 85.50±1.22 to 64.67±3.27 mg/dl, 3 h

after oral administration of the extract. It also significantly lowered blood glucose level in alloxan induced diabetic rat from 331.67±4.90 to 130.33±6.53 mg/dl, 3 h after oral administration of the extract.

Cassia grandis [23]

The aqueous and ethanolic extracts of *C. grandis* (Family: Leguminosae) were evaluated for antidiabetic activity by a glucose tolerance test, in normal rats and alloxan-induced diabetic rats. The aqueous and ethanolic extracts showed that they significantly lowered the blood glucose levels to normal in the glucose tolerance test. In alloxan-induced diabetic rats the maximum reduction in blood glucose was observed after three hours, at a dose level of 150 mg/kg of body weight. The percentage of protection given by the aqueous and ethanolic extracts was 32.72 and 46.42%, respectively.

***Dalbergia sissoo* L.** [26]

The ethanolic extract of *Dalbergia sissoo* L. leaves was administered orally at different doses (250 and 500 mg kg^{-1}) to normal rats. The dose of 500 mg kg-1 was found to be more effective dose in oral route and it decreases Blood Glucose Level (BGL) by 38.2 % in normal healthy rats after 1 day of administration. After daily treatment with the both dose (250 and 500 mg kg^{-1}) of ethanolic *Dalbergia sissoo* extract for 21 days to severely Diabetic (FBG 300-350 mg dL^{-1}) rats, the BGL reduced to 125 mg dL-1 by 250 mg kg-1 and 104 mg dL-1 by 500 mg kg^{-1}.

Ficus glomerata [29]

Diabetes was induced in albino rat models with alloxan monohydrate. *Ficus glomerata* Linn, has been claimed to possess antidiabetic properties by many investigators. The present study was undertaken to screen the hypoglycemic activity of ethanol extracts of leaves of *F. Glomerata*. The results showed that it has significant antihyperglycemic effect in experimental model of diabetes mellitus.

Myristica Fragrans [34]

The petroleum ether (60-80º C) extract of *Myristica fragrans* (PEMF) was administered orally in normal fasted, glucose fed (1.5 g/kg, *p.o.*) and alloxan (120 mg/kg, *s.c.*)- induced diabetic rats (n=5). The blood glucose levels were estimated using glucometer. In addition, changes in body weight, organ (liver, kidney and pancreas) weight, serum lipid profile and blood parameter (haemoglobin, erythrocytes and differential leukocytes) assessed after two weeks in the extract treated diabetic rats. It has been found that, oral pre-treatment with PEMF at dose of 200 mg/kg induced a significant decrease in blood glucose level, i) from 56.5±3.19 (0 h) to 49.75±2.05 mg% (4 h) in normoglycaemic rats, ii) from 145.75±9.65 to 81.5±4.03 mg% in oral glucose tolerance test (OGTT) at ½ h compared to control glucose fed rats, iii) from 305.8±12.49 to 276.6±6.11 mg% after single dose treatment and from 326.25±7.05 to 268.0±9.6 mg% in alloxan-induced diabetic rats after daily treatment of PEMF for two weeks.

O*lea-europea* [36]

Ethanolic and Petroleum ether extracts of *Olea europea* use used and compared with Metformin as standard drug (500mg/kg). Wister strain of either sex was treated with Alloxan (150mg/kg) to induce diabetes. Glucose Oxidase/Perioxidase method was used for the determination of plasma glucose level. The ethanolic extract showed significant decrease in blood glucose level.

Psidium guajava [37]

The antidiabetic effect of *Psidium guajava leaves in* alloxan induced diabetic rats upon Oral administration of ethanolic extract of leaves (250 and 500mg/kg body weight) for 30 days, resulted in significant decrease of blood glucose from 302.67 ± 22.35 to 82.50 ± 04.72 and in a decrease in the activities of glucose-6-phosphatase, fructose-1,6-isphosphatase, aldolase and an increase in the activity of phosphor glucoisomerase and hexokinase in tissues.

Thespesia Populnea [43]

The ethanolic extract of the plant bark (TPBE) and leaf (TPLE) were evaluated for its effect on blood sugar, against the streptozotocin (STZ)–induced diabetic rats and compared it with standard drug glibenclamide. The result of this experimental study indicates that both the ethanolic extract posses' anti-diabetic effect against STZ induced diabetic rats.

***Terminalia catappa* Linn** [44]

Effect of the petroleum ether, methanol, and aqueous extracts of *Terminalia catappa Linn* (Combretaceae) fruit, on fasting blood sugar levels and serum biochemical analysis in alloxan-induced diabetic rats were investigated. All the three extracts of *Terminalia catappa* produced a significant antidiabetic activity at dose levels 1/5 of their lethal doses.

Vinca rosea [47]

The antidiabetic activity of *Vinca rosea* methanolic whole plant extracts in alloxan induced diabetic rats for 14 days. The methanolic whole plant extract at high dose (500 mg/kg) exhibited significant antihyperglycemic activity than whole plant extract at low dose (300 mg/kg) in diabetic rats. The methanolic extracts also showed improvement in parameters like body weight and lipid profile as well as regeneration of β-cells of pancreas in diabetic rats.

CONCLUSION

A large number of plants screened in India and elsewhere for their hypoglycaemic effect, have yielded certain interesting leads, but no plant-based drug has so far reached such an advanced stage of investigation as to replace or reduce the need for the currently available oral anti diabetics. In future studies on plants and plant based products, it would be worthwhile to explore the other possible beneficial effects of plant-based drugs. Such an approach is particularly conducted to abridge the naturally available alternatives of medicines for the treatment of Diabetes mellitus.

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